OMICS Group Conferences

Accelerating Scientific Discovery

International Conference and Exhibition on

Cancer Science & Therapy

15-17 August 2011, Las Vegas, USA

Conference Venue

Renaissance Las Vegas Hotel

3400 Paradise Road, Las Vegas, Nevada , 9169-2770 USA

Main (702) 784-5700, Reservations (800) 750-0980, Meetings (702) 784-5751

Conference Secretariat

5716 Corsa Ave., Suite 110, Westlake, Los Angeles, CA 91362-7354, USA

Phone: +1- 650-268-9744, Fax: +1-650-618-1414, Toll free: +1-800-216-6499

Email: cancerscience2011@omicsonline.org

OMICS Group Journals

A-Z Index

A

- Accounting & Marketing
- Addiction Research & Therapy
- Advances in Robotics & Automation
- Advances in Automobile Engineering
- Aeronautics & Aerospace Engineering Agrotechnology
- AIDS & Clinical Research
- Allergy & Therapy
- Air & Water borne Diseases
- Alzheimer's Disease & Parkinsonism
- Analytical & Bioanalytical Techniques
- Anaplastology
- Anatomy & Physiology
- Andrology-Open Access
- Anesthesia & Clinical Research
- Antivirals & Antiretrovirals
- Applied & Computational Mathematics
- Applied Mechanical Engineering
- Aquaculture Research & Development
- Architectural Engineering Technology
- Arthritis
- Astrophysics & Aerospace technology
- Autacoids
- Autism-Open Access

B

- Bacteriology & Parasitology
- Bioanalysis & Biomedicine
- Biochemistry and Analytical Biochemistry
- Biochemical Pharmacology: Open Access
- Biochips & Tissue Chips
- Bioenergetics: Open Access
- Bioengineering & Biomedical Science
- Bioequivalence & Bioavailability
- Biofertilizers & Biopesticides
- Biometrics & Biostatistics
- Biomolecules
- Bioprocessing & Biotechniques
- Bioremediation & Biodegradation
- Biosafety
- Biosensors & Bioelectronics
- Biotechnology & Biomaterials
- Bioterrorism & Biodefense
- Blood Disorders & Transfusion
- Blood & Lymph
- Brain Disorders & Therapy
- Briefing in Intellectual Property Rights
- Business and Financial Affairs

C

- Cancer Science & Therapy
- Carcinogenesis & Mutagenesis
- Cell and Developmental Biology
- Cell Science & Therapy
- Chemical Engineering & Process Technology
- Chemotherapy: Open Access
- Chromatography & Separation Techniques
- Civil & Design Engineering
- Civil & Legal Sciences
- Clinical & Cellular Immunology
- Clinical Case Reports
- Clinical & Experimental Cardiology
- Clinical & Experimental Dermatology Research
- Clinical & Experimental Ophthalmology
- Clinical & Experimental Pathology
- Clinical & Experimental Pharmacology
- Clinical Pharmacology & Biopharmaceutics
- Clinical Research & Bioethics
- Clinical Toxicology
- Clinical Trials
- Cloning & Transgenesis
- Communicable & Noncommunicable Diseases
- Community Medicine & Health Education
- Computer Science & Systems Biology
- Cytology & Histology

D

- Data Mining in Genomics & Proteomics
- Defense Management
- Dentistry
- Depression and Anxiety
- Diabetes & Metabolism
- Drug Designing
- Drug Metabolism & Toxicology

E

- Earth Science & Climatic Change
- Ecosystem & Ecography Endocrinology & Metabolic Syndrome: Current Research
- Entomology, Ornithology & Herpetology
- Environmental & Analytical Toxicology
- Epidemiology: Open Access
- Emergency Medicine
- Ergonomics
- Electrical & Electronics
- Expert Opinion on Emerging Drugs
- Enzyme Engineering
- Entrepreneurship & Organization Management

F

- Fermentation Technology
- Fertilization : In Vitro
- Food Processing & Technology
- Forensic Research
- Forest Research: Open Access
- Fungal Genetics & Biology

G

- Gastrointestinal & Digestive System
- Genetic Syndromes & Gene Therapy
- Glycobiology
- Glycomics & Lipidomics
- Gynecology& Obstetrics
- Geography & Natural Disasters
- Geology & Geosciences
- Geophysics & Remote Sensing
- Gerontology & Geriatric Research

Contact us at: contact.omics@omicsonline.org

Email Alerts:

OMICS Group Journals would include full text alerts, editorial release, special issue publication, most cited articles etc. that are sent to renowned scientists, academicians, industrialists and research scholars around the globe.

OMICS Group Conferences aims on sending email alerts to Scientific Researchers, Business Entrepreneurs and Pharma, Biotech & Healthcare Industry Developers.

H

- Hair : Therapy & Transplantation
- Health & Medical Informatics
- Hereditary Genetics
- Homeopathy & Ayurvedic Medicine
- Hotel & Business Management
- Human Genetics & Embryology: Current Research
- Hydrology: Current Research
- Hypertension- Open Access

I

- Industrial Engineering & Management
- Irrigation and Drainage Systems Engineering
- Information Technology & Software Engineering
- Internal Medicine

L

- Liver

M

- Marine Science: Research & Development
- Mass Communication & Journalism
- Material Sciences & Engineering
- Medicinal Chemistry
- Medical advancements in Genetic Engineering
- Medicinal & Aromatic Plants
- Medical Diganostic Methods
- Medical Microbiology & Diagnosis
- Membrane Science & Technology
- Metabolic Syndrome
- Microbial & Biochemical Technology
- Molecular Biology
- Molecular Biomarkers & Diagnosis
- Molecular Imaging & Dynamics
- Mycobacterial Diseases

N

- Nanomedicine & Biotherapeutic Discovery
- Nanomedicine & Nanotechnology
- Neonatal Biology
- Nephrology & Therapeutics
- Neurology & Neurophysiology
- Novel Physiotherapies
- Nuclear Energy & Power Generation Technologies
- Nuclear Medicine & Radiation Therapy
- Nutrition & Food Sciences
- Nutritional Disorders & Therapy
- Nursing & Care

O

- Obesity & Weight loss Therapy
- Organ Biology
- Organic Chemistry: Current Research
- Orthopedic & Muscular System: Current Research
- Otolaryngology

P

- Pain & Relief
- Palliative Care & Medicine
- Pancreatic disorders & Therapy
- Pediatrics & Therapeutics
- Petroleum & Environmental Biotechnology
- Pharmaceutica Analytica Acta
- Pharmaceutical Biotechnology
- Pharmaceutics & Drug Delivery Research
- Pharmacoepidemiology & Drug Safety
- Pharmacogenomics & Pharmacoproteomics
- Physical Chemistry & Biophysics
- Plant Pathology & Microbiology
- Postgenomics: Drug & Biomarker Development
- Powder Metallurgy & Mining
- Primary Health Care
- Proteomics & Bioinformatics
- Psychology & Psychotherapy
- Pulmonary & Respiratory Medicine

R

- Radiology: Open Access
- rDNA Technology
- Reproductive System & Sexual Disorders
- Rheumatology

S

- Single Cell Proteins
- Sleep Disorders & Therapy
- Social & Economical Issues of Biotechnology
- Socialomics
- Sports Medicine & Doping Studies
- Spine
- Stem Cell Research & Therapy
- Steroids & Hormonal Science
- Stock & Forex Trading
- Surgery

T

- Telecommunications System & Management
- Textile Science & Engineering
- Thermodynamics & Catalysis
- Thyroid Disorders & Therapy
- Tissue Science & Engineering
- Translational Medicine
- Transplantation Technologies & Research
- Trauma
- Tourism & Hospitality

U

- Urology

V

- Vaccines & Vaccination
- Veterinary Science & Technology
- Virology & Mycology
- Vitamins & Trace Elements

W

- Women's health

Y

- Yoga & Physical Therapy

Contact us at: contact.omics@omicsonline.org

SciTechnol Biosoft

http://www.scitechnol.com

SciTechnol Biosoft is a premier Biosoft and development centric company producing cutting edge intuitive software for the biologists. The company specializes in developing software for use in life science research. Main objective is to study the most recent innovations in different fields of life sciences and translate them into software products that aid the biologists.

Key services include:

- Preparing biosafety requirements for pharma, biotech, health care and lifesciences industries.
- Examine the effectiveness of biosafety regulatory mechanisms, the capacity of industries and institutions to implement biosafety guidelines.
- Data management & distribution.
- Clinical studies of samples for different –omics and different fields of life sciences.
- Preparation and implementation of Software applications & related IT infrastructure in Health care sector.

We work closely with health care organizations to design and development of world class health care solutions serving their needs.

Supporting Journals

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on Cancer Science & Therapy

15-17 August 2011 Las Vegas, USA

ISSN: 1948-5956

Journal of Cancer Science & Therapy

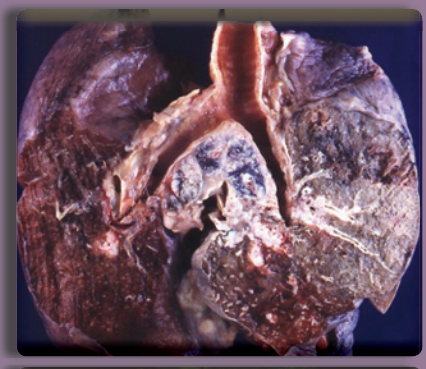
Open Access

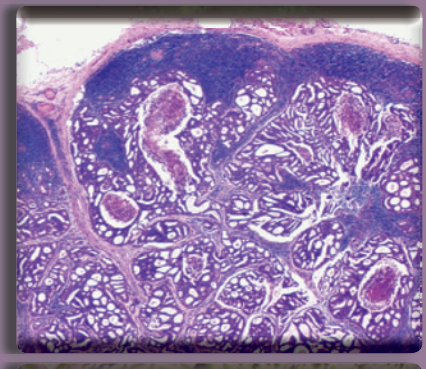
Cancer is a class of diseases in which a cells or a group of cells display uncontrolled growth, invasion and sometimes metastasis. Cancer affects people at all ages with the risk for most types increasing with age.

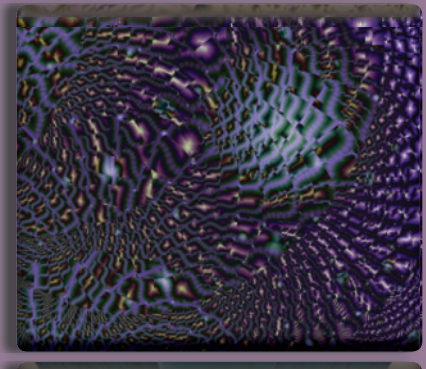
Aims & Scope

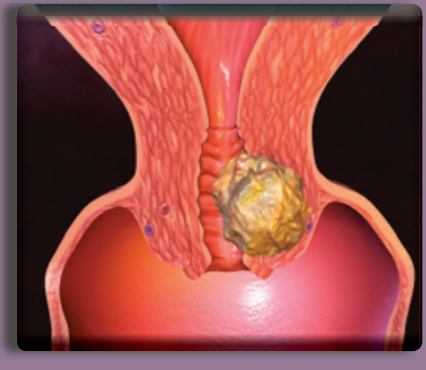
The Journal of Cancer Science & Therapy (JCST) is an Open Access publication which embraces a high quality of original research pertaining to human and animal related cancer diseases, and made available to the readers aware of the threats posed by assorted neoplasm.

Editors & Editorial Board









Journal of Cancer Science & Therapy – Open Access uses online manuscript submission, review and tracking systems of Editorial Manager® for quality and quick review processing.

Submit your manuscript at
http:// www.editorialmanger.com/cancerscience (or)
E-mail to editor.jcst@omicsonline.org

OMICS Publishing Group
5716 Corsa Ave., Suite 110, Westlake, Los Angeles, CA 91362-7354, USA
Tel: +1- 650-268-9744, Fax: +1-650-618-1414, Toll free: +1-800-216-6499
E-mail: omicsonline@omicsonline.org
http://omicsonline.org/jcsthome.php

ISSN: 2157-2518

Journal of Carcinogenesis & Mutagenesis

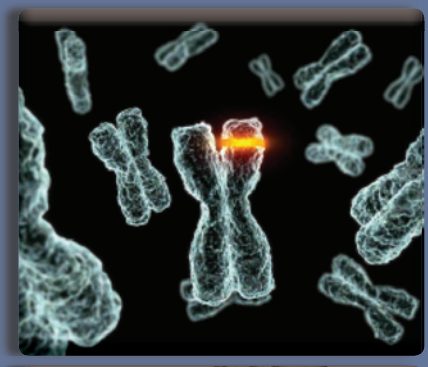
Open Access

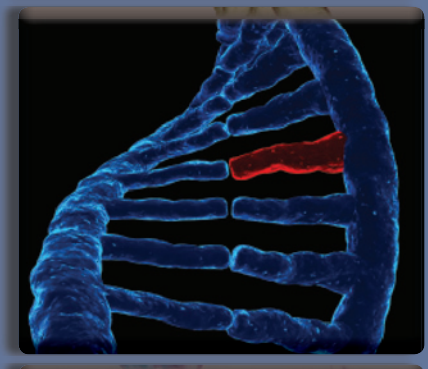
The Journal of Carcinogenesis and Mutagenesis is an international multi-disciplinary journal that focuses on the recognition of cellular responses to DNA damage, apoptosis (cell death), including the inactivation of tumor suppressor genes, and analysis of carcinogenic process by genetic and epigenetic alterations in genes for the study of cancer initiation and progression.

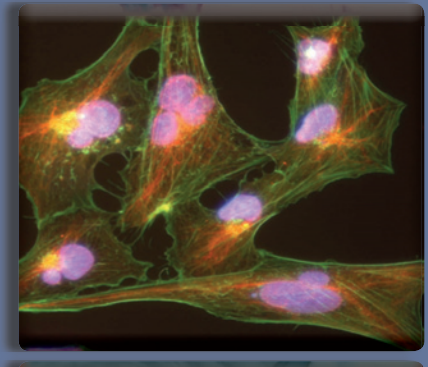
Aims & Scope

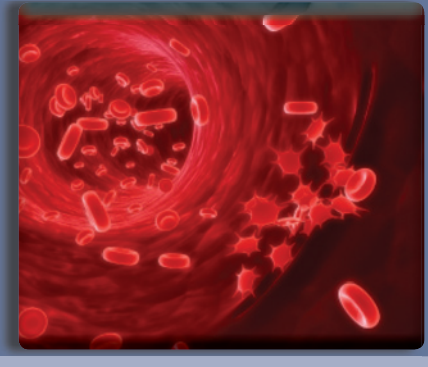
Journal of Carcinogenesis and Mutagenesis publishes original research on the evaluation and characterization of carcinogens or mutagens. The journal also features critical reviews focused on topics of significant interest to specialists in teratology, cancer biology, and mutation research to make aware of cancer to the world.

Editors & Editorial Board









Journal of Carcinogenesis & Mutagenesis - Open Access using online manuscript submission, review and tracking system for quality and quick review processing.

Submit your manuscript at
http://www.omicsonline.org/submission (or)
E-mail to editor.jcm@omicsonline.org

OMICS Publishing Group
5716 Corsa Ave., Suite 110, Westlake, Los Angeles, CA 91362-7354, USA
Tel: +1- 650-268-9744, Fax: +1-650-618-1414, Toll free: +1-800-216-6499
E-mail: omicsonline@omicsonline.org
http://www.omicsonline.org/jcmhome.php

Upcoming Conferences

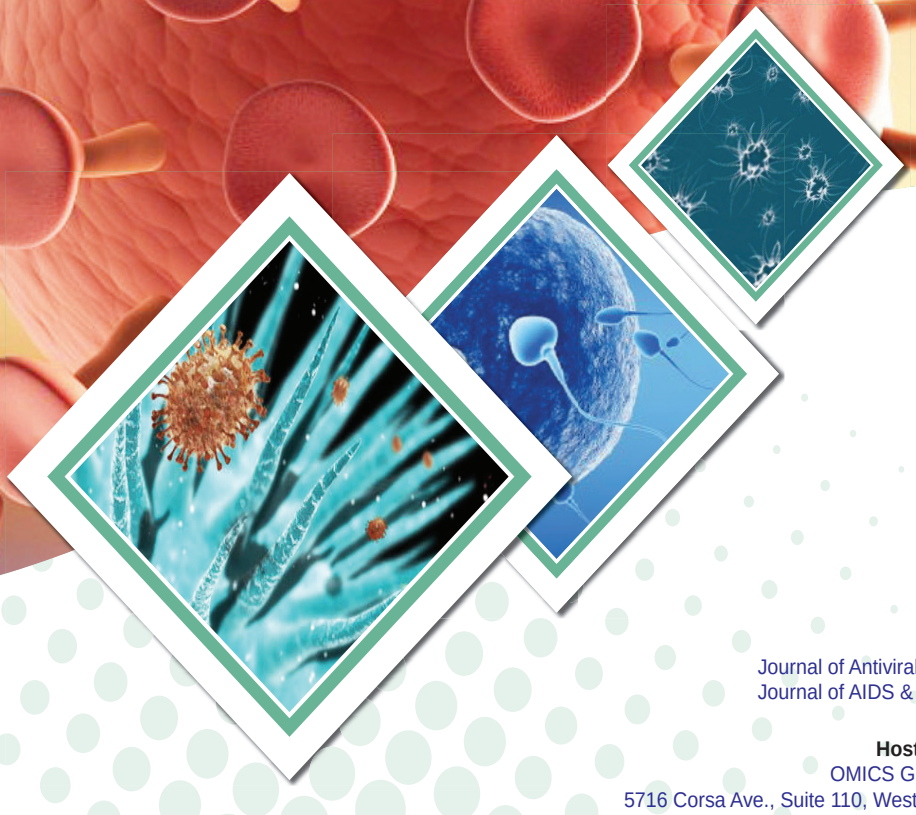
OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on Cancer Science & Therapy

15-17 August 2011 Las Vegas, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on Virology



Operated by:

Editors
Journal of Antivirals & Antiretrovirals
Journal of AIDS & Clinical Research

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake, Los Angeles
CA 91362-7354, USA
Tel: +1-650-268-9744, Fax: +1-650-618-1414
Toll free: 1-800-216-6499(USA & Canada)
E-mail: virology2011@omicsonline.org

Organizing Committee

Date & Venue

5-7 September 2011
Baltimore, USA

http://www.omicsonline.org/virology2011

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on

Pharmaceutical Regulatory Affairs

Operated by:

Editors
Journal of Bioequivalence & Bioavailability
Journal of Bioanalysis & Biomedicine

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake
Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9744, Fax: +1-650-618-1414
Toll free: 1-800-216-6499(USA & Canada)
E-mail: pharma2011@omicsonline.org

Organizing Committee

Sudhakar Akulapalli
Boys Town National Research Hospital, USA

George Perry
University of Texas at San Antonio, USA

Eugenia Kharlampieva
University of Alabama Birmingham, USA

Alexander A. Kamnev
Russian Academy of Sciences, Russia

Hossam M. Ashour
Wayne State Universit Eugene Applebaum, USA

Date & Venue

6-7 September 2011
Baltimore, USA

OMICS Group Conferences
Accelerating Scientific Discovery

2nd World Congress on Biomarkers & Clinical Research

Operated by:

Editors
Journal of Molecular Biomarkers & Diagnosis
Journal of Postgenomics: Drug & Biomarker Development

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: biomarkers2011@omicsonline.org

Organizing Committee

Steven S. Smith
Beckman Research Institute of City of Hope, USA

Paul Wood
President & CEO, Phreedom Pharma Inc, Canada

Philipp Schuetz
University Hospital Basel, Switzerland

Jagat kanwar
Deakin University, Australia

Eyk Schellenberger
Charité –Universitätsmedizin Berlin, Germany

Wen Jin Wu
U.S. Food and Drug Administration , USA

Jens D. Mikkelsen
CNS Pharmacology, NeuroSearch A/S, Ballerup, Denmark

Date & Venue
12-14 September 2011
Baltimore, USA

http://www.omicsonline.org/biomarkers2011

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on

Vaccines & Vaccination

Operated by:

Editors
Journal of Vaccines & Vaccination
Journal of Clinical and Cellular Immunology

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: vaccines2011@omicsonline.org

Organizing Committee

Edmund J. Gosselin
Albany Medical College,USA

Masoud H Manjili
Dr. Masoud H Manjili
Virginia Commonwealth University, USA

Chinnaswamy Jaganath
University of Texas, USA

Ara Hovanessian
Université Paris Descartes, France

Hiroshi Kido
Tokushima University, Japan

Escher, Alan
Loma Linda University,USA

Ennio De Gregorio
Novartis Vaccines and Diagnostics research center,Italy

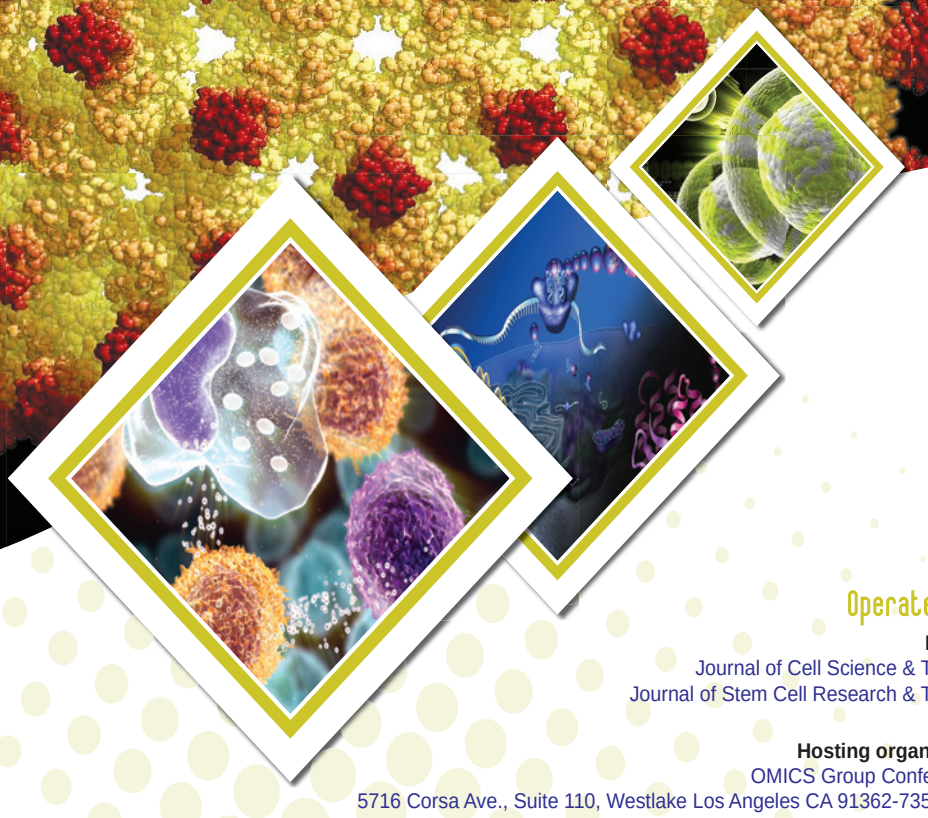
Date & Venue

22-24 Nov 2011
Philadelphia, Marriott Hotel, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on

Cell Science & Stem Cell Research



Operated by:

Editors
Journal of Cell Science & Therapy
Journal of Stem Cell Research & Therapy

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: cellscience2011@omicsonline.org

Organizing Committee

Partha Roy
University of Pittsburgh, USA

Ming Pei
Virginia University, USA

Yadong Wang
University of Pittsburgh, USA

Wan-Ju Li
University of Wisconsin-Madison, USA

Sudhakar Akulapalli
Boys Town National Research Hospital, USA

Samir A. Farghaly
Cornell University, USA

Treena Livingston Arinzeh
New Jersey Institute of Technology, USA

Ken Hayashi
Keio University, Japan

Aline M. Betancourt
Tulane University, USA

Claudia Palena
National Cancer Institute, USA

Date & Venue

29 Nov - 1 Dec 2011
Philadelphia Airport Marriott, USA

http://omicsonline.org/cellscience2011

OMICS Group Conferences
Accelerating Scientific Discovery

2nd World Congress on Biotechnology

Operated by:

Editors
Journal of Biotechnology & Biomaterials
Journal of Microbial & Biochemical Technology

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: biotechnology2011@omicsonline.org

Organizing Committee

Dr. Antony Atala
Wake Forest University, USA

Jimmy Thomas Efird
University of North Carolina, USA

Jagat R. Kanwar
Deakin University,. AUSTRALIA

Yadong Wang
University of Pittsburgh, USA

Sudhakar Akul Yakkanti
Boystown National Research Hospital, USA

Elena Sarropoulou
Institute of Marine Biology and Genetics, Greece

Yehia Mechref
Texas Tech University, USA

Shonkor kumar Das
University of Fukui, Japan

Date & Venue

29 Nov-1 Dec 2011
Philadelphia Airport Marriott, USA

http://omicsonline.org/biotechnology2011

OMICS Group Conferences
Accelerating Scientific Discovery

2nd World Congress on
Diabetes & Metabolism

Operated by:

Editors
Journal of Diabetes & Metabolism
Journal of Steroids & Hormonal Science

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414
Toll free: 1-800-216-6499(USA & Canada)
E-mail: diabetes2011@omicsonline.com

Organizing Committee


Kenneth Maiese
University of Medicine & Dentistry of New Jersey,USA


Maoqing Dong
Mayo Clinic College of Medicine , USA


Pandu Gangula
Meharry Medical College, USA


Sanjay Kapur
ZRT Laboratory, USA


Cheryl S. Hankin
Bio Med Econ, USA


Pierre-Frederic Keller
Cardiology Division University Hospital, Switzerland


Vanessa Routh
Department of Neurosciences New Jersey Medical School,USA


Wayman Wendell Cheatham
Director Navy Medicine R&D Center, USA


Bigelow, James C
Idaho State University, USA


Delia Cabrera DeBuc
University of Miami,USA

Date & Venue

6-8 December 2011
Philadelphia Airport Marriott, USA

http://omicsonline.org/diabetes2011

OMICS Group Conferences
Accelerating Scientific Discovery

OMICS Group World Congress on
Pediatrics & Gynecology

Operated by:

Editors
Gynecology and Obstetrics
Pediatrics and Therapeutics

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: pediatrics2011@omicsonline.org

Organizing Committee

Kenneth Maiese
University of Medicine & Dentistry of New Jersey,USA

Maoqing Dong
Mayo Clinic College of Medicine , USA

Pandu Gangula
Meharry Medical College, USA

Sanjay Kapur
ZRT Laboratory, USA

Cheryl S. Hankin
Bio Med Econ, USA

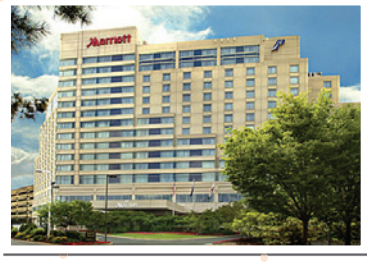
Pierre-Frederic Keller
Cardiology Division University Hospital, Switzerland

Vanessa Routh
Department of Neurosciences New Jersey Medical School,USA

Wayman Wendell Cheatham
Director Navy Medicine R&D Center, USA

Bigelow, James C
Idaho State University, USA

Delia Cabrera DeBuc
University of Miami,USA



Date & Venue

6-8 December 2011

Philadelphia, USA

http://omicsonline.org/pediatrics2011

Metabolomics-2012

International Conference & Exhibition on Metabolomics & Systems Biology

OMICS Group Conferences
Accelerating Scientific Discovery

Operated by:

Editors
Journal of Proteomics & Bioinformatics
Journal of Computer Science & Systems Biology

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414
Toll free: 1-800-216-6499(USA & Canada)
E-mail: metabolomics2012@omicsonline.com

Organizing Committee

Jimmy Efird
University of North Carolina, USA

Zhongming Zhao
Vanderbilt University, USA

Bernd Lepenies
Max Planck Institute, Germany

Sudhakar Akulapalli
Boys Town National Research Hospital, USA

Xue-Long Sun
Cleveland State University, USA

Narasimham L. Parinandi
The Ohio State University College of Medicine, USA

Chulso Moon
The South-Western Medical Center, USA

Chryssostomos Chatgilialoglu
C.N.R. Bologna Research Area, Italy

Janaina Fernandes
Federal University of Rio de Janeiro, Brasil

Samy L Habib
The University of Texas Health Science Center, USA

Date & Venue

20-22 February 2012

San Francisco Airport Marriott, USA

http://www.omicsonline.org/metabolomics2012/

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Biometrics & Biostatistics

Operated by:

Editors
Journal of Biometrics & Biostatistics
Journal of Computer Science & Systems Biology
Journal of Bioengineering & Biomedical Science

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: biometrics2012@omicsonline.org

Organizing Committee


Subir Ghosh
University of California, USA


Rudy Guerra
Rice university, USA


Dongfeng Wu
University of Louisville, USA


Herbert Pang
Duke University, USA


Mark Griffin
University of Queensland, Australia


Philip Rowe
University of Strathclyde, UK


Gui-shuang Ying
University of pennsylvania, USA


Qing Nie
University of California, USA


Yuehua Cui
Michigan State University, USA


Wu Yichao
North Carolina State University, USA

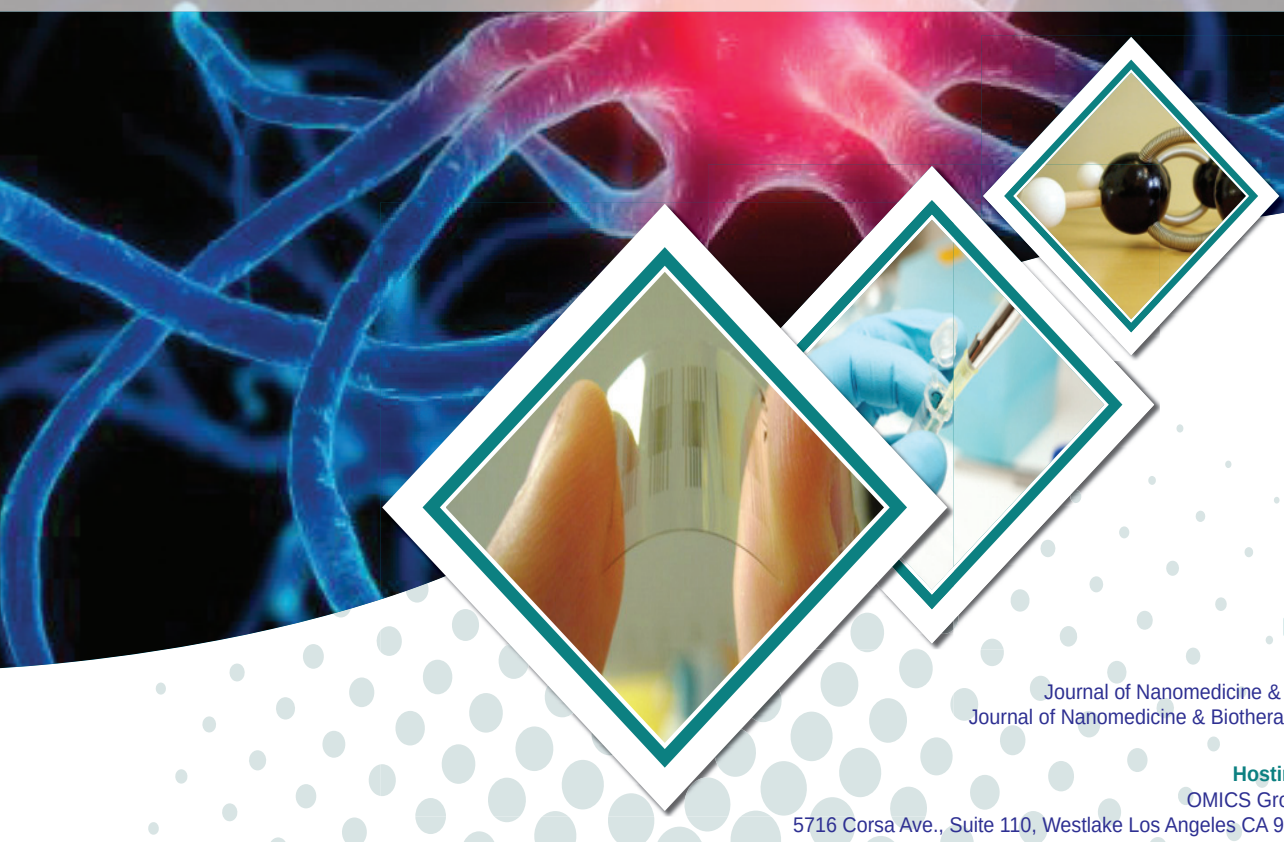
Date & Venue
5-7 March 2012, Omaha, USA

http://omicsonline.org/biometrics2012/

NANO-2012

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on Nanotechnology & Nanomedicine

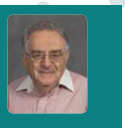


Operated by:

Editors
Journal of Nanomedicine & Nanotechnology
Journal of Nanomedicine & Biotherapeutic Discovery

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414
Toll free: 1-800-216-6499(USA & Canada)
E-mail: nano2012@omicsonline.org

Organizing Committee


Lev Solomon Ruzer
Lawrence Berkeley National Laboratory, USA


W E Merchán-Merchán
University of Oklahoma, USA


Neeraj Vij
Johns Hopkins University, USA


Yongjie (Jessica) Zhang
Carnegie Mellon University, USA


Silvia Muro
University of Maryland, USA


Lan Sun
Sandia National Laboratories, USA


Vikas Tomar
Purdue University, USA


Weibo Cai
University of Wisconsin – Madison, USA


Thomas J. Webster
Brown University, USA


Hai-Feng Frank JI
Villanova University, US

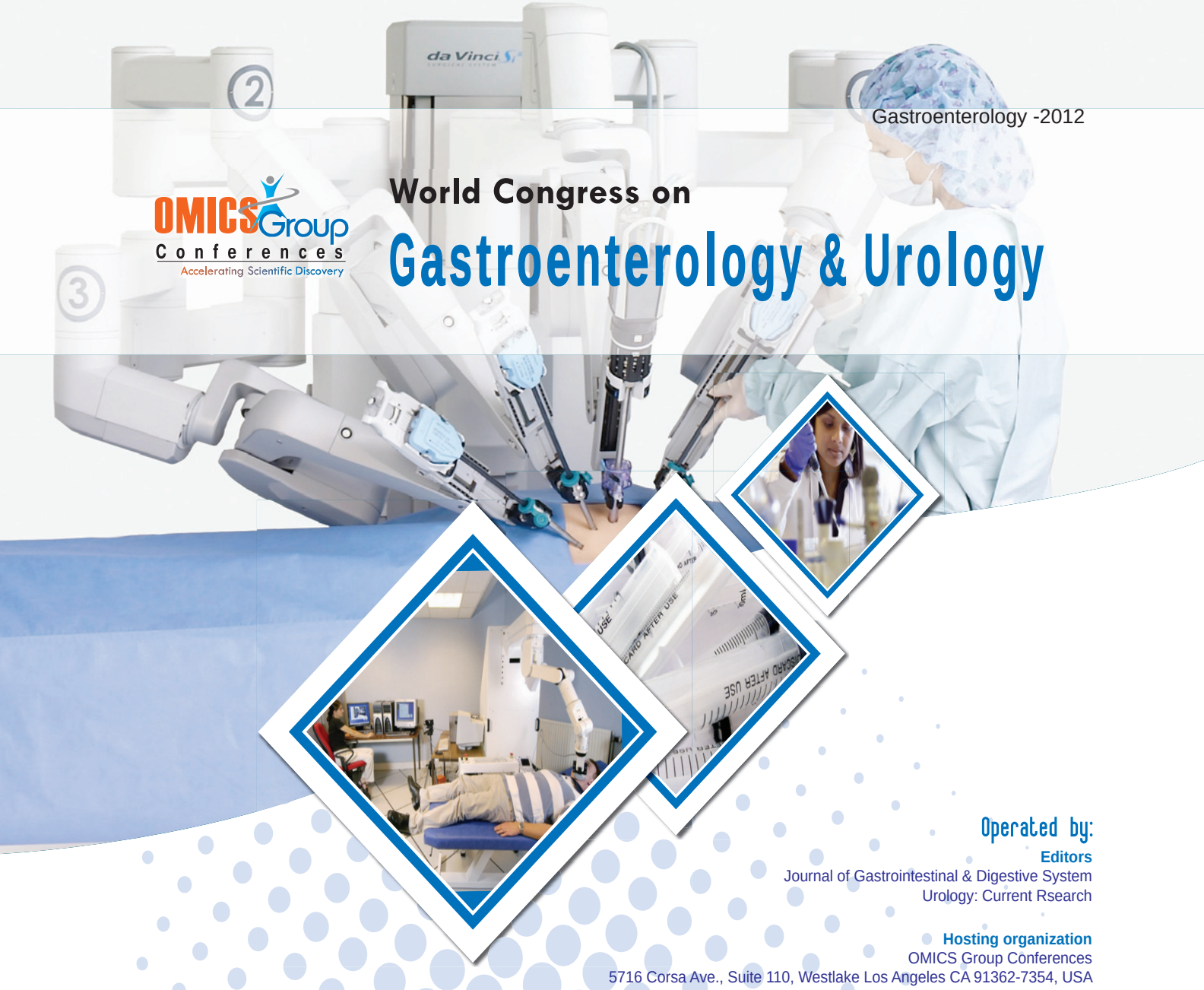
Date & Venue

12-14 March 2012 Omaha, USA

http://www.omicsonline.org/nano2012

OMICS Group Conferences
Accelerating Scientific Discovery

World Congress on
Gastroenterology & Urology



Operated by:

Editors
Journal of Gastrointestinal & Digestive System
Urology: Current Rsearch

Hosting organization
OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: gastroenterology2012@omicsonline.org

Organizing Committee

Inder Perkash
Stanford University, USA

Christos E. Constantinou
Stanford University Medical School, USA

Cherif Boutros
University of Maryland School Of Medicine, USA

Manoop S. Bhutani
The University of Texas MD Anderson Cancer Center, USA

Tauseef Ali
University of Oklahoma Health Sciences Center, USA

Faten N. Aberra
University of Pennsylvania, USA

Radhey Kaushik
South Dakota State University, USA

Sandeep Mukherjee
University of Nebraska Medical Center, USA

Kusum K. Kharbanda
University of Nebraska Medical Center, USA

Natalia Osna
University of Nebraska Medical Center, USA

Date & Venue

12-14 March 2012 Omaha, USA

http://www.omicsonline.org/gastroenterology2012

Key Note Forum

OMICS Group Conferences
Accelerating Scientific Discovery

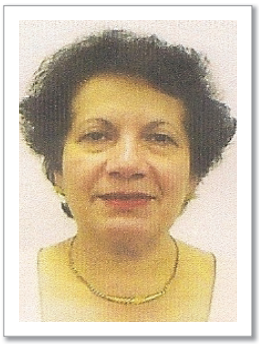
International Conference and Exhibition on Cancer Science & Therapy

15-17 August 2011 Las Vegas, USA

Dr. Michael Mingzhao Xing

Johns Hopkins University School of Medicine, USA

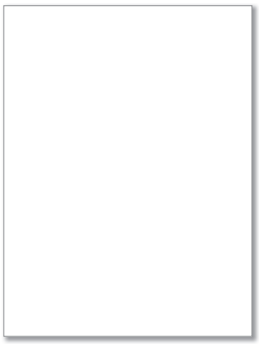
Dr. Mingzhao Xing, M.D., Ph.D., is Associate Professor of Medicine, Oncology and Cellular and Molecular Medicine, Co-Director of the Thyroid Tumor Center, and Chief of the Laboratory for Cellular and Molecular Thyroid Research at the Johns Hopkins University School of Medicine. Following his initial medical training at the Second Military Medical University in Shanghai, China, he obtained a Ph. D. degree in Physiology and Biophysics at Case Western Reserve University in Cleveland. He subsequently completed an internal medicine residency at the Greater Baltimore Medical Center and a clinical fellowship in Endocrinology and Metabolism at the Johns Hopkins University School of Medicine. Upon completing the fellowship, Dr. Xing was recruited to the faculty at the Division of Endocrinology and Metabolism of the Johns Hopkins Hospital. Dr. Xing serves on a number of national and international professional committees/panels, including, for example, National Institute of Health study sections, American Thyroid Association committees, several cancer research grant review panels in European counties. He also serves as a member or editor on a number of subspecialty journals, such as Journal of Clinical Endocrinology and Metabolism, Endocrine-Related Cancer, and Thyroid. Dr. Xing practices clinical endocrinology as a subspecialty consultant and teaching attending at the Johns Hopkins Hospital while also conducting laboratory research as a physician scientist. His main clinical and research interest is in thyroid diseases, particularly thyroid tumors. Supported by the American Cancer Society and NIH R0-1 grants, his laboratory has been studying molecular, genetic and epigenetic mechanisms of thyroid cancer and their clinical translations. His team has published actively in these areas, particularly in relation to the MAP kinase and PI3K/Akt pathways. He is co-holder of a patent on the initial discovery and clinical characterization of the BRAF mutation in thyroid cancer. He has published more than 80 scientific articles. Among his professional recognitions/ awards are the US FAMRI Clinical Innovator Award, Maryland Innovator Award, American Cancer Society RSG Award, and "America's Top Physician" recognition.



Dr. Mahin Khatami

National Cancer Institute, USA

Dr. Mahin Khatami immigrated to USA in 1969 after training in Chemistry (BS) and Science Education (MS) in Iran. She received her MA in Biochemistry from SUNY at Buffalo (1977) and Ph.D. in Molecular Biology from the University of Pennsylvania (UPA, 1980). Her postdoctoral framings were in physiology, protein chemistry and immunology at UVA, Fox Chase Cancer Center & UPenn. She became a Faculty of Medicine at Dept. Ophthalmology-UPA until 1992; and in collaboration with a team of scientists, under direction and support of John H Rockey, MD, Ph.D., she quickly earned her supervisory responsibilities on two major projects; cell/molecular biology of diabetic retinopathy/ maculopathy and experimental models of acute and chronic inflammatory diseases. As a junior faculty, she was perhaps a most productive scientist in the country as she published 39 scientific articles and over 60 abstracts in conference proceedings in the first decade of her academic career. Since 1998, at NCI/NIH, extension of her earlier discoveries on immunobiology of inflammatory diseases became closely relevant to her duties as Program Director-HSA for developing concepts for molecular diagnosis, prevention and therapy of cancer for large clinical trials (Prostate-Long-Colorectal-Ovarian) and designs of cohort clinical studies. Dr. Khatami has lectured internationally; served as scientific judge; consultant to pharmaceutical companies; research advisor; member of professional societies; editorial membership and reviewer activities; symposia organizer; president of Graduate Women In Science, Washington Chapter. Before retiring in 2009, her position title was Assistant Director for Technology Program Development, Office of Technology and Industrial Relations and Program Director-IMAT, Office of Director, NCI/NIH. She is currently Book Editor on Inflammatory Diseases.



Dr. Francois M. Vallete

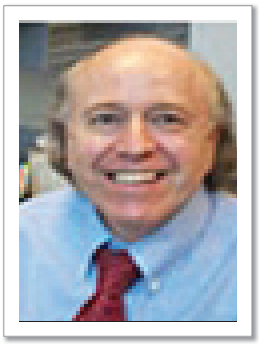
INSERM and Universite de Nantes, France

Dr. François M. Vallette has completed his Ph.D at the age of 26 years from Paris VII University and did postdoctoral studies in the Department of Cell Biology of NYU Medical Center. Currently, he is the director of the Department of Oncogenesis and Targeted Therapies in the Nantes Angers Cancer Research Center in France. He has published more than 80 papers in reputed journals and serving as associate or editorial board member in several journals.

Dr. Stephen W.J. Wang

Millennium Pharmaceuticals Inc, USA

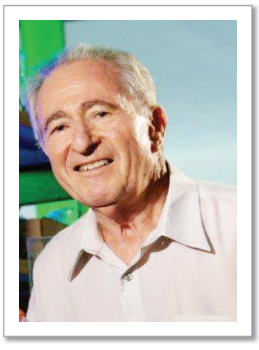
Dr. Stephen Wang received his training in pharmaceutical sciences at the Texas Medical Center under Professor Ming Hu. Dr. Wang currently serves as a principal scientist in the department of Drug Metabolism and Pharmacokinetics at Millennium Pharmaceuticals in Cambridge MA. Previously, Dr. Wang served as a senior scientist in the department of Drug Metabolism and Pharmacokinetics at Merck. Dr. Wang's research interests focus on the disposition of xenobiotics in an effort to improve bioavailability of chemopreventive agents. Dr. Wang has made significant contributions in the field with a consistent publication track record of over 25 manuscripts in peer-reviewed scientific journals and various book chapters.



Dr. Jimmy T. Efird

Brody School of Medicine, USA

Dr. J. T. Efird completed his Doctorate in Epidemiology at Stanford University School of Medicine. He currently is an Associate Professor at Brody School of Medicine, East Carolina University (ECU) and has a joint appointment as Epidemiologist/Chief Statistician in the Center for Health Disparities Research. Prior to joining ECU, Dr. Efird was Director of the Biostatistics Facility at the John A. Burns School of Medicine (Honolulu, Hawaii) and an Associate Member of the Cancer Research Center of Hawaii. Dr. Efird's research interests include brain tumours, soft-tissue sarcomas, and HPV-related cancers.



Dr. Eugene P. Goldberg

University of Florida, USA

Dr. Goldberg FAIMBE, FBSE, joined the faculty of the University of Florida as the Biomedical Program of Excellence Professor in 1975. At Florida, as part in the Departments of Chemistry and Materials Science & Engineering, he helped establish intramural graduate programs in Polymer and Biomedical Sciences. He is now also affiliated with the University's Cancer Center and the Departments of Biomedical Engineering, Pulmonology, and Pharmacology & Therapeutics. His biomedical research interests and activities for the past 35 years have been diverse with strong focus on localized chemotherapy by direct intratumoral drug injection. Pioneering cancer therapy studies were initiated in 1976 as a Visiting NIH Scientist and marked by a seminal 1978;38:1311 Lung Cancer paper on IT Chemoimmunotherapy. Subsequent research was devoted to enhancement of intratumoral chemotherapy using drug-loaded albumin and DNA nanomesospheres as reviewed in JPP 2002;54;159-180. Recent clinical research has been focused primarily on bronchoscopic intratumoral injection of chemotherapy with Drs. Seyhan and Firuz Celikoglu and Dr. Wolfang Hohenforst-Schmidt as reported in Cancer Therapy 2008;6:545-552 and JPP 2010;62:287-295. Dr. Goldberg is the senior author of more than 425 published and presented papers and is on the editorial boards of numerous journals.

Dr. John Thompson

University of Waterloo, Canada. Senesco Technologies Inc., USA

Dr. Thompson received his PhD from University of Alberta and he is professor of Biology and Associate Vice-president, Research at the University of Waterloo, his research interests include Biochemistry and molecular biology of programmed cell death: the molecular basis of membrane deterioration in senescing and aging tissues; comparative aspects of senescence and stress including the role of hormones and the involvement of free radicals; functional genomics of senescence and apoptosis. He is the Chief Scientific Officer for Senesco Technologies Inc., USA and a Fellow of the Royal Society of Canada.

Dr. Shymal Dilip Desai

LSU Health Sciences Center, USA

Dr. Desai obtained her Bachelor of Science and Master of Science in Biochemistry from University of Mumbai, India. She received her Doctorate in Biochemistry from the University of Mumbai, India. She did her post-doctoral fellowship at the UMDNJ-RWJMS in New Jersey USA. She was a faculty member in the Department of Pharmacology at the UMDNJ/RWJMS till 2007. In 2007, she joined the LSUHSC as Assistant Professor in the Department of Biochemistry &Molecular Biology. She has published 20 papers in reputed journals. She currently serves on the editorial board of the three reputed journals.

Dr. Sudhakar Akul

Boys Town National Research Hospital, USA

Dr. Sudhakar Akulapalli (Akul) is the founder Director of Cell Signaling, Retinal and Tumor Angiogenesis Laboratory at Boys Town National Research Hospital, Associate Professor at Creighton University School of Medicine and University of Nebraska Medical Center, Omaha, NE, USA. He did his postdoctoral training at Harvard Medical School, Boston, MA, USA (2003). He has received Ph.D (2001), M.Phill (1997) and M.Sc (1995) degrees in life sciences fromUniversity of Hyderabad; and B.Sc in Biology from Silver Jubilee College (APRDC) Kurnool, SK University (1993) from India. He received President's fellowship (1992), GATE (1996) and CSIR (2007-2000) fellowships from Government of India. He received Mahindra & Mahindra Educational Award (2000) and Young Clinical Scientist Awards from Flight Attendant Medical Research Institute (FAMRI) in 2007 and 2010. He also received Bio-Bio Young Scientist Award from OMICS publishing group; Michael A. O'Connor Young Investigator Award; RO1 grant Award from NIH/NCI and Research Scholar Grant Award from ACS (2010). He is serving as AIBS/NIH-RO1 Grant reviewer for DT study section. He has published more than 35 research articles in several top journals including Science, Cancer Cell, JCI, Blood, PNAS, Gastroenterology, Cancer Research, JBC, IOVS, JCST etc. He is serving as an Executive Editor, Editor and Editorial board member of reputed journals and is serving as a reviewer for 21 scientific journals including JCI, Blood, Circulation, Circulation Research, Cancer research, Clinical Cancer research etc. He was honored by giving a position as Keynote Speaker, Chairman, Co-chairman and organizing committee member for several international conferences including Bio-Bio-2009; Bio-Bio-2010; Anal-Bio2010; Biomarkers & Clinical Research 2010; Diabetes & metabolism 2010 etc.

Scientific Tracks & Abstracts

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on Cancer Science & Therapy

15-17 August 2011 Las Vegas, USA

Track 1(i) 1(ii) 1(iii)

1(i): Cancer Stem Cells and Metastatic Growth

1(ii): Cell Signaling and Membrane Proteins; Inflammation and Inflammatory Factors in Cancer Development

1(iii): Metastatic Cell Growth & Adhesion; Apoptosis & Cell Division

Session Chair

Dr. Lu Zhe Sun
University of Texas Health Science Center at San Antonio, USA

Session Co-Chair

Dr. Caterina La Porta
University of Milan, Italy

Session Introduction

Title: **Blocking cancer metastasis with TGF-beta antagonists**

Dr. Lu Zhe Sun, University of Texas Health Science Center at San Antonio, USA

Title: **Molecular targeting of cancer stem cells by the small molecule dichloroacetate (DCA) through the disruption of the OCT4/PKM2 complex**

Dr. Francois M. Vallette, INSERM and Universite de Nantes, France

Title: **Matrix metalloproteinases in crosstalk between cancer cells and osteoblasts in the bone invasion of oral squamous cell carcinoma**

Dr. Jin Gao, James Cook University, Australia

Title: **Cancer stem cells**

Dr. Caterina La Porta, University of Milan, Italy

Title: **Deconstructing cancer progression: Cancer stem cells and dedifferentiation**

Dr. Carlos F. D. Rodrigues, University of Coimbra, Portugal

Title: **Stat5: From lactogenesis to tumorigenesis**

Dr. Itamar Barash, Institute of Animal Science, Israel

Title: **Inflammatory chemokines in breast cancer: Regulation by genetic and host factors**

Dr. Adit Ben-Baruch, Tel Aviv University, Israel

Track 1(i) 1(ii) 1(iii)

Title: The ESCRT pathway and ubiquitin-binding ability of Tsg101 are required for dynamic Src trafficking and v-Src-mediated invadopodia formation and invasion

Dr. Chun Tu, University of Nebraska Medical Center, USA

Title: Individual chemosensitivity test for personalized therapy in cancer patients

Dr. Jianping Gong, Huazhong University of Science and Technology, P. R. China

Title: Tanshinone II A on apoptosis via SAPK/JNK signal transduction in pancreatic cancer cells

Dr. Peihao Yin, Shanghai University of Traditional Chinese Medicine, China

Title: The anti-tumor effect of fermented curcumin

Dr. Ha-rim Choi, Nambu University, Republic of Korea

Title: Involvement of extracellular proteases ADAM17 and ADAM10 in germ cell apoptosis induced by etoposide

Dr. Ricardo D Moreno, Pontificia Universidad Católica de Chile, Chile

Title: Polypeptide N acetylgalactosaminyl transferases expression in Pancreatic cancer

Dr. Prakash Radhakrishnan, University of Nebraska Medical Center, USA

Blocking cancer metastasis with TGF-beta antagonists

Lu Zhe Sun

University of Texas Health Science Center at San Antonio, USA

Induction of epithelial-mesechymal transition (EMT) has been shown to confer both metastatic and self-renewal properties to breast tumor cells resulting in drug resistance and tumor recurrence. TGFβ is a potent inducer of EMT. We found that chemotherapeutic drug doxorubicin activates TGFβ signaling in breast cancer cells. Doxorubicin induced EMT, promoted invasion and enhanced stem cell properties in the murine 4T1 breast cancer cells in vitro, which were inhibited by a TGFβ type I receptor kinase inhibitor (TβRI-KI). These observations suggest that the adverse activation of TGFβ pathway by chemotherapeutics in the cancer cells together with elevated TGFβ levels in tumor microenvironment may lead to EMT and generation of cancer stem cells resulting in the resistance to the chemotherapy. We investigated the potential synergistic anti-tumor activity of TβR1-KI in combination with doxorubicin in animal models of metastatic breast cancer. Combination of Doxorubicin and TβRI-KI enhanced the efficacy of doxorubicin in reducing tumor growth and lung metastasis in the 4T1 orthotopic xenograft model in comparison to single treatments. Doxorubicin treatment alone enhanced metastasis to lung in the human breast cancer MDA-MB-231 orthotopic xenograft model and metastasis to bone in the 4T1 orthotopic xenograft model, which was significantly blocked when TβR1-KI was administered in combination with doxorubicin. Our results indicate that the combination treatment of doxorubicin with a TGFβ inhibitor has the potential to reduce the dose and consequently the toxic side-effects of doxorubicin, and improve its efficacy in the inhibition of breast cancer growth and metastasis.

Biography

Dr. LuZhe Sun received his Ph.D. degree in Physiology from Rutgers-The State University of New Jersey and UMDNJ-Robert Wood Johnson Medical School in 1990 and obtained his postdoctoral training in Baylor College of Medicine in the US. He became an independent researcher in 1995 as Tenure-track Assistant Professor of Pharmacology in the University of Kentucky School of Medicine and is currently Professor of Cellular and Structural Biology, Dielmann Endowed Chair in Oncology, and Associate Director for Translational Research at the Cancer Treatment and Research Center in the University of Texas Health Science Center. Dr. Sun's main research interest is to elucidate the role of transforming growth factor beta (TGFβ) signaling in tumor progression. He participated in the discovery of the tumor suppressor role of TGFβ type II receptor in hereditary non-polyposis colorectal cancer and pioneered the use of a soluble TGFβ type III receptor and the engineer of a soluble chimeric TGFβ receptor for the inhibition of cancer growth, angiogenesis, and metastasis in various xenograft models of late stage human cancers. His research has been supported with multi-million dollar funding from National Institutes of Health, Department of Defense, the University of Texas Health Science Center, and other private foundations. He has co-authored more than sixty peer-reviewed publications, and serves regularly as scientific reviewer over the past decade for the National Institutes of Health and the Department of Defense in the US.

Molecular targeting of cancer stem cells by the small molecule dichloroacetate (DCA) through the disruption of the OCT4/PKM2 complex

François M. Vallette

INSERM and Université de Nantes, France

It has been postulated that solid tumors originate from a relatively small number of cells called cancer stem cells (CSC). Numerous studies have shown that brain tumor cancer stem cells were highly resistant to cell death and as such might contribute to tumor recurrence by eluding anti-cancer treatments. Like neural stem cells, cancer stem cells form *in vitro* structures called neurospheres. Using a proteomic approach based on two-dimensional DIGE and MALDI-TOF/TOF mass spectrometric identification, we have compared neurospheres derived from rat neural stem cells (NSC) with that derived from rat glioma (CSC) . The major pathway highlighted by this proteomic analysis is glucose metabolism. Inhibition of aerobic glycolysis *in vitro* altered the survival of CSC but not that of NSC. Strikingly, decreasing the non-oxidative glucose metabolism by Dichloroacetate (DCA), a PDK inhibitor, specifically depleted the stem cells population and impaired the growth of tumors *in vivo*. We found that DCA induced CSC differentiation rather than death, through the disruption of a PKM2/OCT4 complex in rat and human glioma. This work has important implications in the treatment of human brain tumors.

Biography

François M. Vallette has completed his Ph.D at the age of 26 years from Paris VII University and did postdoctoral studies in the Department of Cell Biology of NYU Medical Center. Currently, he is the director of the Department of Oncogenesis and Targeted Therapies in the Nantes Angers Cancer Research Center in France. He has published more than 80 papers in reputed journals and serving as associate or editorial board member in several journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Matrix metalloproteinases in crosstalk between cancer cells and osteoblasts in the bone invasion of oral squamous cell carcinoma

Jin Gao, Jingjing Quan, Chuanxiang Zhou and Glenn Francis

School of Dentistry, Griffith University and James Cook University, Australia

This study aims to detect whether matrix metalloproteinases (MMPs) play a role in bone invasion of oral squamous cell carcinoma (OSCC). Condition medium (CM) was collected from osteoblasts (hFOB or OB) and OSCC cells, and used in the indirect co-culture. Gelatine and protein forms of MMP-2/9 were detected by Gelatine Zymograph and Western Blotting. Bone markers, Twist1, Runx2, RANKL and OPG were also analysed using immunohistochemistry. Real-time PCR was utilized to determine the mRNA levels of these genes in OB and OSCC cells following the co-cultures. The Archival OSCC samples of bone invasion were used to confirm the localisation of those molecules in vivo. Results showed that gelatine forms of MMP-2/9 were increased in OSCC cells after co-cultured with hFOB. MMP-2 was also increased at the protein levels. Twist1 was increased, but not for Runx2. The RANKL/OPG ratio in hFOB was increased. Real-time PCR showed a similar expression patterns in co-cultured OB and OSCC cells to that at protein levels by Western blots and in clinical samples by immunohistochemistry. In conclusion: Cell co-culture is a useful model and has effectiveness on changes of MMP expression in OSCC cells in vitro. In addition, an increased RANKL/OPG ratio indicates the recruitment of osteoclasts and osteoblasts in the bone micro-environment of bone invasion of oral cancer cells. This study suggests roles of MMP-2/-9 in regulating the invasion of OSCC into bone.

Biography

Dr. Jin Gao was originally trained as a Dentist in China in 1980s, completed his PhD in late 1990s from the University of Queensland School of Dentistry and postdoctoral studies at the University of Sydney School of Medicine. He was awarded Australian NHMRC Peter Doherty Fellowship to carry out his cancer research career at Queensland University of Technology in 2001. Jin returned to his Academic Dentistry in 2005 at Griffith University, and is now a full Professor in Oral Biology & Oral Pathology at James Cook University.

Cancer stem cells

Caterina La Porta

Department of Biomolecular Science and Biotechnolog, University of Mila, Italy

The majority of human cancer cells are the clonal progeny of an initiating variant tissue cell. Recent investigations of a variety of tumor types have shown that phenotypically identifiable and isolable subfractions of cells possess the tumor-forming ability. This feature of rare cells with tumor-forming potential dividing to produce cells with limited or no tumor forming potential is the basis for the cancer stem cell paradigm. Cancer stem cell research revived a longer-standing idea that many tumors (though not all) were likely to be the spawn of mutated tissue-specific stem cells. We will present the first phenotypic evidence to support this concept.

Biography

Caterina La Porta has completed his Ph.D at the age of 28 years from University of Milan and she is research Associate professor at the same University permanent from 2002. She is the group leader of the Molecular Oncology Laboratory at the Department of Biotechnology of the University of Milan. She has published more than 60 papers international Journals and she is in the editorial board and referee of many International Journals. She has been visiting professor in many outstanding University and she collaborates with many international laboratories in particular in the United States. For more information: www.oncolab.unimi.it

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Deconstructing Cancer Progression: Cancer Stem Cells and Dedifferentiation

Carlos F. D. Rodrigues

Centre for Neuroscience and Cell Biology, University of Coimbra, Portugal

In the last decades cancer has evolved as the most common human disease with lung cancer toping the ranking. All over the world different theories have tried to explain the emergence, development and progression of human tumors, although none have yet fully succeeded on its task. One of the recent and most appealing theories argues that the heterogeneous nature of each tumor encompasses a specific population of cells, with Stem Cells (SCs) like properties, which gives rise to the bulk of the tumor cells with more differentiated phenotypes**1**. Although, these Cancer Stem Cells (CSCs) have been blamed as responsible for tumor recurrence and resistance to conventional therapies**2**, their origin is rather controversial.

Aiming to understand the mechanisms underlying hexavalent chromium [Cr(VI)] induced lung cancer, we succeeded to induce the malignant transformation of the non-tumorigenic bronchial epithelial cell line (BEAS-2B) following exposure to occupational relevant Cr(VI) concentrations**3**. Subsequently, the resulting RenG2 cell line malignant potential was increased following successive rounds of transplantations in athymic nude mice**4**. Metabolic and cell cycle studies revealed that the more malignant RenG2-derivative cell lines (DRenG2 and DDRenG2) have increased glycolytic metabolism and decreased replicative index. Additionally, sphere-formation assays also revealed positive only for DRenG2 and DDRenG2 cell lines and the molecular characterization of those cultures confirmed their CSCs-identity.

Apparently, the increased malignant potential of DRenG2 and DDRenG2 cell lines can be ascribed to a process of cellular dedifferentiation leading to the emergence of CSC-like sub-populations in both cell lines boosting their aggressiveness and resistance.

Biography

Carlos Rodrigues, has 25 years old and is a last year PhD student at the University of Coimbra, Portugal. He has finished his graduation in Biology at the same University in 2008. Since the last year of his graduation he has been focusing his research in trying to highlight the molecular mechanisms underlying hexavalent chromium induced lung cancers and its progression to metastasis. So far he has already published 7 papers (2 original research paper, 1 review and 4 proceedings) and has 2 additional manuscripts under revision.

Stat5: from lactogenesis to tumorigenesis

Itamar Barash

Institute of Animal Science, ARO the Volcani Center Bet-Dagan, Israel

The signal transducer and activator of transcription (Stat5) is a cytoplasmic signaling molecule and a transcription factor which confers the effects of cytokines, polypeptide hormones and growth factors into transcriptional activity. In the mammary gland, Stat5 controls epithelial cell proliferation, lactogenesis, lactation and cell survival. In transgenic mice, we have shown that deregulation of Stat5 activity during the reproductive cycle results in parity-dependent development of mammary tumors in post-estropausal females. Overexpression of the native and constitutively active form of Stat5 cause mainly highly differentiated tumors, while its C-terminally truncated form induced mainly the poorly differentiated carcinomas. Several mechanisms may account to the oncogenic effect of Stat5. (i) DNA damage**.** Production of reactive oxygen species during the vulnerable stage of pregnancy induced significant DNA damage and cellular DNA damage response within three days. Chromosomal breakage, fragmentation and translocations occasionally result in tumorigenesis. (ii) Parity-dependent Histone modifications at the Stat5 binding sites in the cyclin D1 and bcl-x gene promoters during the reproductive cycle. These modifications expose individual cells to the deregulated effect of Stat5 which highly activates these genes. (iii) Silencing tumor suppressers and proliferation antagonists. These distinct metabolic consequences occur during tumor development and mediate the earlier effect of deregulated Stat5. Thus, in association with the protective effect of parity against breast cancer that was reported in epidemiological studies, parity-dependent deregulated levels and activity of Stat5 represent a long-term risk factor. Monitoring Stat5 activity in the breast during the vulnerable stage of pregnancy may help in reducing its oncogenic effect.

Biography

Itamar Barash has received his Ph.D from The Hebrew University of Jerusalem and completed postdoctoral studies at McGill University and the Weizmann Institute. He is the head of the Department of Ruminant Science and Genetics of the Institute of Animal Science of the Volcani Center. He has published more than 43 papers in reputed journals. The current research topics in his lab are: The role of Stat5 in normal mammary development and function and in tumorigenesis; amino acids acting as signal molecules in the mammary gland; Identification of stem cells in the bovine mammary gland.

Inflammatory chemokines in breast cancer: Regulation by genetic and host factors

Adit Ben-Baruch

Ela Kodesz Institute for Research on Cancer Development and Prevention, Tel Aviv University, Israel

Inflammatory chemokines, including CCL2, CCL5, and CXCL8 are major contributors to breast malignancy, acting at many different levels. We have analyzed the regulation of CCL2 and CCL5 expression by inflammatory cytokines in breast tumors. Our analyses indicated that TNFα and IL-1β are expressed by the tumor cells in 90% of breast cancer patients, and that both cytokines potently up-regulated the release of CCL2 and CCL5 by breast tumor cells and by normal breast epithelial cells that are as yet non-transformed. Also, we found that TNFα and IL-1β act directly on breast tumor cells and on non-transformed breast epithelial cells to promote cell characteristics leading to increased invasiveness. Combined with additional findings, we suggest that TNFα and IL-1β from autocrine sources are important up-regulators of CCL2 and CCL5 release in early and advanced stages of disease, as well as of progression-related processes. In parallel, we have analyzed the roles played by genetic and signaling components in the regulation of CCL2, CCL5 and CXCL8 in model systems of fibroblasts and of breast tumor cells. In this part, we focused on two components that undergo oncogenic deregulation in breast cancer, namely the tumor suppressor p53 and the Ras signaling pathway. Our findings provide evidence to intricate modes of interaction between p53, Ras and the chemokines, suggesting that inappropriate regulation of these genetic and signaling components promotes the release of pro-malignancy chemokines in breast cancer. Overall, our findings indicate that cooperation between inflammatory mediators and genetic/signaling components in breast cancer support breast tumor growth and metastasis.

Biography

Dr. Ben-Baruch completed her Graduate studies in Tel Aviv University, Israel. Following her post-doctoral studies at the NIH she returned to Tel Aviv University as a Faculty member, where she started analyzing the roles of chemokines in malignancy. Dr. Ben-Baruch's laboratory was the first to identify the chemokine CCL5 as a key factor supporting breast malignancy. Dr. Ben-Baruch's research has contributed to the current understanding of the role of inflammatory chemokines, primarily of CCL2 and CCL5 in breast cancer. It is now agreed by leading investigators in the field that these chemokines are key detrimental factors in breast cancer that could serve as potential targets for therapy, and for identification of patients-at-risk.

The ESCRT pathway and ubiquitin-binding ability of Tsg101 are required for dynamic Src trafficking and v-Src-mediated invadopodia formation and invasion

Chun Tu

University of Texas M.D Anderson Cancer Center, USA
University of Nebraska Medical Center, USA

ESCRT proteins including Tsg101 are well-established for their role in formation of multivesicular bodies and sorting ubiquitinated endosomal cargoes to lysosomes via their ubiquitin-binding domains. However, genetic ablation studies in mouse models and human cell lines show ESCRT proteins and Tsg101 are required for proliferation, cell viability, and malignant phenotypes of cancerous cells. Utilizing a conditional Tsg101 knockout mouse embryonic fibroblast (MEF) cell line, we show that Tsg101 is indispensible for Src function. Dynamic trafficking of Src at endosomes and translocation of active Src to focal adhesions and invadopodia are impaired when expression of Tsg101 is lost. Blocking Vps4 function by expression of a dominant negative form of Vps4 has similar effect. Viral expression of wildtype Tsg101, but not the N45A mutant, which has lower binding affinity to ubiquitin, restores invadopodia formation and invasivenss of Tsg101-deleted v-Src MEFs. Together, our study reveals a surprising positive role of Tsg101 and probably ESCRT pathway in promoting Src signaling that requires its ability to interact with ubiquitin.

Biography

Chun Tu obtained her ph. D from Washington University at St. Louis in 2004. Her postdoctoral work under Dr. Hamid Band at Northwestern University and University of Nebraska Medical Center focused on how lysosomal trafficking affects Src signaling and invadopoida-associated matrix-degradation and invasion. She is currently an instructor working in Dr. Mien-Chie Hung's lab at University of Texas MD Anderson Cancer Center.

Individual chemosensitivity test for personalized therapy in cancer patients

Jianping Gong, Dong dong Yu and Jichao Qin

Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, P.R. China

To avoid or minimize the side effects and improve the effectiveness of chemotherapeutic agents in advanced gastric cancer and colorectal cancer (CRC) patients, we have developed an *in vitro* model to determine the response of the cells, which were dissociated from surgical tumor samples, to combination chemotherapeutic agents. In additional, a xenograft model was further applied to test the results from *in vitro* studies. If consistent results were obtained, we will explore whether the above experimental systems can finally be indicator(s) to achieve personalized chemotherapy for individual cancer patients. For the sake of simplicity, we refer to Individual Chemosensitivity Test (ICT) as both *in vitro* and *in vivo* experimental systems described above.

The detailed protocol of ICT was described as the following. Fresh surgical tumor samples from individual patients were dissociated into single cells, and then some of the cells were cultured *in vitro* and treated with combined chemotherapeutic agents in two different chemotherapeutic regimens, i.e., Oxaliplatin and Irinotecan-based combination therapies, which are two often-used primary or neoadjuvant or adjuvant chemotherapeutic regimens for gastric cancer and CRC patients. After incubated for 6-8 hours, the cells were harvested to examine the response to the combined chemotherapeutic agents by evaluating the percentage of apoptosis and proliferation. On the other hand, some of the cells from the fresh surgical tumor specimens were implanted in immunodeficient mice (i.e., nude mice), when the tumors became palpable, the same combined chemotherapeutic agents as *in vitro* studies were administered via tail vein injection. After about a month, the individual tumors were harvested and weighed. In *in vivo* experimental system, the response of the cells to the given agents was assessed by monitoring the tumor growth in nude mice upon administration of chemotherapeutic agents. Until now, 21 surgical specimens (9 Gastric cancer and 12 CRC specimens) were conducted for ICT, and encouragingly, the results *in vitro* were highly consistent with those from *in vivo* experimental system.

In brief, we are taking the steps to apply 'right' chemotherapeutic regimens for individual cancer patients based on the results from ICT. Our ultimate goal is to attain personalized chemotherapy for individual cancer patients.

Biography

Jianping Gong has earned his M.D and Ph.D degrees from Tongji Medical College of Huazhong University of Science and Technology in China, and received postdoctoral training from New York Medical College for more than 3 years. Currently, he is a distinguished professor and director of gastrointestinal surgery division in Tongji Hospital, Tongji Medical College of Huazhong University of Science and Technology in China.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Tanshinone IIA on apoptosis via SAPK/JNK signal transduction in pancreatic cancer cells

Peihao Yin

Putuo Hospital, Shanghai University of Traditional Chinese Medicine, China

This study is to investigate the effect of **TS**IIA on **inducing** apoptosis **via SAPK/JNK signal transduction** in **human** pancreatic cancer cells**.** In vitro, MTT assay was used to observe the cytostatic effect in human pancreatic cancer cell line PANC-1 by TSIIA. The apoptosis was assessed in pancreatic cancer cells by immunofluorescence after treatment with TSIIA; apoptosis was determined by Flow cytometry (FCM), p-JNK expression was assayed by Western Blot, and the mRNA expression level of Survivin were detected by Fluorescent Quantitation PCR, compared with the mRNA expression level of Survinvin after treatment with blocking agent. In vitro, the growth inhibitory effect was concentration-and time-dependent. After PANC-1 cells were treated with 8, 16, 32mg/L of TSIIA for 48h, typical morphologic changes of apoptosis were observed by fluorescence microscope using Hoechst staining. When treated with 8, 16, 32mg/L of TSIIA for 48h, the cell apoptotic rates were respectively (8.83±1.51)%,(12.86±2.70)% and (21.24±2.58)%, showing significant difference(P<0.01). After signal transduction pathway of JNK was blocked, the cell apoptotic rates were decreased significantly (P<0.01). Phosphorylation-JNK expression after 1h and the expression was the highest when at 4h. The mRNA expression of the Survivin gene were decreased obviously after treatment with 16mg/L TSIIA for 48h; whereas they were decreased significantly when the transduction pathway was blocked. **TSIIA can induce human** pancreatic **cancer cells apoptosis. The anti**- pancreatic cancer **mechanism of TSIIA might involve down-regulation the expression of the** Survivin **mRNA via** SAPK/JNK **signal transduction pathway.**

Biography

Peihao Yin, as the vice-director of surgery in Putuo hospital affilated to Shanghai University of Traditional Chinese Medicine, he has taken in charge of the prevention and treatment of cancer in Integrative Medicine. Also he is the member of Professional Translation Committee on Chinese Medicine and have been undertaking more than 6 prizes on Science and Technology Commission of Shanghai Municipality. He has published more than 20 papers in reputed journals, including 2 papers in SCI.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The anti-tumor effect of fermented curcumin

Ha-rim Choi[1], Hyung-Sik Kang[2] and Youn-Tae Chi[2]

[1]Department of Food and Nutrition, Nambu University, Republic of Korea,
[2]School of Biological Sciences and Technology, Chonnam National University, Republic of Korea

Curcumin (diferuloylmethane) has been known to suppress tumor progression. To identify curcumin derivatives having more potent anti-tumor activity, we compared the anti-tumor effect of curcumin and fermented curcumin fermented by *bacillus subtillus*. Fermented curcumin (diferuloylmethane) markedly suppressed proliferation of various cancer cells through regulation of cell cycle progression compared to curcumin. Expression of apoptosis-associated genes was elevated by treatment of cancer cells with fermented curcumin in a dose-dependent manner. In addition, fermented curcumin suppressed metastasis by downregulating MMP expression. More importantly, the susceptibility to NK cell-mediated killing of cancer cells was modestly more increased in cancer cells treated with fermented curcumin than in those treated with only curcumin. These findings collectively suggest that fermented curcumin plays an essential role in the regulation of tumorigenecity.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Involvement of extracellular proteases ADAM17 and ADAM10 in germ cell apoptosis induced by etoposide

Ricardo D Moreno

Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Chile

We have recently determined that the extracellular protease TACE/ADAM17 is involved in physiological (constitutive) germ cell apoptosis. The mechanism underlying apoptosis induction in cancer cells has been studied in different cell types, but it is not known whether the same factors participate in viable germ cells. Since testicular cancer primarily affects young males, we used pubertal rats (21 days old) as a model to determine whether etoposide induces apoptosis through TACE/ADAM17 upregulation, akin to physiological process. Germ cell apoptosis induced by DNA damage was associated with an increase in protein levels and cell surface localization of TACE/ADAM17 and ADAM10. On the contrary, apoptosis of germ cells induced by heat stress, another cell death stimulus, did not change levels or localization of these proteins. Pharmacological *in vivo* inhibition of TACE/ADAM17 and ADAM10 prevents etoposide-induced germ cell apoptosis. Gleevec (STI571) a pharmacological inhibitor of p73, a master gene controlling apoptosis induced by etoposide, prevented the increase of TACE/ADAM17 levels. In vitro, using a germ cell line model, etoposide was also able to induce up regulation of ADAM10 and TACE/ADAM17. Pharmacological and genetic inhibition of both enzymes (knockdown) prevented apoptosis induced by etoposide. Our results strongly suggest that TACE/ADAM17 participates in apoptosis of male germ cells induced by DNA damage. Therefore, we have showed a new and a previously unanticipated element in the mechanism of apoptosis induced by etoposide.

Biography

Ricardo Moreno has completed his Ph.D at the age of 26 years from Pontificia Universidad Católica de Chile and postdoctoral studies from Oregon Regional Primate Research Center. He is associate Professor at the Physiology Department (Biological Sciences Faculty, Pontifical Catholic University of Chile). He has published more than 35 papers in reputed journals and serving as associate or editorial board member in several journals.

MUC1-CT regulates UDP: polypeptide N-Acetylgalactosaminyltransferases (ppGalNAc-Ts) expression in pancreatic cancer

Prakash Radhakrishnan and Michael A Hollingsworth

Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, NE 68198-5950

MUC1 is a transmembrane glycoprotein overexpressed and aberrantly glycosylated in most of the human cancers including pancreatic cancer. Overexpression of MUC1 is associated with progression of pancreatic cancer. The MUC1 cytoplasmic tail (MUC1-CT) regulates a variety of genes that are implicated in the process of epithelial to mesenchymal transition (EMT), increased invasiveness and metastasis of cancer cells. In this study we show that overexpression of MUC1 downregulates one of the mucin type *O*-glycan initiating glycosyltransferases, UDP: polypeptide N-acetylgalactosyltransferase-5 (ppGalNAc-T5). The ppGalNAc-T5 is associated with tumor suppressor gene EXT-2. Further, down regulation of MUC1 by shRNA restores and up-regulates ppGalNAc-T5 expression. Our ChIP-on-chip and ChIP analysis reveals that binding of MUC-CT to the ppGalNAc-T5 promoter inhibits the transcription of ppGalNAc-T5. This study suggests that one oncogenic role of MUC1-CT is targeting the tumor suppressor glycosyltransferase GalNAc-T5 and it is the first study to show that MUC1-CT regulates expression of glycosyltransferases in pancreatic cancer cells.

Biography

Prakash Radhakrishnan obtained his Ph.D from University of Madras, India in 2006. His research work under Dr. Michael A Hollingsworth focused on role of Mucin glycans in pancreatic cancer growth and metastasis.

2(i): Biomarkers in Cancer Therapy & Molecular Diagnostics

2(ii): DNA Methylation and Mutation based biomarkers

Session Chair

Dr. Michael Mingzhao Xing

Johns Hopkins University School of Medicine, USA

Session Co-Chair

Dr. Jeff Gildersleeve

National Cancer Institute, USA

Session Introduction

Title: **Prognostic utility of BRAF mutation in thyroid cancer**

Dr. Michael Mingzhao Xing, Johns Hopkins University School of Medicine, USA

Title: **New biomarkers for cancer vaccine research**

Dr. Jeff Gildersleeve, National Cancer Institute, USA

Title: **Signature molecular biomarkers of prognosis of gastric adenocarcinoma: A study of 114 cases using genome-wide technique and FISH**

Dr. Dongfeng Tan, University of Texas MD Anderson Cancer Center, USA

Title: **Biomarkers for therapy with the EGFR inhibitors**

Dr. Helmout Modjtahedi, Kingston University London, UK

Title: **Tumor specific oligomeric forms of protein b23/nucleophosmin**

Dr. Natalia Vladimirova, Russian Academy of Sciences, Russia

Title: **A biomarker and immunomarkers approach for the diagnosis of poorly differentiated neuroendocrine carcinoma**

Dr. M. H. Bukhari, King Edward Medical University, Pakistan

Title: **Methylation array analysis of tissue DNA in oral squamous cell cancer patients in Taiwan**

Dr.Yu Fen Li, China Medical University, Taiwan

Title: **Proximity Ligation for visualization of protein-protein interactions in cancer cell signaling and early cancer detection through novel blood based biomarkers**

Dr. Simon Fredriksson, Olink Bioscience AB, Sweden

Title: **Methylation biomarkers – From discovery to clinical use**

Dr. Tomasz K Wojdacz, University Hospital of Aarhus, Denmark

Title: **Molecular and biochemical evaluation of anti-proliferative effect of (Cichorium endivia, L.) phenolic extracts**

Dr. Ali S. Alshehri, King Khalid University, Saudi Arabia

Prognostic utility of *BRAF* mutation in thyroid cancer

Mingzhao Xing

Division of Endocrinology and Metabolism, Johns Hopkins University School of Medicine, USA

Genetic alteration is the driving force for thyroid tumorigenesis and progression, based upon which novel approaches to the management of thyroid cancer can be developed. The T1799A *BRAF* mutation in papillary thyroid cancer (PTC) has a great clinical promise and is currently being translated from laboratory to the clinic use. Studies from our and other groups have consistently shown that *BRAF* mutation is the most common genetic alteration in thyroid cancer, occurring in about 45% of papillary thyroid cancers (PTC) and 25% anaplastic thyroid cancer. The *BRAF* mutation exerts its oncogenic role through aberrant activation of the MAP kinase signaling pathway. Numerous studies around the world have demonstrated the unique role of *BRAF* mutation in the development of aggressiveness of PTC, in agreement with our initial findings. For example, *BRAF* mutation is closely associated with extrathyroidal invasion, lymph node metastasis, advanced tumor stage, and, importantly, disease persistence/recurrence and even decreased patient mortality. *BRAF* mutation is also associated with loss of radioiodine avidity of PTC, making it difficult to treat this cancer using radioiodine. Numerous studies have demonstrated that *BRAF* mutation is associated with increased expression of tumor-promoting molecules or suppression of tumor-suppressing molecules, providing a molecular basis for the role of this mutation in the progression and aggressiveness of PTC. Recent studies have also demonstrated an important role of *BRAF* mutation in the silencing of iodide-handling genes in PTC, providing a molecular explanation for the association of loss of radioiodine avidity of PTC with *BRAF* mutation. Thus, *BRAF* mutation is a novel and powerful prognostic molecular marker for poorer prognosis of PTC. Use of *BRAF* mutation, which can be detected on preoperative thyroid fine needle biopsy specimens, is expected to become an effective strategy for risk stratification of PTC. This may help resolve several clinical dilemmas encountered in the management of PTC, such as how to determine the extent of surgical and medical treatments of PTC in various clinical settings. It is thus expected that *BRAF* mutation, as a novel prognostic marker in PTC, will have an important impact on thyroid cancer medicine.

Biography

Mingzhao Xing, M.D., Ph.D., is Associate Professor of Medicine, Oncology and Cellular and Molecular Medicine, Co-Director of the Thyroid Tumor Center, and Chief of the Laboratory for Cellular and Molecular Thyroid Research at the Johns Hopkins University School of Medicine. Following his initial medical training at the Second Military Medical University in Shanghai, China, he obtained a Ph. D. degree in Physiology and Biophysics at Case Western Reserve University in Cleveland. He subsequently completed an internal medicine residency at the Greater Baltimore Medical Center and a clinical fellowship in Endocrinology and Metabolism at the Johns Hopkins University School of Medicine. Upon completing the fellowship, Dr. Xing was recruited to the faculty at the Division of Endocrinology and Metabolism of the Johns Hopkins Hospital. Dr. Xing serves on a number of national and international professional committees/panels, including, for example, National Institute of Health study sections, American Thyroid Association committees, several cancer research grant review panels in European counties. He also serves as a member or editor on a number of subspecialty journals, such as Journal of Clinical Endocrinology and Metabolism, Endocrine-Related Cancer, and Thyroid. Dr. Xing practices clinical endocrinology as a subspecialty consultant and teaching attending at the Johns Hopkins Hospital while also conducting laboratory research as a physician scientist. His main clinical and research interest is in thyroid diseases, particularly thyroid tumors. Supported by the American Cancer Society and NIH R0-1 grants, his laboratory has been studying molecular, genetic and epigenetic mechanisms of thyroid cancer and their clinical translations. His team has published actively in these areas, particularly in relation to the MAP kinase and PI3K/Akt pathways. He is co-holder of a patent on the initial discovery and clinical characterization of the BRAF mutation in thyroid cancer. He has published more than 80 scientific articles. Among his professional recognitions/awards are the US FAMRI Clinical Innovator Award, Maryland Innovator Award, American Cancer Society RSG Award, and “America’s Top Physician” recognition.

New biomarkers of cancer vaccine research

Jeffrey C. Gildersleeve
National Cancer Institute, USA

Cancer vaccines have significant potential as therapeutics to treat cancer, but they typically only provide a clinical benefit in a subset of patients. To optimize the clinical use of cancer vaccines and to better understand the factors that affect clinical responses, there have major efforts to identify predictive biomarkers (markers that could be used to select patients that are likely to have a positive response) and biomarkers of efficacy (markers that could be used to determine if a patient being treated with a cancer vaccine is having a positive response to the treatment). Current biomarker research has focused a variety of factors, such as T cell responses, circulating tumor cells, and cytokine production. One area that has been largely understudied is immune responses to glycans. Cancer cells undergo major changes in carbohydrate expression during the onset and progression of the disease, and aberrantly expressed glycans can serve as important targets for natural immune surveillance and/or for immune responses induced by vaccines. Our group has developed a carbohydrate microarray or "glycan array" which enables us to profile immune responses to a wide range of carbohydrate antigens in a high-throughput fashion. This presentation will focus on the development of the glycan array and its application to the identification of new biomarkers for cancer vaccine research.

Biography

Jeff Gildersleeve completed his Ph.D. at Princeton University in 1999 and carried out postdoctoral studies at The Scripps Research Institute from 1999-2003. He is currently an Investigator at the National Cancer Institute in the Chemical Biology Laboratory. His research focuses on the development of glycan array technology and its application to cancer biomarker research. He has published 32 papers and has served as a reviewer for numerous scientific journals and granting agencies. In 2006 he received the NCI Director's Innovation Award and in 2010 was selected by the Editors of Molecular BioSystems as an "Emerging Investigator".

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Signature molecular biomarkers of prognosis of gastric adenocarcinoma: A study of 114 cases using genome-wide technique and FISH

Dongfeng (Dan) Tan

University of Texas MD Anderson Cancer Center, USA

Background: Accumulated evidence suggests that multiple genetic alterations are involved in the complex carcinogenetic process of gastric adenocarcinoma (GAC). Although a number of genetic changes have been reported in GAC, including amplification of *CMET and FGFR2*, mutation of *E-cadherin and KRAS*, and loss of heterozygosity on 5q and 18q, the molecular events leading to GAC and its progression remain largely unknown. To assess global molecular changes in GAC, we use whole genomic assay to evaluate human GAC samples.

Methods: Oligonucleotide array comparative genomic hybridization (aCGH) was performed on 46 GAC samples using a high-density (244K) aCGH system (Agilent Technologies). For each aCGH probe, each sample was classified as having normal, gained, or lost DNA copy number based on log 2 ratio thresholds of 0.15. An independent set of tissue arrayed samples (n=68) was further validated by fluorescent in-situ hybridization (FISH) by using probes visualizing 19q13.3 (red signal) and the centromere (green signal). Amplification of 19q13.3 was defined if the ratio of 19q13.3 to centromere is greater than 2.2. The mean patient's survival follow-up time was 58 months.

Results: aCGH identified 1271 genes with DNA copy loss and 1449 genes with DNA copy gain in gastric cancer. Among these identified genes, 11 deleted and 198 amplified genes were observed to have significant association with patient's survival. Forty-eight of amplified genes were specifically located on chromosome 19q13.3, including *CRX, DACT3, DKKL1, EHD2, EMP3, HIF3A, HRC, IGFL2, IGFL3, KPTN, LIG1, PNKP,* and *PTOV1*. Compared with all other patients, those (n=14) with gene amplification on 19q13.3 had a significantly poorer prognosis ($p<0.01$), independent of other conventional prognosis factors including TNM stage. These results were further confirmed by FISH method and amplification of 19q13.3 was identified in 18 cases with unfavorable clinical outcome.

Conclusions: This genome-wide study identified a panel of critical genes associated with progression of GAC. Amplification of the genes on chromosome 19q13.3, a possible signature event in gastric carcinogenesis, represents a potentially useful prognostic biomarker for this aggressive malignancy. Further functional studies are needed to confirm the potential value of these genes in the management of gastric cancer.

Biography

Dr. Dongfeng (Dan) Tan is a professor at MD Anderson Cancer Center. After medical education and graduate study (1978-1987) in Tongji Medical College, Wuhan, Dr. Tan did postgraduate training in pathology and genetics at Essen University in Germany (1987-90) and Columbia University (1991-94) in New York. After pathology residency at Yale University Medical Center, Connecticut, from 1994 to 1998, he completed an oncologic surgical pathology fellowship at Memorial Sloan-Kettering Cancer Center in New York. Certified by American Board of Pathology in 1998, Dr. joined Roswell Park Cancer Institute as an assistant professor of pathology in 1999. In 2004, he became an associate professor at The University of Texas (UT) Health Science Center at Houston. In 2006, he joined the faculty of UT M. D. Anderson Cancer Center. Currently, Dr. Tan focuses on oncological pathology and molecular diagnostics. Dr. Tan has published more than 120 peer-reviewed articles, one textbook, and a number of book chapters. In recognition of his contributions to the field, Dr. Tan has been invited to present at a number of national and international meetings as well as grand rounds at varied institutions. He has also served on grant review committees for private and government agencies, and has been invited to serve on the editorial boards of ten peer-reviewed journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Biomarkers for therapy with the EGFR inhibitors

Helmout Modjtahedi
Kingston University London, UK

Since the early 1980s, abnormal expression and activation of the epidermal growth factor receptor (EGFR) family members, in particular EGFR and HER-2, have been reported in a wide range of human epithelial malignancies and in some studies have been associated with poor clinical outcomes. These discoveries have lead to the strategic development of several types of inhibitors. Some of these inhibitors namely anti-EGFR monoclonal antibodies [(mAbs) cetuximab and panitumumab], anti-HER-2 mAb trastuzumab, small molecule EGFR tyrosine kinase inhibitors [(TKIs) gefitinib, erlotinib], or a dual EGFR and HER-2 TKI (lapatinib), have been approved by the FDA for the treatment of patients with head and neck, metastatic colorectal, pancreatic, breast cancers or gastric cancers. Despite these advances, two major outstanding challenges associated with the use of the EGFR inhibitors are the lack of reliable predictive markers for response to therapy with the EGFR inhibitors and the duration of response which can be short in some of these patients. In some studies, the presence of EGFR gene amplifications or somatic mutations, mutated KRAS or PTEN, the expression of autocrine EGFR ligands (e.g. epiregulin, amphiregulin), other members of the EGFR family (e.g. HER-2, HER-3) or heterologus growth factor receptor (e.g. IGF-IR and c-Met) or development of skin rash were associated with the response or resistance to treatment with the EGFR inhibitors. However, all patients with wild type KRAS, for example, do not respond to therapy with the EGFR inhibitors. In this presentation, I shall discuss these challenges and developments todate regarding the establishment of more reliable predictive markers for response to therapy with the EGFR inhibitors.

Biography

Dr Helmout Modjtahedi is Reader in Cancer Therapeutics at Kingston University London. He completed his PhD (1989-1993) followed by 6 years of postdoctoral studies at The Institute of Cancer Research, University of London. In 1999, he joined University of Surrey as a Clinical Lecturer in Tumor Immunology and in 2007 moved to Kingston University London. His research to date has been focused upon targeting of EGFR family members with monoclonal antibodies and small molecules tyrosine kinase inhibitors. He has published more than 50 papers and book chapters and is serving as an editorial member on several journals.

Tumor specific oligomeric forms of protein b23/nucleophosmin

N.M.Vladimirova

Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow

In tumor cells nicleophosmin is overexpressed. According to the latest literature data the gene of nucleophosmin most frequently underwent modifications (mutations, deletions, translocations) during malignant blood disorders. Structural state of nucleophosmin in solid tumor is less studied. We have developed a strategy for isolation and structural analysis of nucleophosmin from HeLa cells. The protein forms functioning in human tumor cells have been characterized. The site of protein truncation has been established and the ability of truncated nucleophosmin to form SDS-resistant oligomers has been shown for the first time. We have analyzed the monomer-oligomer state of B23 in human tumor cell of various origin such as HeLa, Hep G2, MCF-7, NGP, K-562, Jurkat, Ramos, U-87, JMR-32; in rat tumor C6 cells, normal rat tissues (brain, liver, kidney, heart, lung). We have created special antipeptide antibodies which specifically react either with oligomeric or monomeric forms in contrast to monoclonal antibodies (FC82291, Sigma) that recognize nucleophosmin monomers and oligomers together. The SDS-stable oligomers were detected in all tumor cells, but were not detected in normal tissue cell lysates. For the first time we described essential differences in the level and localization of B23 oligomers and monomers in glioma (C6, U-87) and neuroblastoma (JMR-32) cells. This work was supported by the RFBR (project No. 09-04-00713-a) and the Program "Fundamental Sciences for Medicine" (project 2009-2011).

Biography

Natalya Vladimirova has been a Senior Researcher at Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences (Russia) since 1987. She graduated from Lomonosov Moscow State University in 1972 with a degree in chemistry. Since that time she has been working in Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry and studying the structure and functions of different proteins. She got a PhD degree in 1979. Vladimirova has more than 70 scientific publications, carries out scientific seminars for students. She is a scientific supervisor of post-graduate students. During last seven years she has been studying the role of nucleolar proteins in carcinogenesis and apoptosis, paying special attention to protein B23/nucleophosmin.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

A biomarker and immunomarkers approach for the diagnosis of poorly differentiated neuroendocrine carcinoma

M. H. Bukhari

King Edward Medical University, Lahore, Pakistan

Background: Pathologic evaluation of tumor tissue is the key for establishing a correct diagnosis and for selecting the appropriate therapy for patients with poorly differentiated neuroendocrine carcinoma (PDNECA). Here, we evaluated the role of histopathology and immunohistochemistry in the diagnosis and subclassification of primary PDNECAs at a single institution with multidisciplinary expertise in neuroendocrine oncology. Methods: Clinico-pathologic data from 80 adult patients, aged: 25-76 yrs (mean 42 yrs years), Patients: 51 M/29 F, with primary PDNECA of the lung 42, colon 33, pancreas 19, gall bladder 3, liver 2 and miscellaneous 17 who had undergone biopsy/resection at our institution were included. Data were collected from pathology archives, consultation files, tumor registries, and social security indexes. All available slides were independently reviewed by 3 pathologists for histological subtyping and immunohistochemical evaluation of each case.

Results: Histopathology was adequate for diagnosing pure small cell (SCCA) and large cell neuroendocrine carcinoma (LC-NECA). Immunohistochemistry was useful in supporting the diagnosis of PDNECA. Overall, chromogranin, synaptophysin, NSE, and CD56 were positive in 44/75 (60%), 72/77 (94%), 24/28 (88%), and 22/25 (88%) cases, respectively. Immunoreactivities for other markers for primary PDNECAs from various organs were as follows: TTF-1, 16/24 (67%) pulmonary and of 0%for nonpulmonary; α-fetoprotein (AFP), 2/2 (100%) in hepatic vs. non-hepatic; anti-cytokeratin (CAM 5.2), 16/19 (85%) pancreatic, 5/6 (83%) pulmonary; CK-7, 15/19 (79%) pancreatic and.83% Pulmonary vs. 28-50% in non-pancreatic/pulmonary/colonic, CDX2 was 100% in small intestine primaries and 100% negative in pancreatic and Gall Bladder NEC, carcinoembryonic antigen (CEA), 5/5 (100%) colonic; CK20, 23/27 (85%) colonic. Ki-67 index ranged from 20-70% (median: 45%). There was a strong correlation between mitotic count and Ki-67 index (*r +0.953*).

Conclusions: Histopathology can be used to subclassify PDNECA cases into small-cell, large-cell, and mixed small and large cell subtypes, as well as other histological subtypes. However, for patients with PDNECA of unknown origin, a panel of immunohistochemical markers (TTF1, CK7, CK20, and CDX2) may be helpful in pointing toward the primary site. Practical utility of AFP to differentiate between primary hepatic and extra-hepatic PDNECA merits further investigation.

Biography

Dr Bukhari completed his doctorate in Surgical Pathology with the theoretical and practical combination of Histopathology, Immunohistochemistry and PCR at the King Edward Medical University in 2007. After his doctorate he attended the special course of Breast Pathology in Harvard School of Public Health in 2009. He has started work with Prof Abbas Iqbal and Eyyad H A Kamel on Chemothearpeutic effect of Sanatinib.e in triple negative patients and HER 2 Positive cases.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Methylation array analysis of tissue DNA in oral squamous cell cancer patients in Taiwan

Yu-Fen Li, Yi-Hsiu Hsiao and Chien-Kuo Tai

China Medical University, Taiwan

Purpose: The aim of this study is to perform a genome-wide methylation profile of 1,505 CpG sites of 807 cancer-associated genes and search for diagnosis and screening biomarkers for oral squamous cell cancer (OSCC).

Methods: Buccal tissue samples of 40 OSCC patients obtained from the tissue bank of China Medical University Hospital were served as the case group. A total of 15 normal samples composed the control group. Specificity, sensitivity, and the area under the Receiver Operating Characteristic curve (AUC) were calculated along with 5-fold cross validation to evaluate the accuracy of a predictive model.

Results: Thirty-four single CpG sites with both the sensitivity and specificity higher than 70% were selected as the classifier. A total of 8 panels consisted of two or three CpG sites showed a perfect specificity and a high sensitivity (85%~90%). The panel of genes ASCL1 and FLT4 represented the best combination with a perfect specificity, 90% of sensitivity, AUC=95%, and 92.6% (standard error 0.1%) of the mean correct classification rate in 5,000 times of the 5-fold cross validation.

Conclusions: In the present study we found the methylation status of the selected CpG sites might have a great potential to serve as the diagnostic biomarkers for OSCC. These promising candidate CpG sites deserve for further study in the early diagnosis and screening of OSCC.

Biography

Yu-Fen Li has completed her Ph.D in 2004 at University of Southern California. She has published more than 25 papers in reputed journals.

Chien-Kuo Tai has completed his Ph.D from University of Southern California and postdoctoral studies from UCLA. He is an associate professor at National Chung Cheng University.

Proximity ligation for visualization of protein-protein interactions in cancer cell signaling and early cancer detection through novel blood based biomarkers

Simon Fredriksson
Olink Bioscience, Sweden

The *in situ* proximity ligation assay (*in situ* PLA) is a novel method for detecting protein-protein interactions in native fixed cells and tissue samples. The assay provides localized single molecule data visualized by fluorescence microscopy and quantified by objective counting. Target protein interaction pairs are bound by primary antibodies in a standard immuno-staining reaction, and when bound within a few tens of nanometres distance of each other, an amplified single molecule DNA based reporter is generated. The amplification product of the reporter is visible as a bright spot and remains locally attached to the site of the interaction also revealing sub cellular localization.

A large number of cell signalling study examples will be presented showing the utility of the technology and how it can provide novel insights in cancer pathway behaviour. The ability to study protein-protein interactions in situ using co-incidence binding by pairs of primary target specific antibodies opens a new realm of biomarker opportunities based on activity of proteins rather than abundance.

Another incarnation of the PLA technology takes advantage of the protein to DNA conversion for use in multiplexed quantification of putative biomarkers in plasma samples. Data from multiplexed PLA in a colorectal cancer biomarker study will be presented detecting 75 proteins in 2 micro litres of plasma with 5 log linear range with sensitivities down to low femto Molar. A pilot study of 140 samples will be presented.

Biography

Dr. Fredriksson is the Chief Scientific Officer at Olink Bioscience (Uppsala, Sweden) and has been a key figure in inventing and developing the proximity ligation assay for protein detection. After obtaining his PhD in molecular medicine in 2002 at Uppsala University he spent four years at Stanford University implementing PLA into a senstivite high throughput cancer biomarker research tool. He is a co-founder and board member of Olink, focused on the commercialization of the in situ and in solution PLA technologies.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Methylation biomarkers – From discovery to clinical use

Tomasz K Wojdacz

University and University Hospital of Aarhus, Denmark

Methylation is a process of "turning off" the genes, which is implicated in the pathology of cancer and in many other disorders. The methylation-based biomarkers are highly promising candidates for both early diagnosis and treatment of many diseases. There are four primary fields of use for the in-vitro diagnostic biomarkers:

1. Diagnosis

2. Prognosis/Prediction

3. Prevention

4. Pharmacoepigenomics

The methylation biomarkers have already been shown to fulfill the requirements of each of the above categories. Therefore vast majority of research in the field focuses currently on discovery and validation of methylation based biomarkers for clinical use. The initial steps of the identification/discovery procedure should normally employ two technologies: the technology allowing for genome wide screening for disease related methylation changes and the single PCR based methodology. The technologies allowing scanning for the genome wide methylation changes normally display high level of intra experimental data variation and therefore cannot be directly applied in diagnostic settings. Therefore the PCR based technologies has to be used to: firstly validate the genome wide screening findings and secondly to develop a test that can be applied in diagnostic settings. We have successfully combined state of the microarray technology: Roche/NimbleGene MicroArrays and the Methylation Sensitive High Resolution Melting (MS-HRM), for methylation biomarkers development and validation. The new workflow allowed us to discover and successfully perform clinical validation of 20 novel breast cancer methylation biomarkers. Overall, the technical specifications of our new workflow meet requirements for the complete platform for methylation biomarkers discovery, validation and diagnostic application.

Biography

Tomasz K Wojdacz holds an MSc degree in biotechnology and PhD in medical sciences. His research work focuses on epigemetics and development of methylation biomarkers for clinical applications. His work also involves leading entrepreneurship initiatives between scientists and commercial partners. Dr Wojdacz currently holds position at the University of Aarhus, Denmark. The Danish Chamber of Commerce has recently recognized Dr Wojdacz's work on providing a link between academic world and biomedical industry partners and awarded Tomasz with prestigious Reinholdt W Jorck and Hustrus price. Dr Wojdacz's has also been awarded with Lundbeck Foundation Talent award 2010.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Molecular and biochemical evaluation of anti-proliferative effect of (*Cichorium endivia,* L.) phenolic extracts

Ali S. Alshehri[1] and Hafez E.E[2]

[1]King Khalid University, Faculty of Science, Saudi Arabia
[2]Mubarak City for Scientific Research and Technology Applications, Egypt

Polyphenolic compounds are widely distributed in the vegetable kingdom and are therefore consumed regularly in the human diet. Medicinal plants are considered to be the most hopeful way for cancer treatment. The *Cichorium endivia,* L. plant materials were collected from different regions in Tanuma, Saudi Arabia. Methanol extraction was carried out and the HPLC analysis showed that, the extract containing four main compounds with different concentrations. The anticancer activity of the plant root extract was examined on three different cell lines (hypatocarcinoma cells, breast cancer cells and colon cancer cells). The extract degrees of activity was measured by determining cytotoxcity for the three cell lines compared with anticancer drug 5 FU (5-fluorouracil**).** The gene expression for the DNA cancer markers; P53, Bcl2, TNF and interleukin IL-4, IL-6 and IL-2 were examined using real time PCR. The expression of the P53 was high both in cells treated with FU and root extract but the expression in colon cancer was lower than liver cancer and breast cancer in successive manner. Expression of Bcl2 was high in cell lines treated with root extract compared with the FU, yet this expression still was low compared with the control ones. The TNF expression was high in the cells treated with the phenolic root extract but the expression of the TNF was high in HPG2 cells and decreased in both HTC116 and MCF7 respectively. The expression level of IL-2, IL-4 decreased in the examined cell lines treated with both root extract and with 5FU as well. In case of the IL-6 expression was high in cells treated with the root extract compared with the treated cells with 5FU and control cell lines. Thus, *Cichorium endivia*, which contains a combination of phenolic compounds, represents an enjoyable means of anticancer especially for Hypatocarcinoma.

Track 2(iii) 2(iv)

2(iii): Prognostic biomarkers

2(iv): Biomarkers based on Cancer Types

Session Chair
Dr. Jimmy Efird
Brody School of Medicine, USA

Session Co-Chair
Dr. Shyamal Dilip Desai
LSU Health Sciences Center, USA

Session Introduction

Title: **Season-of-Birth as a prognostic factor of survival time follow a diagnosis of cancer**

Dr. Jimmy Efird, Brody School of Medicine, USA

Title: **Molecular screening for Lynch syndrome population based approach using immunohistochemistry and methylation analysis**

Dr. Lars Henrik Jensen, University of Southern Denmark, Denmark

Title: **Gold nanoparticles and nanotechnology for cancer biomarker discovery and research**

Dr. Qun Huo, University of Central Florida, USA

Title: **Combination of Notch1 and Notch2 as prognostic marker on Patients with colorectal cancer**

Dr. Dake Chu, The Fourth Military Medical University, China

Title: **Novel role for orphan receptor PXR in Cancer**

Sridhar Mani, Albert Einstein College of Medicine, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Season-of-Birth as a prognostic factor of survival time follow a diagnosis of cancer

Jimmy T. Efird
Brody School of Medicine, USA

Evidence of an association between survival time and date of birth would suggest an etiologic role for a seasonally variable environmental exposure occurring within a narrow perinatal time period. Risk factors that may exhibit seasonal epidemicity include diet, infectious agents, allergens, and antihistamine use. Typically data has been analyzed by simply categorizing births into months or seasons of the year and performing multiple pairwise comparisons. This paper present a statistically robust alternative, based upon a trigonometric Cox regression model, to analyze the cyclic nature of birth dates related to patient survival. Disease birth-date results are presented using a sinusoidal plot with peak date(s) of relative risk and a single P value that indicates whether an overall statistically significant seasonal association is present. Advantages of this derivative-free method include ease of use, increased power to detect statistically significant associations, and the ability to avoid arbitrary, subjective demarcation of seasons.

Biography

Dr. J. T. Efird completed his Doctorate in Epidemiology at Stanford University School of Medicine. He currently is an Associate Professor at Brody School of Medicine, East Carolina University (ECU) and has a joint appointment as Epidemiologist/Chief Statistician in the Center for Health Disparities Research. Prior to joining ECU, Dr. Efird was Director of the Biostatistics Facility at the John A. Burns School of Medicine (Honolulu, Hawaii) and an Associate Member of the Cancer Research Center of Hawaii. Dr. Efird's research interests include brain tumours, soft-tissue sarcomas, and HPV-related cancers.

Molecular screening for Lynch syndrome. population based approach using immunohistochemistry and methylation analysis

Lars Henrik Jensen

Department of Oncology, Vejle Hospital and University of Southern Denmark, Denmark

Microsatellite instability (MSI) in colorectal cancer is one of the few prognostic markers and markers of cancer biology that have made it from bench to bedside. MSI tumors have a better prognosis and may respond differently to chemotherapy, but here we will focus on MSI and screening for the hereditary cancer syndrome, Lynch syndrome, which affects 2-5 % of all colorectal cancer patients.

MSI is variable length mutations in tumor DNA caused by deficiency of DNA mismatch repair. Dysfunction of this repair system is caused by inactivation of any of the repair enzymes MLH1, MSH2, MSH6, or PMS2. It can be measured either on the DNA level as MSI or on the protein level with loss of expression of the affected protein. Lynch syndrome is caused by hereditary mutations in any of the four mismatch repair genes. About 15 % of all colorectal cancers have MSI, but not more than one in three of these are caused by germline mutations. The rest is caused by a sporadic phenomenon, promoter hypermethylation of MLH1.

Based on an exploratory study and a validation study, we have established a strategy for molecular screening for Lynch Syndrome with initial immunohistochemistry and in the case of MLH1 deficiency also promoter methylation analysis. The strategy is now implemented in our region and will be followed prospectively.

Several obstacles and challenges have to be met to bring knowledge from the laboratory to the patients. Molecular screening for Lynch syndrome may serve as a template for how to do this successfully.

Biography

Lars Henrik Jensen is a medical doctor from University of Aarhus. He completed his Ph.D in 2007 from University of Southern Denmark and has been an exchange visitor at University of Southern California. His primary areas of research are gastrointestinal cancers, clinical trials, and molecular markers.

Gold Nanoparticles and Nanotechnology for Cancer Biomarker Discovery and Research

Qun Huo

Nano Science Technology Center, University of Central Florida, USA

Nanotechnology is bringing ground-breaking tools and new capabilities to biomolecule research and medical diagnosis. Gold nanoparticles as one of the most extensively studied nanomaterials, have many interesting and unique optical properties. These properties make gold nanoparticles as excellent optical probes for biomolecular imaging and assay applications. Based on the light scattering property of gold nanoparticles, our group has recently developed a nanoparticle-enabled dynamic light scattering assay (NanoDLSay) technology for biomolecular detection and analysis. This technique detects proteins, DNAs and other biomolecular targets by monitoring the size change of the gold nanoparticles caused by target analyte binding. In the last few years, we have investigated heavily on the use of NanoDLSay technique for cancer biomarker research. From our study, we made several new findings: (1) a prostate cancer biomarker, prostatic acid phosphatase (PAP), is significantly more complexed or aggregated in prostate cancer tissue than in the normal and BPH (benign prostate hyperplasia) tissue; (2) the concentration of certain serum protein-complexed VEGF (vascular endothelial growth factor) in blood serum is decreased in prostate cancer compared to normal and benign prostate conditions; and (3) we discovered a new protein complex from the nucleus of a pancreatic cancer cell line, *Panc-1*. In this talk, we will explain the principle of NanoDLSay technology and its broad applications in cancer biomarker research.

Biography

Qun Huo received her Ph.D. from University of Miami in Chemistry in 1999. After completing a two-year postdoctoral work at University of Miami, she joined North Dakota State University as an assistant professor in 2001. In 2005, she became an associate professor in the NanoScience Technology Center at University of Central Florida. She has published more than 60 peer-reviewed papers and her research focus is gold nanoparticles and nanotechnology for biomedical applications. She received the prestigious National Science Foundation CAREER award, NIRT (Nanotechnology Interdisciplinary Research Team) award and she is currently a New Florida 2010 Boost Scholar award recipient.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Combination of Notch1 and Notch2 as Prognostic Marker on Patients with Colorectal Cancer

Dake Chu
The Fourth Military Medical University, China

Background: Aberrantly activated Notch signaling has been shown to play a key role in carcinogenesis and progression of various human malignancies. However, the prognostic roles of Notch1 and Notch1 are still uncertain. In this study, we investigated the expression of Notch1 and Notch2 in colorectal cancer to determine their prognostic value.

Methods: The protein expression of Notch1 and Notch2 was examined by immunohistochemistry in 1003 clinical colorectal cancer specimens. Statistical analysis was carried out to assess associations of Notch1 and Notch2 expression with survival of patients with colorectal cancer.

Results: Significantly negative correlation between Notch1 and Notch2 was found in colorectal cancer ($P<0.001$). Notch1 and Notch2 were proved to be inversely correlated with tumor differentiation, depth of invasion, lymph node metastases, distant metastasis, TNM stage and survival of patients, suggesting opposite function of the two receptors. Notch1 and Notch2 were proved to be adverse independent prognostic predictors ($P<0.001$). Moreover, a synergistic effect of positive Notch1 and negative Notch2 coexpression on predicting poor overall survival was proved.

Conclusion: Notch1 and Notch2 may be independent adverse prognostic predictors for patients with colorectal cancer. These results would contribute to identify more efficient prognostic predictors and therapeutic targets.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Novel Role for orphan receptor PXR in Cancer

Sridhar Mani
Albert Einstein College of Medicine, Bronx, NY

The nuclear receptor pregnane X receptor (PXR) is activated by a range of xenochemicals, including chemotherapeutic drugs, and has been suggested to play a role in the development of tumor cell resistance to anticancer drugs. PXR also has been implicated as a regulator of the growth and apoptosis of colon tumors. Here, we have used a xenograft model of colon cancer to define a molecular mechanism that might underlie PXR-driven colon tumor growth and malignancy. Activation of PXR was found to be sufficient to enhance the neoplastic characteristics, including cell growth, invasion, and metastasis, of both human colon tumor cell lines and primary human colon cancer tissue xenografted into immunodeficient mice. Furthermore, we were able to show that this PXR-mediated phenotype required fibroblast growth factor (FGF) 19 signaling. PXR bound to the FGF19 promoter in both human colon tumor cells and "normal" intestinal crypt cells. However, while both cell types proliferated in response to PXR ligands, the FGF19 promoter was activated by PXR only in cancer cells. Taken together, these data indicate that colon cancer growth in the presence of a specific PXR ligand results from tumor-specific induction of FGF19. These observations may lead to improved therapeutic regimens for colon carcinomas.

Biography

Sridhar Mani (Shri) is a Professor of Medicine and Genetics at the Albert Einstein College of Medicine, Bronx, NY. He was the Founding Director of the Phase I Experimental Therapeutics Program at the Montefiore/Einstein Cancer Center. He received his MD degree (1990) from the Mount Sinai School of Medicine, New York, NY followed by further postdoctoral training in Internal Medicine (Board Certified)(1990-1992) and Hematology/ Oncology (Board Certified, Onc 1992-1995) at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, CT. Subsequently, he was the program leader for gastrointestinal oncology at the University of Chicago, Chicago, IL. During his tenure as a medical student, he did summer workat Rockefeller and then as a postdoctoral fellow at Yale, he studied under Dr. Eric Fearon on the role of DCC in colon cancer. In 1998, he returned to NY (Albert Einstein College of Medicine) to develop a Phase I Program in Oncology and a laboratory effort on drug metabolism. He is the recipient of the Clinical Investigator Award from the Damon Runyon Foundation (New York) and presently is an NIH funded Investigator on the role of orphan nuclear receptors in metabolism. He is a permanent member of the Developmental Therapeutics Study Section of NCI and serves as an editorial board member for Cancer Research, Clinical Cancer Research and Molecular Cancer Therapeutics (AACR). He has more than 100 peer- reviewed papers in journals like Science, Cancer Research, Clinical Cancer Research, Molecular Pharmacology, Molecular Endocrinology, Molecular Cancer Therapeutics, and Journal of Clinical Oncology.

3: Advances in cancer detection and imaging

Session Chair
Dr. Wolfgang Hohenforst-Schmidt
Klinikum Coburg GmbH, Germany

Session Co-Chair
Dr. Vikas Kundra
University of Texas M.D. Anderson Cancer Center, USA

Session Introduction

Title: **Imaging of exogenous gene expression for personalizing therapy**

Dr. Vikas Kundra, University of Texas M.D. Anderson Cancer Center, USA

Title: **DynaCT as a new tool for onsite and realtime navigation in the lung**

Dr. Wolfgang Hohenforst-Schmidt, Klinikum Coburg GmbH, Germany

Title: **Individualized chemo-radiation therapy based on quantitative functional imaging**

Dr. Dag Rune Olsen, University of Bergen, Norway

Title: **Targeting EGFR for fluorescence optical imaging of cancer**

Dr. Haibio Gong, LI-COR Biosciences Inc., USA

Title: **Squamous cell cancer of the head and neck - preoperative TNM staging with functional computed tomography imaging**

Dr. Agnieszka Trojanowska, Medical University of Lublin, Poland

Title: **Digital imaging in mammography helping enhancing the detection & diagnosis of breast lesions**

Dr. Bhawna Dev, Sri Ramachandra University, India

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

DynaCT as a new tool for onsite and realtime navigation in the lung

Wolfgang Hohenforst-Schmidt
Coburg Klinic, Germany

DynaCT is a quite new mode of rotational fluoroscopy that provides CT like images with an angiographic system (Siemens AG Healthcare, Forchheim, Germany). This innovative imaging modality has found its way into a variety of interventional procedures. Image acquisition is achieved in approx. 8 seconds by a C-arm rotation of 220 degrees and an acquisition of 450 images. A volume set is reconstructed on workstation and is available for assessment in less than 1 minute in the interventional suite. This volume can than be further processed and overlayed on the fluoro image to guide procedures. Since the C-arm gantry is open DynaCT is well suited for hybrid interventions. Therefore established applications include cardiovascular therapy (electrophysiology, endovascular aortic repair and transcatheter aortic valve replacement), neurointerventions for cerebral aneurysms and interventional oncology.

Obtaining soft tissue information without administration of contrast medium is until now a less explored application field. We hereby describe how DynaCT could support the growing field of pneumology and its focus on diagnosing and treating early stage lung cancer. In that context our 2 DynaCT-suites themselves serve as a standard thoracical computertomography (TCT), a sophisticated fluoroscopy for all kinds of bronchological interventions and as an conjunct of 3-dimensional CT information projected into fluoroscopy images. Thereby real-time and onsite navigation without additional tools (like superdimension) are easily possible. This technique is regularly applied since autumn 2010 with very favourable results and could be part of a daily workflow for local ablation therapies in NSCLC like Intratumoral Chemotherapy or Radiofrequency Ablation.

Biography

Dr. Wolfgang Hohenforst-Schmidt works as a senior physician executive in the field of interventional pulmology including chest oncology, interventional cardiology and intensive care medicine since more than one decade. He is author of the national guideline commitee on Pulmonary Hypertension (Dtsch Med Wochenschr 2010; 135: S102-115). In interventional pulmology he published new methods like perthoracical endopulmonary ultrasound to guide peripheral cancer biopsies (49th Congress of the German Society of Pulmology (DGP) 2008, Lübeck, P79) and reported for the first time surprising survival rates in NSCLC-patients following an interventional program that used controlled submaximal physical exercise as adjunct treatment to standard therapy (Medical Tribune 2010; 31/32: S16). On the 16th World Congress of Bronchology in Budapest he presented surprising preliminary data on survival of patients treated with ITC in combination with intravenous chemotherapy (16th WCB 2010, Budapest, A-0190).

Individualized chemo-radiation therapy based on quantitative functional imaging

Dag Rune Olsen

University of Bergen Faculty of Science, Norway

Functional imaging provides non-invasive quantitative information about biological and physiological processes of relevance for the response to treatment, and may as such be critical for the development of individualized cancer therapy. PET-imaging - with appropriate tracers - enables visualization of the tumor energy metabolism, cellular proliferation, apoptosis, angiogenesis, hypoxia as well as receptor status, whereas tracer kinetics can be quantified from 4D PET imaging. Dynamic contrast enhanced (dce) MR imaging can be utilized in deriving voxel-wise information about e.g. blood perfusion of the tumor as well as information about the extra-cellular space. Tumor hypoxia has been shown to correlate to quantitative dce-MR images. Based in diffusion weighted MR imaging, the apparent diffusion of water molecules can be measured and information about cellular integrity of tumor tissue can be derived. MR spectroscopy provides quantitative information about various metabolites in the tumor tissue.

Vast amount of information about biological features that - directly or indirectly – are of importance for the response to therapy requires advanced mathematical tools in the search for complex mechanism and relationships. Artificial neural networks (ANN) is one example of such strategies that can be utilize in computer assisted clinical decision -making. ANN analysis of various quantitative MR parameters have e.g. shown to be able to predict response to chemo-irradiation in pre-clinical tumor models.

Quantitative functional imaging provides information about tumor biological features in addition to that of genomics and proteomics, and should be integrated into a cancer systems biological approach towards individualized cancer therapy.

Biography

Dag Rune Olsen holds a Ph.D in biomedical physics, University of Oslo. He has been department head/head of research at the Institute of Cancer Research, The Norwegian Radium Hospital, Oslo, and professor of biomedical physics, University of Oslo. Professor Olsen is now Dean of Science at the University of Bergen. He has published more than 100 papers in international peer-review journals. Olsen is member of editorial boards and international advisory boards of international scientific journals as well as member of the board of the European Society of Therapeutic Radiology and Oncology. He is the recipient of the 2008 Klaas Breur Award.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Targeting EGFR for fluorescence optical imaging of cancer

Haibiao Gong
LI-COR Biosciences, USA

Dysregulation of epidermal growth factor receptor (EGFR) is associated with many types of cancers. It is of great interest to noninvasively image the EGFR expression *in vivo*. Among different modalities, fluorescence optical imaging has the advantage of low cost, easiness of handling and simplicity for multiplexing. Fluorescence in the near-infrared (NIR) spectral region is especially desirable due to its reduced background and high penetration capability. Various EGFR-targeting molecules have been studied for molecular imaging. These include antibodies, antibody fragments, natural ligand EGF, nanobody and affibody. A couple of examples will be discussed, with the focus on IRDye® 800CW labeled EGF (EGF800) and EGFR-specific affibody (Eaff800).

Both EGF800 and Eaff800 were characterized for binding/uptake using EGFR-overexpressing cells. When used for *in vivo* tumor imaging, the signal intensities of EGF800 had a good correlation with tumor sizes. In an orthotopic prostate tumor model, the tumor growth was successfully tracked by EGF800. *In vivo* imaging study of Eaff800 was conducted in A431 xenograft tumors. The accumulation of EGF800 in the tumor could be identified 1 hr post-injection, and became most prominent after 1 d. The specificity of Eaff800 was confirmed by its high level of binding/uptake by A431 cells and low binding/uptake by HER2-overexpressing cells. In combination with an HER2-specific probe Haff682, Eaff800 could be used to distinguish between A431 (EGFR-overexpressing) and SKOV3 (HER2-overexpressing) tumors. Interestingly, the organ distribution pattern and clearance rate of Eaff800 were different from those of Haff682. While Haff682 accumulated predominantly in the kidney, more Eaff800 was found in the liver.

Biography

Haibiao (Herbert) Gong earned a Ph.D. degree in molecular biology at National University of Singapore. He did his postdoctoral research at University of Pittsburgh, School of Pharmacy, and joined LI-COR Biosciences as a research scientist in 2007. His research focus at LI-COR is near-infrared fluorescence imaging. He has published more than 30 papers in reputed journals.

Squamous cell cancer of the head and neck - preoperative TNM staging with functional computed tomography imaging

Agnieszka Trojanowska
University Medical School in Lublin, Poland

Squamous cell cancer (SCC) of the head and neck , like other malignancies, should be reported with regard to TNM classification and treated accordingly. Sole anatomic imaging has its drawbacks, as early lesion detection often remains challenging, and non-neoplastic processes, especially inflammation, can mimic malignancies.

Computed tomography perfusion (CTp) is a technique that allows quick qualitative and quantitative evaluation of tissue perfusion by generating maps of blood flow (BF), blood volume (BV), and mean transit time (MTT). Perfusion CT has been found to be useful for non-invasive diagnosis of many diseases like cerebral ischemia and infarction, tumoral neo-angiogenesis, differentiation between malignant and benign process and for tumour response to radio- and chemotherapeutic treatment. Recent studies point, that CTp parameters may provide reliable information on vascularization of lymph nodes and may reflect angiogenic activity, helping to understand the changes occurring when malignant process invades the lymph node.

CTp is becoming a powerful tool in oncology and head and neck surgery. Depicting differences in tissue perfusion between different structures, shows promise in distinguishing malignant infiltration.

Biography

Agnieszka Trojanowska has completed her Ph.D at the age of 26 years from Lublin Medical University and postdoctoral studies from the same university. She has been working as senior research fellow in Radiology Department in Lublin Medical University for last 10 years. She is a specialist in head and neck radiology, and at present the head of Polish Society of Head and Neck Radiology. She has published 38 papers in reputed journals and has been serving serving as a reviewer in 4 international journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Digital imaging in mammography helping enhancing the detection & diagnosis of breast lesions

Bhawna Dev

Department of Radiology & Imaging Sciences, Sri Ramachandra University , India

The medical imaging field has been considerably impacted in recent years by the emergence of digital imaging modalities, including **Computed Radiography** (CR) and **Digital Radiography** (DR).

The similarities between CR and DR technology are the resultant image is in the digital format, the image formats are compatible for storage in the digital Picture Archiving and Communication System (PACS) and the appearance of the digital images can be manipulated.

Digital imaging permits computer-aided detection which provides a supportive role to Radiologist during diagnosis. Computer aided detection also commonly known as **Computed Aided Diagnosis** (CAD), uses a computer program to detect features likely to be of clinical significance in images and highlights it. **Digital Breast Tomosynthesis** is a newly emerged digital mammography technique that produces a 3-dimensional image of the breast.

The high spatial resolution and wide acquisition angle results in the production of mammography images with unparalleled image quality which enables better analysis of the type and size of lesions as well as microcalcifications compared to conventional methods. **Contrast Digital Mammography (CDM)** It has been shown that the growth and metastatic potential of tumors can be directly linked to the extent of surrounding angiogenesis. This motivates the use of contrast medium uptake imaging methods to aid in the detection of cancer. The important advantages of digital imaging is an overall decrease of radiation dose to the patient, tolerance to over or under exposure, possibility to utilize post-processing techniques that can make the image diagnostically better.

Biography

Dr Bhawna completed her graduation from Guru Nanak Dev University , Amritsar and her post graduation – M.D. Radio diagnosis from Sri Ramachandra University, Chennai India in the year 2000. She is presently working as Professor of Radiology in Sri Ramchandra University Chennai, India.

She has special interest in Oncology and is expert in performing non-vascular image guided interventions like radio frequency ablation , vertebroplasty & image guided biopsies may it be vertebral, muscular ,mediastinal structures , visceral organs or breast .

She is the co- founder & resource person for Indian Academy Of CT guided interventions "IACTI". She has been conducting various CME programmes and hand on workshops for years together.

She has multiple international & national publications to her credit. She has won numerous awards and has been a constant winner for Case of The day awards in RSNA.

4: Cancer: Management & Prevention

4(i): Diet & Physical Exercise

4(iii): Environmental Factors

Session Chair
Dr. Anna Enblom
Karolinska Institute, Sweden

Session Co-Chair
Dr. Ann Fonfa
The Annie Appleseed Project, USA

Session Introduction

Title: **"PACThe": Programme of accompanying women after breast Cancer treatment completion in thermal resorts: Preliminary results on 125 patients at one-year follow-up**

Dr. Y J. Bignon, Centre Jean Perrin, France

Title: **Patient advocate perspectives on integrative oncology – Diet & physical exercise, managing unwanted effects, environmental factors**

Dr. Ann Fonfa, The Annie Appleseed Project, USA

Title: **Preventive medicine: Hope or Hype?**

Dr. Amr Amin, UAE University, U.A.E

Title: **Cancer and palliative care in Africa: case of Cameroon**

Dr. Koanga Mogtomo M. L, University of Douala, Cameroon

Title: **Level of physical leisure and daily living activities in cancer patients undergoing radiotherapy**

Dr. Anna Enblom, Karolinska Institute, Sweden

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

"PACThe": Programme of Accompanying women after breast Cancer treatment completion in Thermal resorts: Preliminary results on 125 patients at one-year follow-up

Yves-Jean BIGNON

Centre Jean Perrin, FRANCE

Quality of life (QOL) is greatly impaired in women just after completion of the treatment for their breast cancer (BC). High body mass index (BMI) at BC diagnosis impaired the survival prognosis. Adjuvant chemotherapy is significantly associated with weight gain, which is linked to increased mortality of BC. First interventional nutrition trials demonstrate a positive effect on global mortality. Increasing physical activity seems to have even more benefits. Nevertheless no European trials were undertaken.

Objectives: improvement of the QOL, avoid weight gain, reduce overweight in high BMI women, increase physical activity for women in complete remission of BC just after completion of their treatment including chemotherapy

Programme: Randomization is made before the ninth month after completion of treatment: one arm with individual standard recommendations at home, one arm with 10-women-groups in an intensive multi-disciplinary 13 days-course of personalized education for protective nutrition and physical activity (full pension in one of three spas).

Intermediate results: 117 were randomized in the "spa" arm, 116 in the control group (CG). 125 women were followed-up at one year (51% overweight or obese).

- CG gained weight while spa group lost 4% of weight ($p<10^{-7}$).
- Physical activity level is stable in CG and significantly increased in spa group (p=0,005).
- QOL increased in both group, significantly in only spa group ($p=7< 10^{-7}$)
- Depression is significantly improved in the spa group ($p=7x\ 10^{-5}$)

Conclusion: efficiency of PACThe reinforced programme looks high compared to CG, on QOL, physical activity level, control of weight gain.

Biography

After MD. in oncology (1984) and PhD. in molecular biology (1991), Pr. YJ Bignon joined as geneticist the University of Auvergne at the Cancer Center Jean Perrin in France, after a post-doctoral position at UCSD (USA). YJ Bignon pioneered oncogenetics in France (1988), and developed research on hereditary predisposition to breast cancers and tertiary prevention (nutrient-genetics relationships).

YJ Bignon published 258 papers in peer-review journals (5,200 citations), H index at 31, made 300 conferences and 500 communications in scientific meetings, co-owners 5 patents. YJ Bignon is the scientific director of the Centre Jean Perrin since 2004.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Patient Advocate Perspectives on Integrative Oncology – Diet & Physical Exercise, Managing Unwanted Effects, Environmental Factors

Ann E. Fonfa

The Annie Appleseed Project, USA

From the perspective of a person with cancer, there is NO separation between management of the unwanted (usually called 'side') effects and diet and physical exercise. Why is that? Because both appropriate nutrition and physical movement have been shown to be effective tools in reducing many of the negative short and long-term outcomes of conventional cancer treatments.

As advocates we think more emphasis is needed about simple steps any person with cancer can take to get healthier to better deal with conventional treatments. Is everyone seeing a nutritionist or exercise counselor? Why not? These services should be available at all cancer centers, and be known to all oncology professionals treating people. Additionally since so many with cancer face the risk of recurrence, counseling on nutrition and physical exercise would be of value there as well. We find simple ways to encourage people to move in healthier directions, and we find them very interested. Research is also needed that looks at combining a variety of healthy behaviors including the use of 'green' cleaning and personal care products, detoxifying the body from the continual assault of pollutants in our atmosphere and the use of some dietary supplements – some of which have been well-defined in individual studies, ie fish oil, probiotics, vit D, etc. We've heard arguments about the difficulty but remain unimpressed by that. Our mission is providing information for people with cancer, and we do it on a large-scale via our website, online since June 1999, reaching millions of English-speaking people.

Biography

Ann E. Fonfa was diagnosed with breast cancer at the age of 44 (1993). She became interested in a variety of issues that she though badly handled. Happily more than half of the list has been addressed. Comorbidities made her unable to take chemotherapy and explored alternative medicine. She founded Annie Appleseed Project educating others about what she found. She's Florida Field Coordinator for National Breast Cancer Coalition, Advocacy co-chair, Florida Breast Cancer Foundation, Chair, Risk Reduction Working Group, SFLCCC, author of one published paper, coauthor of many. Reviews for Cochrane and other organizations. Serves on many varied panels.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Preventive medicine: Hope or Hype?

Amr Amin
UAE University, UAE

Cancer is the second leading cause of morbidity and mortality worldwide. Billions of dollars have been spent to study cancer and tremendous advancements in the understanding and treatment of cancer have been made. Nevertheless, as effective cures for a variety of cancers continue to elude us, natural protection against cancer has been receiving a great deal of attention lately not only from cancer researchers and patients, but also from physicians. There is compelling evidence from epidemiological and experimental studies that highlight the importance of compounds derived from plants "phytochemicals" to reduce the risk of colon cancer and inhibit the development and spread of tumors in experimental animals. More than 25% of drugs used during the last 20 years are directly derived from plants, while the other 25% are chemically altered natural products. Still, only 5-15% of the approximately 250,000 higher plants have ever been investigated for bioactive compounds. The advantage of using such compounds for cancer treatment is their relatively non-toxic nature and availability in an ingestive form. An ideal phytochemical is one that possesses anti-tumor properties with minimal toxicity and has a defined mechanism of action. This presentation will shed some light on numerous herbal remedies that have shown potential protective effects against cancer along with other illnesses that are currently represented in the area at alarming rate. Finally, "whether the drug discovery and pharmaceutical industry in Middle East have gone far enough" is a concern that remains to be carefully addressed.

Biography

Prof. Amin is a graduate faculty at UAE University who supervised many graduate theses. He earned his PhD from University of Illinois at Chicago and received a postdoctoral training at University of Pennsylvania School of Medicine. After joining UAEU Prof. Amin's focus was redirected to the field of preventive medicine. His lab is interested in natural product's protection against diabetes and cancer. He has published many articles, reviews and book chapters in reputable journals. He serves on the editorial boards and as a reviewer of many international journals. Prof. Amin is also the recipient of many national and international awards.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Cancer and palliative care in Africa: Case of Cameroon

Koanga Mogtomo ML and Ngono Ngane RA
University of Douala, Cameroon

Cancer-related pain has become a major problem worldwide. Pain can be caused by cancer, cancer treatment or by the side effects of treatment. At every stage of the cancer trajectory there is also emotional pain for both patients and the family. The dimension of these problems is worse in developing countries, especially countries in Africa, where there is a lot of ignorance about cancer, negative cultural beliefs about illness causes, poverty and lack of government policy on cancer control. Late presentation in hospitals with pain, no option of cure and poor supportive care is therefore very common. Denial, anxiety about the future, fear of loss of income and fear of dying contribute to late hospital visits. Cancer pain was a target symptom and cancer the disease when the strategy was developed. With appropriate education and availability of essential drugs, adequate pain relief can be achieved in more than 85% of cancer patients using simple techniques such as opioids, nonopioid analgesics and adjuvant medications. However, for many countries in Africa, availability of opioid analgesics is a major challenge for effective cancer pain treatment. The mean consumption of morphine for the African region was the lowest of all the WHO regions of the world, at0.7 mg/capita. South Africa ranked the highest at 3.4 mg/capita. Where the drugs are available, cost is a major constraint, as is lack of knowledge.

Culturally appropriate and affordable palliative care is also being promoted within Africa by the African Palliative Care Association in collaboration with several international donors. Palliative care emphasizes pain and symptom control, and psychosocial and spiritual support, thus ensuring the best quality of life for patients and support for families. In line with the WHO Community Health Approach to Palliative Care, Uganda has evolved a suitable model for Africa that emphasizes home care, which is mostly delivered by relatives who are supported by specially trained palliative nurse prescribers, an outpatient clinic and a day care hospice. Such models can be adopted to provide cost effective cancer pain relief in other African countries. . In fact by our experience on the field in Cameroon, This is a plaidoyer for the involvement of the government of Cameroon in collaboration with international agencies, to introduce in the national cancer policy the Uganda palliative care models. This suitable model could be developed through public-private partnerships, and standards improved and services upgraded to include advanced pain treatment options. The development of multidisciplinary pain clinics should also be encouraged so that local institutions would be able to include cancer pain management and research in the curriculum of their trainees.

Biography

KOANGA MOGTOMO MARTIN LUTHER has completed his Ph.D at the age of 31 years from University “LA SAPIENZA” ROMA ITALY and postdoctoral studies from University “LA SAPIENZA” ROMA ITALY. He is senior Lecturer at Department of Biochemistry, Faculty of Science, University of Douala Cameroon and head of Molecular virology and viral oncology Virology unit. He has published more than 15 papers in reputed journals and serving as an editorial board member of repute.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Level of physical, leisure, and daily living activities in cancer patients undergoing radiotherapy: which patients will need additional support to restore activity level after end of therapy?

Anna Enblom[1,2,3] and Kristin Campbell[3]

[1]Osher Centre for Integrative Medicine, Department of Clinical Neuroscience, Karolinska Institute, Sweden.
[2]RehabVäst, County Council of Östergötland, Sweden,
[3]Department of Physical Therapy, University of British Columbia, Canada

The aim of this longitudinal study was to describe level of physical, leisure and daily activities during and after radiotherapy, and to identify characteristics associated with not restored activity level one month after end compared to start of therapy. Patients (n=196) undergoing abdominal/pelvic radiotherapy at start, weekly during radiotherapy (median 5 weeks) and at a follow-up four weeks after the end graded their activity level using category-scales. The proportions of patients who decreased activity level between start and end of therapy, and the corresponding proportions who increased activity level between end of therapy and follow-up, were: physical exercising (34%, 36%), walking (26%, 25%), leisure activities (44%, 47%), social interaction (15%, 11%), housework (34%, 29%), shopping (28%, 21%) and activities in general (28%, 38%). Characteristics associated with not restored activity level at follow-up compared to at start (decrease in ≥one activity) were: colon-rectal compared to gynecological/testicular tumors (Relative Risk, RR, 1.5, p=0.049), age >65 compared to <65 years (RR 2.8, p=0.039), lower education compared to academic education (RR 1.5, p=0.038), ability to perform all daily activities at start compared to lower ability (RR 1.4, p=0.048), and experiences of anxiety (RR 1.6, p=0.016), depressed mood (RR 1.7, p=0.003), or low quality of life (QoL) (RR 1.9, p=0.003) at follow-up. The conclusions are that activity level decreased during radiotherapy. Activity level re-increased after the end in most patients, but increased more seldom in older, anxious, depressed patients experiencing low QoL, implying that these sub-groups may need additional support to restore their activity level.

Biography

Dr. Anna Enblom completed her Ph.D at Linkoping University, Sweden, with a thesis regarding acupuncture for emesis as a side-effect of radiotherapy. After postdoctoral studies at the Karolinska Institute, Sweden, she is currently visiting the University of British Columbia, Canada, as a post-doctoral researcher. Her research area is supportive care in cancer patients and survivors using non-pharmacological therapies, especially acupuncture and physical exercising.

4(ii): Chemoprevention

Session Chair
Dr. Stephen W.J. Wang
Millennium Pharmaceuticals Inc, USA

Session Co-Chair
Dr. Jaime A. Yáñez
Alcon Laboratories Inc., USA

Session Introduction

Title: **Mechanistic studies of the bioavailability barrier network (BBN) and its negative impact on the disposition and chemopreventative efficacy of dietary phytochemicals**

Dr. Stephen W.J. Wang, Millennium Pharmaceuticals Inc., USA

Title: **Bioreactive compounds for cancer chemoprevention**

Dr. Jaime A. Yáñez, Alcon Laboratories Inc., USA

Title: **Beyond the pyramid: Diet and alternative compounds for cancer prevention**

Dr. Jeffery G. Herman, University of California San Francisco, USA

Title: **What do you mean I can't take my vitamins anymore? A qualitative review of nutritional supplement use during cancer treatment**

Dr. Alina Barnett, University of California San Francisco, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Mechanistic Studies of the Bioavailability Barrier Network (BBN) and its Negative Impact on the Disposition and Chemopreventative Efficacy of Dietary Phytochemicals

Stephen W.J. Wang

Drug Metabolism and Pharmacokinetics, Millennium Pharmaceuticals Inc, USA

Polyhydroxlyated phytochemicals such as flavonoids, isoflavonoids and resveratrol have received major attention for their abilities to decrease the risk of coronary heart disease, ischemic stroke and most importantly prevent various forms of cancer including but not limited to colorectal and lung. However, a major conundrum observed in the clinic is that these chemopreventative phytochemicals all have extremely poor bioavailability.

To investigate the mechanisms in which our body can limit the amount of phytochemicals in the systemic circulation, we investigated the disposition of phytochemicals in four aspects of 1) absorption 2) distribution 3) metabolism and 4) excretion/elimination. Utilization of in vitro (e.g., ATPase assays, Cell lines, Vesicular transport assays), in situ (simultaneous 4-intestinal site perfusion models) and in vivo (e.g., knockout animals) methods as well as modeling & simulation (i.e., PBPK), we have discovered a barrier network which explains this observed phenomenon. Overall, this barrier network is not only governed by the following: 1) metabolism of these phytochemicals (typically phase II) 2) elimination of metabolites utilizing active transporting proteins (ABC efflux transporters) but is also dependent on the interaction between these two steps. This mechanism of coupling is extremely important as it governs the dispositional process of phytochemicals.

However, additional complexities are introduced as we attempt to disrupt this coupling process and observe an unexpected compensation via other proteins (both metabolic and transporters) within the same superfamily. Therefore, we propose here a bioavailability barrier network worthy of further characterization in order to better understand the disposition of phytochemicals.

Biography

Dr. Stephen Wang received his training in pharmaceutical sciences at the Texas Medical Center under Professor Ming Hu. Dr. Wang currently serves as a principal scientist in the department of Drug Metabolism and Pharmacokinetics at Millennium Pharmaceuticals in Cambridge MA. Previously, Dr. Wang served as a senior scientist in the department of Drug Metabolism and Pharmacokinetics at Merck. Dr. Wang's research interests focus on the disposition of xenobiotics in an effort to improve bioavailability of chemopreventive agents. Dr. Wang has made significant contributions in the field with a consistent publication track record of over 25 manuscripts in peer-reviewed scientific journals and various book chapters.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Bioactive Compounds for Cancer Prevention

Jaime A Yáñez

Drug Metabolism and Pharmacokinetics (DMPK), Alcon Laboratories, Inc., Fort Worth, USA

Consumption of bioactive compouds could be close to 1 g/day in our diet, making them the largest source of anti-oxidants. Dietary sources include fruits, vegetables, cereals, legumes, chocolate, and plant based beverages such as juices, tea, and wine. Extensive biomedical evidence suggests that bioactive compounds no matter their class may contribute to the prevention of cardiovascular disease, cancer, osteoporosis, diabetes, and neurodegenerative diseases. They have been also shown to exhibit beneficial effects on capillary permeability and fragility, to have anti-platelet, hypolipidemic, anti-hypertensive, anti-microbial, anti-viral, anti-allergenic, anti-ulcerogenic, cytotoxic, anti-neoplastic, anti-inflammatory, anti-atherogenic, and anti-hepatotoxic activities.These potential health benefiting properties may call for development of these compounds into future therapeutic agents. The content of bioactive compounds is also potentially influenced by food processing and storage conditions, which can result in transformation of flavonoids, and loss of flavonoid content. This presentation will briefly cover some relevant current statistics about cancer, dietary recommendations and the different family of bioactive compounds that have exhibited chemopreventive properties in selected foods coverings pre-clinical and clinical studies that have been performed to identify their potential chemopreventive effects after dietary consumption.

Biography

Dr. Yáñez received his Ph.D. in Pharmacology and Toxicology from Washington State University on 2008. His graduate research centered on stereospecific bioanalytical, pharmacokinetics and pharmacodynamics of chiral flavonoids. After graduating he joined Schering-Plough (later Merck) where he worked in the DMPK Biodisposition group working mainly with HCV drugs PK studies and in-silico modeling in order to bring GastroPlus into the Biodisposition group. He currently works for Alcon where he works with various glaucoma and intraocular pressure (IOP)-lowering agents and closely works with regulatory submissions in the DMPK department. He continues his research interests on PK/PD, bioactive compounds and health effect of various traditional plants. For this, he collaborates with various universities in Peru and Spain where he serves as research consultant, reviewer for grant submissions, and provides seminars in various subjects. Dr. Yáñez is member of various scientific and honor societies in the US, Europe and Latin America. He has about 50 peer-reviewed reviews, articles, and books chapters.

Beyond the Pyramid: Diet and Alternative Compounds for Cancer Prevention

Jeffery G. Herman
University of California San Francisco, USA

Personal dietary choices have long-term health consequences, with important roles in disease development and incidence including heart disease, diabetes, and cancer. It is estimated that 30-40% of all cancers can actually be prevented by adopting a well-balanced diet and other healthy lifestyle choices (e.g. reduced stress, increased exercise). The scope of dietary intervention research with regards to cancer prevention and treatment is large; ranging from dietary restriction such as specific amino acid restriction (tyrosine/phenylalanine) to dietary supplementation including curcumin and saw palmetto.

In the past, nutritional experiments have largely focused on the relative immediate effects of dietary intervention with regards to alterations of important signaling pathways. These experiments have often exhibited moderate and somewhat inconclusive effects in vitro, in vivo, and in the clinic; however, as new innovative research is beginning to illustrate, dietary intervention is not strictly about immediate and direct effects. Through the alteration of essential protein, genetic and epigenetic expression, the effect of diet and nutrition on cancer and disease incidence is subtle with long-term consequences which can span generations. By understanding these subtle dietary effects with regards to overall health, novel biomarkers for cancer incidence may be discovered and novel drug targets could be developed.

In order to achieve a truly successful use of diet in the prevention of cancer, we must move beyond laboratory and clinical research, and also begin to focus on dietary education, of patients, the general public and the medical community.

Biography

Dr. Jeffery Herman achieved his PhD in Pharmacology/Toxicology from the Washington State University under the mentorship of Dr. Gary G Meadows. Dr. Herman has worked at top research facilities including Oregon Health Science University and San Francisco Veteran Affairs Medical Center/University of California San Francisco. Dr. Herman's research interests largely lie in the role of dietary and nutritional intervention of cancer and other diseases. Dr. Herman has published papers in peer reviewed scientific journals, maintains a successful science and nutrition website and is an active science/medical writer.

What Do You Mean I Can't Take My Vitamins Anymore? A Qualitative Review of Nutritional Supplement Use During Cancer Treatment

Alina Barnett

UCSF Benioff Children's Hospital, CA 94143, USA

Complementary and alternative medicine (CAM) and over-the-counter (OTC) drug use among patients undergoing chemotherapy is increasingly prevalent with estimates reaching nearly fifty percent. Studies suggest that health care professionals rarely have complete medication lists on file for patients receiving chemotherapy. Concomitant OTC and CAM use during chemotherapy could potentially lead to severe drug interactions; a problem that is compounded when health care professionals are unaware of patient non-prescribed or alternative therapy use. The present study provides a literature review of both OTC and CAM use by patients undergoing chemotherapy as well as healthcare professional perception regarding patient OTC and CAM preferences. Non-disclosure of CAM and OTC use is postulated to occur for a variety of reasons: (1) a patient perception that healthcare professionals are displeased with alternate therapies, (2) misleading OTC packaging and (3) misunderstandings of the possible dangers that OTC and CAM products can cause regarding potentially severe interactions with chemotherapy. Understanding patient motivation to use CAM and OTC products during chemotherapy could improve open communication between patients and healthcare providers. Patient disclosure of OTC and CAM use to pertinent healthcare providers during clinic visits as well as more thorough documentation of all medications, would allow for an accurate medication list that may reduce potential drug interactions during chemotherapy.

Biography

Dr. Alina Barnett completed her Doctor of Pharmacy degree at Washington State University and is a Pediatric Clinical Pharmacist at UCSF Benioff Children's Hospital and an Assistant Clinical Professor at UCSF School of Pharmacy. Dr. Barnett's research interests lie in effective medication counseling in the adolescent oncology and transplant patient and innovative clinical pharmacy teaching techniques.

5(v): Cancer: Gene expression & Protein Profiling; Surgery & Laparoscopy

Session Chair
Dr. DaZhi Liu
University of California at Davis, CA USA

Session Co-Chair
Dr. Robert Grützmann
University hospital Carl Gustav Carus, Germany

Session Introduction

Title: **Novel Anti-microRNA strategies for Glioblastoma treatment without cognitive side effects**

Dr. Da Zhi Liu, University of California at Davis, USA

Title: **New tissue acquisition tools for translational research**

Dr. Jaak Ph. Janssens, European Cancer Prevention Organization, Belgium

Title: **Prediction of survival and response to adjuvant therapy in pancreatic cancer**

Dr. Robert Grützmann, University hospital Carl Gustav Carus, Germany

Title: **Current advances in rectal cancer surgery**

Dr. Manish Chand, Royal Marsden Hospital, UK

Title: **Laparoscopic total mesorectal excision: Experience with 74 patients**

Dr. Hosseini SV, Shiraz University of Medical Sciences, Iran

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Novel Anti-microRNA Strategies for Glioblastoma Treatment without Cognitive Side Effects

DaZhi Liu and Frank R Sharp
University of California at Davis, USA

Treatments for glioblastoma multiforme (GBM) and other brain tumors produce long-term cognitive dysfunction. Explanations for this decline often include a treatment that blocks proliferation of neural progenitor cells (NPCs) in the hippocampus and the peri-ventricular zones and/or damaging mature neurons (MNs) in the hippocampus, which plays a critical role in memory and learning. Therefore, we hypothesized that inhibitor(s) of glioblastoma cell (GBC)-specific molecules that are under-expressed in NPCs or MNs might block proliferation of GBCs (i.e. glioblastoma growth) without harming NPCs or MNs. Accordingly we performed microRNA (miRNA), mRNA and protein expression profiles in GBCs, NPCs and MNs. Our data demonstrated that many transcripts (miRNAs, and mRNAs) were differentially expressed in GBCs compared to both NPCs and MNs; the changes of protein expression were consistent with those of mRNA expression with a few exceptions. Decreased expression of selected GBC specific miRNAs (e.g., miR-298, miR-9, miR-330) was associated with increased expression of their putative oncogene mRNA targets (e.g., Anxa1, Skap2, Tgfb1, Pdgfrb, Ckdn2c) in cell proliferation pathways. In addition, over expression of GBC specific miRNAs (e.g., miR-10b, miR196b, miR-196c, miR-211) was associated with decreased expression of their putative neuronal differentiation mRNA targets (e.g., Il1rapl1, Nfasc, Unc5a, Slit1, Robo1, Nrp1) in axon guidance/ tumor suppressor pathways. Inhibition of miR-10b, which was highly expressed in GBCs compared to both NPCs and MNs, blocked the *in vitro* proliferation of GBCs without affecting NPC and MN survival. This provides a model for development of treatments that target GBCs that do not affect NPCs and MNs.

Biography

DaZhi Liu has completed his Ph.D from Shanghai Institute of Materia Medica. After the postdoctoral studies, he becomes a professional researcher in University of California at Davis. He has published more than 25 papers in reputed journals and serving as an editorial board member of the Journal of Cytology & Histology.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

New tissue acquisition tools for translational research

Jaak Ph. Janssens
European Cancer Prevention Organization, Belgium

Histological and molecular examinations are a prerequisite to understand diseases, determine optimal individualized care, and identify targets for potential novel therapies. Despite this key role of tissue based research the act of biopsy still remains troublesome. New direct and frontal biopsy technologies are emerging with the aim to alleviate the bottleneck of inappropriate minimal invasive interventions. Their recent availability provides a good occasion to look into the subject of tissue acquisition problem, i.e. not enough high quality tumor tissue in sufficient quantity. .The new instruments for minimal invasive procedures were evaluated to generate data on the usefulness to provide enough high quality tissue for omic research in comparison to diagnostic surgery for various soft tissues and bone lesions throughout the body. Recent single and multicenter studies provide evidence in more than 1000 patients that macrobiopsies, such as the Spirotome and Coramate, give tissue samples between 150 and 300 mg of highly specified parts of the diseased area in a way very similar to open surgery. In addition, biopsy procedures are increasingly more patient friendly with appropriate comfort and safety. The new macrobiopsies are less expensive, making molecular biology at reach for every oncological patient, company and health care provider. Direct and frontal macrobiopsies open new avenues for future bio-banking, pharmacogenomics, omic research and personalized medicine. It is anticipated that drug discovery and clinical implementation of targeted therapies will be highly facilitated and that clinical research time for multicenter trials will be significantly shortened.

Prediction of survival and response to adjuvant therapy in pancreatic cancer

Robert Grützmann

Department of Visceral, Thoracic, and Vascular Surgery, University Hospital Carl Gustav Carus, Germany

Despite all efforts, patients with pancreatic ductal adenocarcinoma (PDAC) have a poor prognosis. Currently, adjuvant therapy provides a modest increase in median survival time of two to six months. New approaches are needed to individualize therapy based on molecular prognostic signatures to further improve patient survival.

In a multicentre study, gene expression profiles were analyzed from freshly frozen samples from 30 patients who underwent surgical resection of PDAC, and a network based approach to identify genes prognostic for survival was devised. The prognostic genes were validated using quantitative RT-PCR and immunohistochemistry on an independent set of 412 formalin-fixed, paraffin-embedded PDAC samples. Signature classifiers were created using support vector machine-based learning, and their accuracy was assessed with Monte Carlo cross-validation.

Our approach identified seven candidate marker genes prognostic for overall survival. Based on immunohistochemical staining for these markers, we developed signatures to predict the survival of patients with and without adjuvant therapy. Both signatures were independently predictive of survival and superior to established clinical prognostic factors such as grade, tumor size, and nodal status. The first signature (six genes) identifies a high and a low risk group after resection followed by adjuvant therapy (hazard ratio [HR] = 2.0, p = 0.001). The second signature (five genes) identifies a high and a low risk group after resection without adjuvant therapy (HR = 1.53, p = 0.009). For both signatures, the difference in median survival between the identified risk groups was five months.

We present a genome-wide screen for gene expression markers for predicting survival after resection in pancreatic cancer patients. Accurate predictors of outcome and response to adjuvant therapy can be used to personalize and thereby improve therapy.

Biography

Prof. Grützmann has completed his medical studies at the Charite (Berlin, Germany). He than became a qualified general surgeon with subsequent qualification in pancreatic surgery. His scientific interest is the molecular basis of pancreatic cancer. He has published more the 60 papers and book chapters. He is leader of the pancreatic surgery at the University hospital Carl Gustav Carus Dresden, Germany and leader of the pancreatic cancer laboratory at the same University hospital.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Current advances in rectal cancer surgery

Manish Chand
Royal Marsden Hospital, UK

Surgical treatment of rectal cancer has evolved massively over the last 30 years. The foremost challenge for surgeons managing rectal cancer since Ernest Miles' description of surgical treatment more than 100 years ago has been to improve local recurrence rates. The increasing effectiveness of novel oncological therapies has been a great benefit to the long-term survival for patients. However, the standardized surgical technique of total meosrectal excision has probably been the single most effective factor in the significant reduction in local recurrence rates seen over the last 30 years. The current issues revolve around the safety and appropriateness of laparoscopic rectal cancer surgery. The benefits of laparoscopy in surgery in general are well documented, even with regards to colonic cancer. But rectal cancer provides a number of additional challenges. Specialist units report local recurrence rates in open surgery of around 6-8% and this must be the minimum standard for laparoscopic surgery. Yet, the goal of laparoscopic surgery must not be to achieve parity with open surgery, but to improve on the important oncological parts of the operation and move beyond the dexterity of the open surgeon. The arguments for and against laparoscopic rectal cancer surgery are presented.

Biography

Manish Chand is a Surgeon and Senior Research Fellow at the prestigious Royal Marsden Hospital in the UK currently working on his PhD having published more than 30 peer-reviewed articles. He is in the final years of specialist colorectal training having worked in units such as Basingstoke and Kings College, London. He has a particular interest in laparoscopic surgery and rectal cancer. As part of his interests he runs several laparoscopic training courses in the UK. Outside medicine he is a keen sportsman and holds an MBA degree.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Laparoscopic total mesorectal excision; experience with 74 patients

Hosseini SV, Bananzadeh A, Ghahramani L and Bahrami F
Shiraz University of Medical Sciences, Iran

Introduction: Total mesorectal excision (TME) is the cornerstone of surgical treatment for extraperitoneal rectal cancer. The aim of the present study is to present our experience in 74cases with laparoscopic TME

Methods: A retrospective review of 74 cases of laparoscopic TME was performed between 2007 and 2010.

Results: 74 patients with low and middle rectal cancer were treated with laparoscopic TME. 69 patients (93%) with advanced rectal cancer were treated preoperatively with neoadjuvant radiochemotherapy. Distal pathologic margin of all cases was more than 1 cm. Conversion rate was about 4% (3 cases) . There were 17 post operative complications including post operative ileus (9 patients), urinary retension (5 patients) and wound infection (3 cases).

Conclusion: Our experience shows that laparoscopic TME is a safe and oncologically acceptable procedure. However, it remains a complex technique, requiring an adequate learning curve.

Track 5, 5(i(a)) 5(i(b))

5: Cancer Therapy

5(i(a)): Radiotherapy & Chemotherapy

5(i(b)): Radiotherapy & Chemotherapy

Session Chair
Dr. Sherif G. Nour
Emory University School of Medicine, USA

Session Co-Chair
Dr. Liang Xu
University of Kansas Cancer Center, USA

Session Introduction

Title: Magnetic resonance imaging guided thermal ablation for cancer
Dr. Sherif G. Nour, Emory University School of Medicine, USA

Title: Molecular cancer therapy via modulating autophagy
Dr. Liang Xu, University of Kansas Cancer Center, USA

Title: Pathobiology and prevention of bone Loss caused by cancer chemotherapy
Dr. Cory J Xian, University of South Australia, Australia

Title: What is the optimal treatment for metastatic colorectal cancer?
Dr. Esther Una Cidon, Clinical University Hospital, Spain

Title: Biomarkers in relation to response of preoperative radiotherapy in rectal cancer patients- A Swedish rectal cancer clinical trial of preoperative radiotherapy
Dr. Xiao-Feng, Sun University of Linköping, Sweden

Title: The effect of preoperative chemoradiotherapy on lymph nodes harvested in laparoscopic TME for rectal cancer
Dr. Stefano Scabini, Salita Della Adonnetta, Italy

Title: Intensity modulated radiotherapy in chemoreduced retinoblastoma
Dr. Aman Sharma, All India Institute of Medical Sciences, India

Title: Retrospective analysis of total skin electron beam radiation therapy in cutaneous t-cell lymphoma- a developing nation experience
Dr. Manoj Kumar B, All India Institute of Medical Sciences, India

Title: Acute or subacute cor pulmonale: When should we look for malignancies?

Dr. Raniero Di Giovambattista, Hospital of Avezzano, Italy

Title: Different expression of ERK1/2 and pERK proteins in MDA-231 and MCF7 cells after chemotherapy with doxorubicin or docetaxel

Dr. Aliakbar Taherian, Kashan University of Medical Science, Iran

Title: Treatment with AS101 sensitizes acute myeloid leukemia cells (AML) to chemotherapy by disrupting the interaction between the integrin VLA-4 and Fibronectin: Mechanisms of action and clinical applications

Dr. Benjamin Sredni, Bar-Ilan University, Israel

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Magnetic Resonance Imaging Guided Thermal Ablation for Cancer

Sherif G. Nour

Emory University Hospitals and School of Medicine, USA

Although thermal treatment of localized malignancies has been practiced under direct surgical and laparoscopic visualization, much of the excitement over expanding the therapeutic uses of radiofrequency and other forms of thermal energy has been provoked by the advancements in imaging technology. The ability to perform thermal treatment of cancer percutaneously under image guidance has changed thermal ablation from an adjuvant surgical technique to a minimally invasive alternative that is more suited to poor surgical candidates. Unlike radiation therapy, thermal ablation can be repeated multiple times without concern for cumulative dose effects.

The primary contribution of image guidance to needle-based thermal treatment is securing safe, precise electrode delivery into the targeted pathology. The ideal electrode trajectory during actual procedure execution is sometimes significantly different from that suggested on the pre-procedure imaging data owing to shift of anatomical structures when using modified patient positions during treatment. Once the electrode is successfully delivered into the targeted tumor, image guidance adds to treatment efficacy by optimizing electrode position within the pathological tissue and by enabling confident inclusion of an adequate 'safety margin' to the ablated volume.

Compared to ultrasound and CT, the major contribution of MR imaging is its ability to monitor the zone of tissue destruction during the procedure therefore providing real-time guidance for energy deposition and permitting accurate tumor destruction. Other than its ability to define the treatment endpoint, MRI guidance is also advantageous in certain situations such as when a tumor is not adequately visualized on ultrasound or CT or when the complex anatomical location of a tumor renders multiplanar image guidance a safer approach, such as in liver dome lesions.

Biography

Dr. Nour is one of the world's leaders in the field of interventional MRI. For more than a decade, he dedicated his pre-clinical and clinical research to optimizing MRI guided interventions and to developing new minimally invasive tretmant approaches under MRI guidance. He is currently the Director of interventional MRI program at Emory University. He has 25 peer-reviewd original manuscripts published in leading medical journals. He also has 60 peer-reviewed proceedings manuscripts and research abstracts, 8 textbook chapters, and 7 filed patent applications in the field of interventional MRI.

Molecular cancer therapy via modulating autophagy

Liang Xu

Departments of Urology and Radiation Oncology, University of Kansas Cancer Center, USA

Radioresistance markedly impair the efficacy of cancer therapy. Anti-apoptotic Bcl-2 family proteins such as Bcl-xL, Bcl-2 and Mcl-1 are overexpressed in prostate cancer and contribute to prostate tumor initiation, progression and resistance to radiotherapy. A natural BH3-mimetic, small molecule inhibitor of Bcl-2, (-)-gossypol, shows promise in ongoing Phase II clinical trials for human prostate cancer. We have recently shown that (-)-gossypol preferentially induces autophagy in androgen-independent (AI) prostate cancer cells that have high levels of Bcl-2 and are resistant to apoptosis, both in vitro and in vivo, but not in androgen-dependent cells with low Bcl-2 and sensitive to apoptosis. Our results demonstrate for the first time that (-)-gossypol can also interrupt the interactions between Beclin1 and Bcl-2/Bcl-xL at the endoplasmic reticulum, thus releasing the BH3-only pro-autophagic protein Beclin1, which in turn triggers the autophagic cascade. (-)-Gossypol-induced autophagy is Beclin1- and Atg5-dependent, together with Bcl-2 downregulation and Beclin1 upregulation. (-)-Gossypol increased autophagy induced by X-ray radiation in the AI prostate cancer cells. Orally administered (-)-gossypol achieved a much greater efficacy with long-term tumor regression when used in combination with ionizing radiation. (-)-Gossypol significantly enhances the anti-tumor activity of radiotherapy in vitro and in vivo, and represents a promising new regime for treatment of hormone-refractory human prostate cancer with overexpression of Bcl-2. Our data provide new insights into the mode of cell death induced by Bcl-2 inhibitors, which would facilitate the rational design of clinical trials by selecting patients who are most likely to benefit from the Bcl-2-targeted molecular therapy.

Biography

Dr. Liang Xu obtained his M.D. and Ph.D in China and did postdoctoral studies in Louvain University in Belgium, Stanford University and Georgetown University in USA. He has been an Assistant Professor at University of Michigan and now an Associate Professor with Tenure at University of Kansas. He has published more than 75 papers and serving as an editorial board member of multiple journals. He holds many USA and international patents including two agents in Phase I and II clinical trials. His major research interest is molecular cancer therapy targeting cancer and cancer stem cells.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Pathobiology and prevention of bone Loss caused by cancer chemotherapy

Cory J Xian
University of South Australia, Australia

Cancer chemotherapy often induces bone loss or osteoporosis in cancer patients and survivors; yet the underlying mechanisms remain unclear and currently no specific adjuvant treatments are available to reduce these side effects. This study characterized damaging effects and action mechanisms of commonly used anti-metabolites methotrexate (MTX) and 5-fluoruracil (5-FU) on bone formation and osteoporosis in rats, and investigating effects of supplementary treatments with clinically used antidote folinic acid and some nutraceuticals which are known to possess anti-inflammatory, anti-oxidant, and/or anti-resorptive properties. We found that MTX or 5-FU chemotherapy increases expression of proinflammatory cytokines (TNF-α, IL-1β, IL-6, RANKL) and attenuates Wnt/β-catenin signaling in bone and bone marrow stromal cells. MTX or 5-FU chemotherapy causes osteoporosis by reducing bone formation, decreasing pool of bone marrow osteoprogenitor cells and differentiation of bone forming cells osteoblasts, enhancing adipocyte differentiation, increasing formation of bone-resorptive cells osteoclasts, resulting in bone loss and marrow adiposity. Supplementation with folinic acid attenuated MTX damaging effects on growth plate and production of primary bone. Oral doses of some nutraceuticals preserved osteoprogenitor cell content and bone formation, suppressed expression of osteoclastogenic factors in bone, osteoclast number on bone surface and bone resorption, and/or minimized accumulation of marrow fat. Sustaining/activating Wnt signaling by blocking its antagonist(s) also abrogated the bone defects. These observations suggest that cancer chemotherapy causes bone defects by damaging multiple compartments in the bone, and that some supplementary treatments may be beneficial in preserving bone integrity during chemotherapy.

Biography

Prof Xian obtained his PhD in 1993 from Murdoch University (Australia). He has been interested in fundamental and strategic research into tissue growth, injury repair and roles of growth factors/cytokines and progenitor cells. His earlier research positions include those at Child Health Research Institute (Australia), University of North Carolina at Chapel Hill (USA), Flinders University, University of Adelaide and Women's and Children's Hospital (Australia). Since 2001, he has been leading his research group (currently at University of South Australia) conducting bone growth and repair research. He serves as Associate Editors for 4 journals and editorial board members for 8 international scientific journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

What is the optimal treatment for metastatic colorectal cancer?

Esther Uña Cidón

Department of Oncology, Clinical University Hospital, SPAIN

Colorectal cancer is the second leading cause of death from cancer in the developed countries. Although great efforts have been made to early diagnosis a relevant number of cases will present metastases. The natural history of metastatic Colorectal Cancer (mCRC) has dramatically evolved in the recent years thanks to the introduction of modern chemotherapy.

Nowadays with the new drugs, such as oxaliplatin and irinotecan or modern drugs based on molecular targets (bevacizumab or cetuximab) the response rate has increased to 50% and the survival has been improved not only progression free survival, which has reached 12 months, but also overall survival which is longer than 2 years.

Despite this progress many questions remain to be answered, mainly those related to the sequential regimens, drug rotation, alternant or intermitent schedules, optimal duration of chemotherapy, the role of maintenance chemotherapy and the role of doublets or triplets.

The optimal duration of chemotherapy is very important because it has a direct influence on the patient quality of life, survival and costs.

There are several studies addressing this topic and the alternatives we have, such as “stop and go”, intermittent strategies or maintenance of only several agents and these studies reinforce the frequent behaviour of the oncologists to stop the treatment when the patient has obtained the maximum response. But there are some methodological problems in the analyzed trials which have determined that not all the professionals agree with this proposal.

With this context it is essential to perform well designed clinical trials incorporating new drugs and addressing these questions. This presentation tries to review all these controversial points.

Biography

Medical training in Medical Oncology at University Hospital of Oviedo where she collaborated in a Pharmacokinetic Laboratory combining traslational research (cancer drug sensitivity) in cancer. Doctorate courses and Advanced Studies Certificate in Research in Cancer with the best qualification (BQ). PhD with a project “Colon Cancer Follow-up Strategies and their Cost-effectiveness” with BQ. She works in Medical Oncology Department at Clinical University Hospital of Valladolid where she´s been carried out several clinical projects mainly in Digestive Tumors (Gastric and CRC) related to new prognostic/predicitive factors, tumour markers and its clinical utility, biomarkers...In this moment she is carrying out several clinical and pathological projects in CRC and Gastric Cancer. She has completed a Master in Palliative Medicine and other in Molecular Oncology. She´s awarded in two times with National Awards “Profesor Barea” to the best projects related to health management and cost in 2009 and in 2010.

She also works as an Oncology Associated Professor and she´s more than 70 communications to International/National Congress in Oncology and Health Care Quality and Management (HCQM), more than 40 articles published in relevant International and National Scientific Journals (SJ), including HCQM and she´s a reviewer of SJ such as: “European Journal of Surgical Oncology”, “Journal of Oncology Pharmacy Practice”, “Clinical Medicine: Oncology”, “World Journal of Gastroenterology”... She is member of the Editorial Board of “Global Journal of Surgery” and Editor in chief of a Review Book of Colorectal Cancer which is in development. She is member of Spanish Society of Medical Oncology, American Society of Clinical Oncology, European Association of Cancer Research, International Society of Gastrointestinal Oncology and Society for Translational Oncology among others. She has been invited several times to be a speaker in International Congress.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Biomarkers in relation to response of preoperative radiotherapy in rectal cancer patients- A Swedish rectal cancer clinical trial of preoperative radiotherapy

Xiao-Feng Sun

Institute of Clinical and Experimental Medicine, Linköping University, Sweden

The introduction of preoperative radiotherapy (RT) in the treatment of rectal cancer has reduced the frequency of local recurrence and improved patient survival, and RT is now a part of the standard treatment regime in Sweden. However, it is still a major problem that there are unknown factors contributing to variations in recurrence and survival after RT and surgery among rectal cancer patients with the same tumour stage, therefore it is important to search for biological markers that might influence recurrence and survival, and to identify the patients who benefit from RT.

The study included primary tumours from 163 rectal cancer patients who participated in a clinical trial of preoperative RT (87 patients without and 76 with RT before surgery), alone with the corresponding distant and adjuvant normal rectal mucosa, as well as lymph node metastasis.

We have examined p53, WRAP53, p73, survivin, apoptosis, Cox-2, legumain, FXYD-3, MAC30, PRL, ATM, Ki-67, CD163, PPARδ and PINCH, by PCR using confronting two-pair primers and electrophoresis, immunohistochemistry, Western blot and TUNEL.

Expression of WRAP53, p73, Cox-2, legumain, FXYD-3, MAC30, PRL, ATM, PPARδ increased from either distant or adjacent normal mucosa to primary tumour. In the RT group, overexpression of p53, WRAP53, p73, Cox-2, legumain, FXYD-3 and PRL was related to less tumour necrosis or apoptosis, increased incidence of local or distant metastasis, and an unfavourable prognosis independent of both the tumour stage and differentiation. However, none of these effects was seen in the non-RT group. In further interaction analyses, the correlations with prognostic significance of these factors were different between the patients with RT and the patients without RT.

In conclusion, certain biomarkers were independent prognostic factors in patients receiving preoperative RT for rectal cancer, which might provide additional information for selecting patients for preoperative RT.

Biography

Xiao-Feng Sun is professor at Department of Oncology, Institute of Clinical and Experimental Medicine, University of Linköping, Sweden.

Xiao-Feng Sun started medical education in 1977 and obtained MD in 1982 and Msc in 1988 in China. She moved to Sweden in 1989 and obtained PhD in 1993 at Linköping University, Sweden, and did her postdoctor training at Lund University, Sweden, and became professor at Onoclogy in 2005 at Linköping University, Sweden.

Her work focuses on study of genetic alterations in colorectal cancer patients and cell lines, in order to find biomarkers for identifying high-risk individuals, selecting patients who will benefit from chemo/radiotherapy, and evaluate patient prognosis, as well as the mechanisms of biomarker effects.

She has published 132 original full-length publications and three review papers in various international journals, such as Lancet, JNCI, J Clin Oncol, Clin Cancer Res, and Oncogene, and two book chapters.

Dr. Sun has received numerous international, national and local grants/award:

Dr. Sun serve as editorial board member in six international journals, and as reviewers for more than 30 international journals.

Dr. Sun is a member of numerous professional organizations, including Association of International Union Against Cancer Fellows (UICC), American Association for Cancer Research (AACR), European Association for Cancer Research (EACR), Gastrointestinal Society of Oncology, Swedish Society of Medicine, Swedish Society of Oncology, Swedish Cancer Society, and Swedish Proteomics Society.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The effect of preoperative chemoradiotherapy on lymph nodes harvested in laparoscopic TME for rectal cancer

Stefano Scabini, Edoardo Rimini, Andrea Massobrio, Emanuele Romairone, Renato Scordamaglia and Valter Ferrando

Department of Emato-Oncology, San Martino Hospital, Italy

Background: Adequate lymph node resection in rectal cancer is important for staging and local control.This study aims to verify the effect of neoadjuvant chemoradiation, as well as some clinicopathological features, on the yield of lymph nodes in rectal carcinoma.

Matierial and methods: Data on consecutive patients who had laparoscopic total mesorectal excision for rectal adenocarcinoma at a single cancer center between July 2005 and July 2010 were reviewed. No patient had any prior pelvic surgery or radiotherapy. Patients had neoadjuvant chemoradiotherapy if they were stage II or III.

Results: A total of 79 patients were included. The mean age was 67.1 years (range 36-84). Twenty-six patients (33%) received neoadjuvant therapy before resection. The mean number of lymph nodes removed was 14.4 (range 3-39) per specimen. There was less lymph node yield in patients who received neoadjuvant therapy (11.6 vs. 15.6, p 0.05). Only 46% of patients who had preoperative therapy had 12 lymph nodes or more in the specimen as opposed to 64% of those who had surgery upfront (p: 0.03). Other factors associated with lower lymph node yield included stage (p 0.03) and grade (p 0.007) of the tumour. Age, sex, site, type of operation, surgeons and pathologists did not affect the number of lymph nodes removed.

Conclusion: in laparoscopic surgery preoperative chemoradiotherapy for rectal cancer results in reduction in lymph node yield. Early cancer and low-gradind also associated with retrieval of fewer lymph nodes.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Intensity modulated radiotherapy in chemoreduced retinoblastoma

Aman Sharma

Dr. B. R. A. Institute Rotary Cancer Hospital (IRCH), All India Institute of Medical Sciences (AIIMS), India

Background: Intensity modulated radiotherapy (IMRT) has the potential of reducing dose to adjacent critical structures, achieves better target coverage, dose uniformity and sharp dose fall-off. Therefore, aim of our present study is to assess the feasibility of IMRT as a focal therapy for chemo-reduced group II retinoblastoma with regard to target coverage and sparing adjoining critical normal structures.

Material and methods: Six patients of chemo reduced group II retinoblastoma were undertaken for the study. Radiation therapy planning was done with all immobilized in supine position by a thermoplastic cast under general anesthesia. Planning CT was done with 3mm slice thickness and Gross Tumor Volume (GTV) was delineated in CT images as per the post chemotherapy clinical, radiological and opthalamoscopic examination under anesthesia findings. A margin of 2mm was given to generate Clinical Target Volume (CTV), a further expansion of 4mm was given for Planning Target Volume (PTV). The delineated organs at risk (OAR) include optic nerve, temporal lobe, hypo-thalamo pituitary axis (HPA), lacrimal gland, orbit, cornea and the retina. Nine field non-coplanar beam arrangement was used for IMRT planning in the Pinnacle TPS for Elekta synergy linear accelerator. The planning objectives were: prescribed dose of 45Gy/25f for PTV and HPA<37.5Gy temporal lobes<37.5Gy, lacrimal gland <34Gy, orbit<20Gy, lens<10Gy, cornea <23Gy and retina<40 Gy.

Results: IMRT achieved adequate coverage to the PTV. For all patients, 95% of the PTV was covered by 98% of the isodose line. The calculated Conformity Indices (TVRI/VRI) were 0.9391±0.96. Homogeneity Indices (I_{max}/RI) were 1.1475±0.55. Quality of coverage indices (I_{min}/RI) were 0.80±0.40. For ipsilateral OAR doses, the maximum dose to the brain stem was 5.155±1.45Gy and temporal lobe was 40.65±0.53Gy. Maximum dose to the optic chiasm was 8.94±2.51Gy. Optic nerve maximum dose was 45.81±1.74Gy and cornea max dose was 24.98±12.32Gy. Similarly, max dose for the lens and HPA were 15.51±4.50Gy and 8.505±2.86Gy, respectively. Maximum dose to the lacrimal was 34.41±10.32Gy and mean was 20.62±3.37Gy. Orbital mean doses were 16.04±4.34Gy. The maximum doses to the retina were 45.50±1.72Gy and mean doses were 30.75±1.67Gy.

Conclusions: Delivery of IMRT as a focal therapy in chemo-reduced group II retinoblastoma is feasible and provides adequate dose coverage to the target volume. The IMRT spares the adjoining critical normal structures with the given priority apart from the lens.

Biography

Dr Aman Sharma MBBS IGMC Shimla (1997-2003), Medical officer incharge Ex-HPHS(2003-2006), MD Radiation oncology (2006-2009) Regional Cancer Centre IGMC Shimla, Ex-Fellowship Neuroradio-oncology TATA Memorial Hospital Mumbai(sept2009-dec2010), presently work as Senior Resident in All India Institute of Medical Sciences New Delhi. He has conducted a prospective randomized phase III trial in locally advanced HNSCC, scientific paper presented at 13 chapter AROI, review article accepted in NNP, abstract accepted for poster ASCO, three abstracts submitted in ESTRO & head and neck conference.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Retrospective analysis of total skin electron beam radiation therapy in cutaneous t-cell lymphoma- A developing nation experience

Manoj Kumar B
All India Institute of Medical Sciences, India

Introduction: Total Skin Electron beam Therapy (TSET) is an effective therapeutic strategy in the management of advanced Cutaneous T-cell lymphoma. The presents study reports the retrospective analysis of patients treated with TSET at our center.

Material & Methods: A total of 12 patients of Cutaneous T-cell lymphoma were analyzed from January 2004 to March 2011. Patients were treated with Elekta Precise Linear accelerator with HDR mode of 3000cGy/min at isocenter. All the patients were treated as per the Stanford technique, delivering a total dose of 36Gy with a dose of 1.2Gy/f/day using 4MeV electron beam. Out of 6 fields planned, 3 fields per day were delivered alternatively. In all the sessions nails and eyes were shielded with 3mm lead shield. Boost dose of 10 Gy was delivered to the self-shielded regions.

Results: Out of 12 patients studied, nine had stage IIB disease. Seven patients achieved complete remission following TSET while 5 patients died of progressive disease during treatment. After completion of radiation, seven patients continued on PUVA therapy. The main complication observed were non hematological toxicities: four patients had grade III skin reaction and rest patients had grade II dermatitis. At median follow up time of 3.5 years, four patients were alive without any disease. Three patients died due to relapse in non cutaneous sites within 2 years.

Conclusion: Total Skin Electron Beam Therapy was well tolerated and found to be effective treatment of advanced Cutaneous T-cell lymphoma.

Biography

Dr. Manoj Kumar Behera has completed MD in Radiation Oncology from Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, one of the premiere institutes in Radiation oncology in India in 2009. Now he is in 2nd year of Senior Residency (SR) in All India Institute of Medical Sciences (AIIMS). He is specifically interested in SBRT/SRT, brachytherapy and Clinical oncology research as well as patients care.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Acute or subacute cor pulmonale: When should we look for malignancies?

Raniero Di Giovambattista
Hospital of Avezzano, Italy

Recently we observed a case of a 51-year-old women who died in our hospital for respiratory distress related to a widespread invasion of the pulmonary vessel by metastatic cells of a gastric cancer. Autopsy showed an indifferentiated carcinoma of the gastric fundus with diffuse permeation of the pulmonary vascular and lymphatic channels. Acute respiratory failure and severe pulmonary hypertension was the first clinical presentation of the malignancy. Echo 2D examination showed marked dilatation and D-shape right ventricular (RV) deformation. PAP max was 80 mmHg. D-Dimer 1230 mg/dl. Angio-CT scan of the chest permitted us to rule out our first clinical diagnosis of acute pulmonary thromboembolism (PE).

4 months ago a new, similar case came to our attention. A 62 year-old-man who suffered in the past of COPD, was admitted to our hospital after a brief clinical observation in another facilities, complaining of progressive, severe dyspnea and weakness. He dated the onset of progressive deterioration of his symptoms about 1 month earlier, in absence of fever, chest pain, palpitations or significant changes of the BP. Heart rate at entry was 110/min, BP 105/60 mmHg, D-Dimer value was 3650 mg/dl. Echo 2D showed dilatation and RV D-shape deformation. PAP max measured by echo was about 100 mmHg. Even in this case the chest CT-scan failed to demonstrate pulmonary thromboembolism. On the fifth day of the hospital stay he died of respiratory failure. Autopsy showed a signet ring carcinoma of the stomach with diffuse permeation of the pulmonary vascular and lymphatic channels.

In the last 12 months we observed 2 cases of subacute cor pulmonale as the first clinical presentations of massive, microscopic pulmonary tumor embolism (PTE) arising from gastric cancer. The clinical presentation as acute or subacute RV pressure overload and respiratory distress is a very rare but a fatal complication of cancer, and often a post-mortem diagnosis. When present, adenocarcinoma - more frequently arising from stomach, breast, lung, gallbladder, colon or prostate - is the most common histological tumor type. The tumor involvement of the pulmonary vessels develops from either lymphangitic and/or hematogenous spread. In both cases we observed, as well has been reported in literature, the first clinical diagnosis was pulmonary embolism. D-dimer values were very high. Echocardiographic examination showed signs of acute, severe right ventricular pressure overload and positivity of the Mc Connell sign. This instrumental findings together with the severity of respiratory distress and a shock index > 1 (defined as heart rate divided by systolic blood pressure) observed in both our cases , reinforced in our mind the first clinical suspect of massive P.E. Microscopic PTE and pulmonary thomboembolism are clinically almost indistinguishable, and PTE is often mistaken for thromboembolism. Oxygen desaturation is generally more severe in PTE's patients. D-Dimer values might be as high as they are actually seen in the course of PE. Chest angio CT-scan plays a pivotal role for ruling out the diagnosis of acute pulmonary thromboembolism. Large pulmonary arteries indeed are generally involved in the course of thromboembolic disease: filling defects in the large pulmonary vessels and/or pulmonary infarction are quite always demonstrated by CT-scan. By contrast, with the exception of choriocarcinoma or hepatoma which may provoke acute cor pulmonale by large vein invasion, the tumor emboli usually occlude small vessels and produce subacute cor pulmonale. The parenchyma can be normal or near to normal in these patients. The cases we described remind physicians to consider unknown malignancies as a direct (not thrombus-mediated) causes of acute or subacute cor pulmonale. Chest CT-scan is usually negative in this clinical scenario, so in this case we should look for malignancies. The 2 cases we observed represent in our view also a reminder for physicians and sonographers that echocardiographic examination is a very useful tool to demonstrate pulmonary hypertension and acute right ventricular pressure overload, but not always is able to put light on the etiology of pulmonary hypertension. Take home messages from our experience:

- Unknown adenocarcinoma may have its first clinical presentation as acute or (more frequently) subacute cor pulmonale. It is a very rare but a fatal complication of cancer, and often a post-mortem diagnosis.
- Microscopic PTE and pulmonary thomboembolism are clinically almost indistinguishable, and PTE is often mistaken for thromboembolism. AngioCT-scan is the tool of choice for ruling out the diagnosis of pulmonary thromboembolism as a cause of acute or subacute cor pulmonale
- Echocardiography is quite always useful to evaluate the severity of pulmonary hypertension (PH) and right ventricular overload. Is not the right tool to establish the etiology of PH.

If chest CT-scan fails to demonstrate either the presence of emboli in the large pulmonary vessels as well parenchymal abnormalities which well fit the severity of PH and respiratory failure, we should always look for malignancies.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Different expression of ERK1/2 and pERK proteins in MDA-231 and MCF7 cells after chemotherapy with doxorubicin or docetaxel

Aliakbar Taherian and Tahereh Mazoochi

Kashan Anatomical Research Center, Kashan University of Medical Science, Iran

Objective(s): Curative treatment of breast cancer patients using chemotherapy often fails as a result of intrinsic or acquired resistance of the tumor to the drug. In this study, cytotoxicity and the expression of Erk1/2 and phospho-Erk was compared in MDA-231 (ER-) and MCF7 (ER+) cell lines after treatment with doxorubicin (DOX) or docetaxel (DOCT).

Materials and Methods: Cell cytotoxicity of DOX or DOCT was calculated using MTT assay. Immonofluorescent technique was used to show Mdr-1 protein in MDA-231 and MCF7 cells after treatment with DOX or DOCT. The expression of ERK1/2 and phpspho-ERK was assayed with immunobloting.

Results: Comparing IC_{50} values showed that MDA-231 cells are more sensitive than MCF7 cells to DOX or DOCT. Immonofluorescent results confirmed the expression of Mdr-1 in these two cell lines after DOX or DOCT treatment. In MDA-231 cells the expression of ERK1/2 and pERK was decreased after DOX treatment in a dose-dependent manner. In contrast in MCF7 cells the expression of ERK1/2 and pERK was increased after DOX treatment. DOCT treatment resulted the same result with less significant differences than DOX.

Conclusion: The heterogeneity seen in cell lines actually reflects the heterogeneity of breast cancers that is why, patients categorized in one group respond differently to a similar treatment. These results emphasize the importance of a more accurate classification and a more specific treatment of breast cancer subtypes.

Keywords: Breast Cancer, pERK, MDA-231, MCF7, Doxorubicin, Docetaxel

Biography

Aliakbar Taherian completed his bachelor of science in Biology in Tarbiat Moallem University in Tehran. After a few years he was accepted in Medical School of Tehran University and received his Master of Science in Human Histology. After working in Kashan university of Medical Sciences for a few years teaching Human Histology to Medical students, he received a scholarship from the university to study his PhD. He was accepted in University of Saskatchewan to work with Dr. Patrick Krone and Nick Ovsenek in the Anatomy and Cell Biology Department. During his study he would publish two papers (1,2) and clone two genes (submitted to Genbank). After completing his PhD he worked as a postdoc in the same department with Dr Haas for a few years. In the postdoc period, He published one paper and has another submitted paper (3,4). Now he is working in Kashan University of Medical Sciences, teaching Human Histology to medical and paramedical students. Besides teaching he has a few research projects that occupies most of his time in university and home. The project that has been recently completed and submitted for publication (5) is about the different responses of breast cancer to chemotherapy.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Treatment with AS101 sensitizes acute myeloid leukemia cells (AML) to chemotherapy by disrupting the interaction between the integrin VLA-4 and Fibronectin: Mechanisms of action and clinical applications

Benjamin Sredni, Adi Bazar and Yona Kalechman

Faculty of Life Sciences, Bar-Ilan University, ISRAEL

Bone marrow minimal residual disease (MRD) causes relapse after chemotherapy in patients with acute myelogenous leukemia (AML) due to acquired drug resistance - this is induced by the attachment of the integrin receptor VLA-4 on leukemic cells to its ligand fibronectin (FN) on bone marrow stromal cells. We show that the non toxic compound AS101, previously shown to exert anti tumoral effects *in-vitro* and *in-vivo*, sensitizes AML cells to ARA-C only when leukemic cells are plated on FN but not on BSA-coated plates. This was associated with a significant decrease in pAkt and Bcl-2. The sensitizing effect of AS101 was also correlated with the ability of AS101 to deactivate VLA on AML cells. In a model of SCID mice implanted with leukemic cells either from established AML cell lines or with leukemic cells expressing high VLA-4, obtained from AML patients, co-treatment with AS101 and chemotherapy significantly increased mice survival while chemotherapy alone exerted only a modest effect. Furthermore, the combined treatment resulted in the elimination of leukemic cells from all organs tested. Moreover, mice transplanted with AML cells that express low VLA-4, considerably reacted to chemotherapy alone as expressed by increased survival, while co-treatment with AS101 resulted in similar effects. Importantly, AS101 increases migration of leukemic cells expressing high VLA-4 from the Bone-Marrow to the peripheral blood enabling their sensitization to chemotherapy.

We propose that treatment with AS101 currently used in treatment of cancer patients, combined with chemotherapy, has a potential to eradicate MRD and prolong survival of AML patients.

Biography

Prof. Benjamin Sredni, Head of The Cancer, AIDS and Immunology Research Institute at Bar-Ilan University in Israel - completed his Ph.D at Bar-Ilan and was a visiting scientist and associate many times at the Laboratories of Immunology, NIH, , US. Sredni served as Chief Scientist of the Ministry of Health in Israel and is Dean of the School of Graduate Studies at Bar-Ilan. He is a member of numerous reputed scientific organizations and was President of the Israel Association of Immunology. He has published over 175 papers in reputed journals and is guest editor in a special issue of Seminars of Cancer Biology.

5(iii): Hormone Replacement Therapy

5(iv): Molecular-Targeted Therapies

Session Chair
Dr. Paul J. Higgins
Albany Medical College, USA

Session Co-Chair
Dr. David Vesely
University of South Florida Medical School, USA

Session Introduction

Title: Expression of the p53 target SERPINE1 (PAI-1) gene is required for human tumor cell migration upon plastic conversion to a Stem Cell- like phenotype in response to TGF-ı1+EGF

Dr. Paul J. Higgins, Albany Medical College, USA

Title: Molecular targets of cardiac hormones in cancers

Dr. David Vesely, University of South Florida Medical School, USA

Title: Beta-glucans as anticancer agents

Dr. Anshu Agrawal, University of California, USA

Title: Mechanical blocking of cancer cell division by Progerin

Dr. Olga Moiseeva, University of Montreal, Canada

Title: The transcriptional landscape of nasopharyngeal carcinoma defined by RNA-seq

Dr. MU Sheng Zheng, Sun Yat-sen University Cancer Center, China

Title: Nanoformulated nanocarriers with modified lactoferrin for cancer and bio-distribution through MRI

Dr. Jagat R. Kanwar, Deakin University, Australia

Title: Alternative splicing of Kruppel-like factor 4 plays a role in colorectal tumorigenesis

Dr. Seung Joon Baek, University of Tennessee, USA

Title: **Inhibition of adenoid cystic carcinoma cell growth and metastasis by knockdown of ADAM 10 expression via RNA interference**

Dr. Qin Xu, Ninth people's Hospital, China

Title: **Peptide-targeted chemotherapy for breast cancer**

Dr. Chin-Tarng Lin, National Taiwan University Hospital, Taiwan

Title: **Targeting the BCR-ABL tyrosine kinase in chronic Myeloid Leukemia as a model of rational drug design in cancer**

Dr. Adriana Zamecnikova, Kuwait Cancer Control Center, Kuwait

Title: **Microtubule: A target for withaferin-a induced cell death**

Dr. Kamalini Ghosh, University of Calcutta, India

Title: **Molecular basis of anti-inflamatory strategies in cancer cachexia**

Dr. Marilia Seelaender, University of Sao Paulo, Brazil

Title: **Adenovirus Library for Novel Transductional Targeting**

Dr. Yamamoto Masato, University of Minnesota, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Expression of the p53 target SERPINE1 (PAI-1) gene is required for human tumor cell migration upon plastic conversion to a stem cell-like phenotype in response to TGF-β1+EGF

Paul J. Higgins
Albany Medical College, USA

The emergence of highly aggressive, cancer stem cell-like, subtypes of human squamous cell carcinoma (SCC) reflects increased transforming growth factor-β1 (TGF-β1) synthesis and epidermal growth factor receptor (EGFR) amplification. Cooperative TGF-β/EGFR signaling promotes cell migration and induces expression/activation of proteases (e.g., plasminogen, MMPs) and protease inhibitors that regulate stromal remodeling resulting in the acquisition of an invasive phenotype. Paradoxically, plasminogen activator inhibitor type-1 (SERPINE1,PAI-1), the major inhibitor of plasmin generation, is also upregulated under these conditions and is an early event in tumor progression. Increased PAI-1 expression temporally and spatially modulates plasmin-initiated pericellular proteolysis, preserving a stromal scaffold permissive that facilitates invasive potential. Combined TGF-β1+EGF treratment was used to investigate mechanisms underlying induced epithelial-to-mesenchymal transition (EMT) in *ras*-transformed human keratinocytes. Dual stimulation with TGF-β1+EGF resulted in keratinocyte "plasticity" and pronounced colony dispersal. Transcriptome analyses indicated that cells undergoing EMT expressed high β1 integrin levels and possessed stem cell-like characteristics. The most up-regulated transcript encoded PAI-1, an established marker of aggressive carcinoma cells and a functional promoter of cell migration suggesting that PAI-1 plays a critical role in epithelial stem cell biology. PAI-1 knockdown alone effectively inhibited TGF-β1+EGF-dependent cell scattering, indicating a functional role for this SERPIN in the dual-growth factor model of induced motility. Identification of signaling networks and their effect on specific invasion-promoting target genes, such as PAI-1, may lead to the development of pathway-specific therapeutics that impact late-stage events in human cutaneous epithelial tumor progression. Supported by grants from the NIH (GM57242) and the NYSDOH Empire State Stem Cell Trust Fund (C024312).

Biography

Dr. Paul J. Higgins received his Ph.D. in molecular biology from New York University. He was a post-doctoral fellow and Assistant Member at the Memorial Sloan-Kettering Cancer Center before assuming the Directorship of the Center for Cell Biology & Cancer Research at Albany Medical College. Dr. Higgins has published more than 250 papers, served on a number of NIH and international review panels and is an Editor of various biomedical journals. He was the recipient of the University of Florida College of Medicine Excellence Award in Molecular Medicine in 2008.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Molecular targets of cardiac hormones in cancers

David L. Vesely

James A. Haley Veterans Hospital/University of South Florida Health Sciences Cardiac Hormone Center, USA

One gene in the heart synthesizes four peptide hormones, i.e., long-acting natriuretic peptide, vessel dilator, kaliuretic peptide and atrial natriuretic peptide. These four peptides decrease up to 97% of human pancreatic, breast, colon, ovarian, kidney and prostate adenocarcinomas as well as glioblastomas of the brain, small-cell and squamous cell lung carcinoma cells in cell culture. When infused subcutaneously for 28 days with weekly fresh hormones at 3 nM min^{-1} kg^{-1} body weight in athymic mice, they eliminate up to 80% of the human pancreatic adenocarcinomas, 2/3rds of human breast adenocarcinomas, and up to 86% of human small-cell lung cancers with treated mice living a normal lifespan. These cancers never reoccur in the primary site in the lifespan of the mice. Their mechanisms(s) of action in cancer cells includes a 95% inhibition of Ras, 96% inhibition of ERK 1/2 kinases, and 98% inhibition of MEK 1/2 kinases. Mitogens such as epidermal growth factor which stimulate Ras and ERK 1/2 kinases have their effects completely blocked by these cardiac hormones. The cardiac hormones do inhibit ERK 1/2 kinases in healthy cells. In addition to inhibiting the Ras-MEK 1/2-ERK 1/2 kinase cascade, they enter the nucleus as shown by Immunocytochemical techniques where they inhibit DNA synthesis.

Biography

David L. Vesely, M.D., Ph.D., completed his M.D. and Ph.D. degrees simultaneously in 3 years at the University of Arizona Medical School and did his post-graduate training at the University of Miami Medical School. He is Chief of Endocrinology, Diabetes and Metabolism at the James A. Haley Medical Center and Professor of Medicine, Molecular Pharmacology and Physiology and Director of the Cardiac Hormone Center at the University of South Florida Medical School, Tampa, Florida, USA. He is the author of 315 peer-reviewed articles and 3 books. He received the 2007 Service to America Career Achievement Medal.

Beta-glucans as anticancer agents

Anshu Agrawal, Sudhanshu Agrawal and Sudhir Gupta

Department of Medicine, University of California-Irvine, USA

Pattern-recognition receptors (PRRs) detect molecular signatures of microbes and initiate immune responses to infection. Immune responses generated by prototypical PRRs such as Toll-like receptors (TLRs) have been widely investigated. In contrast, the immune responses initiated by other classes of putative PRRs remain ill defined. C-type lectins are a class of PRRs that recognize carbohydrate structures which are often part of microbial pathogens. Dectin-1 is a C-type lectin receptor present on dendritic cells that recognizes fungal β-glucans. Our investigations suggest that Dectin-1 is not just an antigen uptake receptor but also a modulator or initiator of adaptive immune responses. Human dendritic cells stimulated with Curdlan, Dectin-1 agonist prime CD4 Th17 responses via IL-23 production. Furthermore, these CD4 T cells induce differentiation of B cells to secrete IgG and IgA. More importantly; these dectin-1 stimulated dendritic cells promote the expansion and differentiation of granzyme B expressing cytotoxic T lymphocyte that display high cytolytic activity against target tumor cells *in vitro*. The capacity of Curdlan-stimulated human DCs to induce differentiation of these cells makes them attractive target for manipulations in clinic against cancer.

Biography

Anshu Agrawal completed Ph.D. from Central Drug Research Institute, Lucknow and subsequently worked as a Research Scientist in the division of immunology at ICGEB, India. She won a scholarship to work in France and after completing postdoctoral studies is now working as a faculty in the Department of Medicine, University of California, Irvine since last 6 years. She is the recipient of the New Scholar award in aging from the Ellison Medical Foundation. She has published more than 30 papers and serves as an editorial board member and reviewer for several journals. Her primary area of interest is dendritic cells, innate immunity and aging.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Mechanical blocking of cancer cell division by progerin

Olga Moiseeva
University of Montreal, Canada

The nuclear lamina is a fibrous structure underneath the inner nuclear membrane. One of the main components of lamina is the intermediate filament protein lamin A. Different lamin A mutations lead to development of a wide range of diseases, termed laminopathies. The most severe laminopathy is Hutchinson-Gilford progeria syndrome (progeria), which is characterized by premature aging, but not accompanied by an increase in cancer incidence. Progerin is a lamin A mutant with 50-aa deletion near the C-terminus. The inhibition of cancer cell proliferation by progerin is a consequence of accumulation of polymeric progerin formations in lamina that physically blocks mitosis.

Based on our results with progerin, we propose to use a mechanical approach in cancer therapy. Such an approach might work despite the mutations present in cancer cells, and therefore can be also effective at the late stages of cancer development. The disadvantage of the mechanical approach is that this approach could be toxic for normal dividing cells. To decrease the toxicity, targeted therapy can be used. Theoretically, this mechanical approach does not have to be limited to the nuclear lamina since different targets can be physically blocked inside and outside the cells. For example, a stable polymeric cage could be created around cancer cells to provide a physical barrier to proliferation that could act independently of any mutations. Any or several specific cancer receptors can be used, including those promoting proliferation. A wide range of polymeric nanoparticles is now available, magnetic nanoparticles can also be used.

Biography

Olga Moiseeva has completed her Ph.D from Pushchino State University and postdoctoral studies from University of Montreal.

The transcriptional landscape of nasopharyngeal carcinoma defined by RNA-seq

Mu-Sheng Zeng

State Key Laboratory in South China, Sun Yat-sen University Cancer Center, China

Next-generation sequencing technology is a powerful and cost-efficient tool for ultra-high-throughput transcriptome analysis. We applied paired-end RNA-seq to generate a deep unbiased transcriptome map of a EBV positive nasopharyngeal carcinoma (NPC) cell C666 and normal cell NPEC2. Using effective bioinformatics pipelines, we unambiguously detected many differentially expressed genes, novel transcripts, a variety of transcript isoforms and chimeric transcripts. Most importantly, we have identified a novel fusion gene which might play a oncogenic function in pathogenesis of NPC. Finally, we found that 78% EBV genes are transcribed, which indicate that the expression pattern of EBV in NPC is more complex than previously expected.

Biography

Dr. Zeng received his PhD degrees from Sun Yat-sen University of Medical Sciences and then worked as a postdoctoral fellow at the Department of Radiation Oncology in Tufts University-New England Medical Center in Boston. Currently, Dr. Zeng is a principal investigator in the State Key Laboratory in South China, China. He has published more than 30 papers in reputed journals.

Dr. Zeng's research on EBV variation led to the analysis of the whole genomic sequence from a Cantonese NPC derived EBV. The studies on cellular oncogenes led to identification of the potential role of the polycomb protein Bmi-1 in NPC as well as establishment of Bmi-1 immortalized nasopharyngeal epithelial cell lines. His current research focuses on the molecular events required for early transformation of nasopharyngeal epithelial cells as well as early diagnosis of NPC.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Nanoformulated nanocarriers with modified lactoferrin for cancer and bio-distribution through MRI

Jagat R. Kanwar, Rupinder Kanwar and Ganesh Mahidhara

Institute for Technology and Research Innovation (ITRI), Deakin University, Australia

Background: At nano scale, the fundamental and vital properties of matter can be changed, which can be used for daunting task such as oral administration of bio-macromolecules to be able to achieve sustained delivery, controlled release, target specific delivery and combinatorial therapy.

Objectives: Main objective of the study was to develop, characterize and see the bio-distribution of iron saturated lactoferrin protein loaded novel ceramic nanocarriers to deliver orally and monitor these tumours MRI imaging in xenograft colon cancer.

Methods and Results: In our study, we demonstrate the formulation of a novel alginate enclosed, chitosan coated ceramic anti cancer nano carriers (ACSC NC). These NC were loaded with multi-functional anti cancer bovine lactoferrin (bLf), a natural milk based protein, for improvement of intestinal absorption, in order to develop a novel platform to carry anti cancer protein and/or peptides for oral therapy. Size, morphology, internalization and release profiles of the ACSC NC under varying pH were determined. Furthermore, uptake of these NC *in vitro* in colon cancer cell lines was analyzed, by measuring the endocytosis and transcytosis. NCs were characterised through various physical and biological assays. Transcytosis studies indicate the transcytosis of the NC, with minimal damage to the Caco-2 cell monolayer. In conclusion, these NC can be used for future targeted protein/peptide or nucleic acid based drug delivery to treat fiddly diseases such as cancer and neurodegenerative disorders. Lf+ loaded ACSC NC significantly reduced tumour vascularity and blood flow, and increased anti-tumour cytotoxicity, tumour apoptosis and the infiltration of tumours by leukocytes. Lf+ increased the average weight of the spleens of tumourbearing mice by ~20%, accompanied by a major increase in the numbers of particular leukocyte subsets in the spleen. CD4+, CD8+, NK, IFN-γ+-expressing and dendritic cell numbers in the spleen were significantly ($P<0.001$) increased compared to corresponding cell numbers for mice maintained on the control diet. Lf+ bound to the intestinal epithelium and was preferentially taken up within Peyer's patches. It increased the production of Th1 and Th2 cytokines within the intestine and tumour, including TNF, IFN-γ, as well as nitric oxide that have been reported to sensitize tumours to doxorubicin chemotherapy. Importantly, it restored both red and white peripheral blood cell numbers depleted by doxorubicin chemotherapy, potentially fortifying the mice against cancer. In summary, bLf is a potent natural adjuvant and fortifying agent for augmenting cancer chemotherapy, but needs to be saturated with iron and administered orally in Lf+ loaded ACSC NC to be effective. Bio-distribution of iron saturated lactoferrin was determined my MRI and confirmed by other imaging techniques. We also compared our results with the doxorubicin and taxol loaded ACNC-NPs.

Conclusion: Taken together, our results are highly encouraging for the development of combination nano-therapeutic strategies that combine gene silencing and drug delivery to provide more potent and targeted therapeutic, especially in late and metastatic breast cancer.

Biography

Dr Kanwar is an immunologist and molecular biochemist with an international reputation in investigating fundamental and applied molecular aspects of cancer and chronic inflammation. He did his PhD from Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. Before joining Deakin University in 2006, he was a Senior Scientist/Senior Research Fellow in the University of Auckland, Auckland, New Zealand. During the past decade his research both academic and commercial has centered on understanding the pathophysiological mechanisms and/or finding treatments for a variety of chronic inflammatory diseases and different types of cancer. Dr Kanwar has published 55 research articles, 12 invited reviews and 5 book chapters, in highly ranked, international, peer-reviewed journals. These publications have added to the body of knowledge in the fields of immunology, cancer gene therapy, nanomedicine, cell biology and biotechnology, and have extended these disciplines. He is a key inventor on 9 international patents and has provided consultancy to 5 Biotechnology based companies. He is a member of editorial board for 7 international journals and a nominated member of more than 12 national and international societies including American Society of Nanomedicine. He has extensive and close collaborations with colleagues from New Zealand, Australia, Singapore, India, China and USA.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Alternative splicing of Kruppel-like factor 4 plays a role in colorectal tumorigenesis

Seung J. Baek and Jae Hoon Bahn

University of Tennessee College of Veterinary Medicine, USA

Most human genes undergo alternative splicing, and many abnormal splicing processes are associated with human diseases. However, the molecular relationship between alternative splicing and tumorigenesis is not well understood. Here, we found novel Krüppel-like factor 4 (KLF4) splicing variants produced by exon skipping in human cancer cell lines as well as colon tumor tissues. To elucidate mechanism of the KLF4 alternative splicing, we developed KLF4 minigene system and found that RNA binding motif protein 5 (RBM5) plays an important role in KLF4 splicing, as assessed by gain and loss of functional studies. Several anti-tumorigenic compounds were also tested for the KLF4 splicing. Interestingly, sulindac sulfide restored wild type KLF4 ($KLF4_L$) expression and this is mediated by dephosphorylation of RBM5. Another splicing variant, small KLF4 ($KLF4_S$), localizes in the cytoplasm and nucleus, and antagonizes transcriptional activity of wild type KLF4. Our data suggest that RBM5 plays a pivotal role in the alternative splicing of KLF4, and these splicing variant forms may impact tumorigenesis.

Biography

Dr. Seung Baek completed his Ph.D from University of Maryland School of Medicine and postdoctoral studies from NIEHS/NIH. He is the director of Lab of Environmental Carcinogenesis. He has published more than 85 papers in reputed journals and serving as an editorial board member of several journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Inhibition of adenoid cystic carcinoma cell growth and metastasis by knockdown of ADAM 10 expression via RNA interference

Zhiyuan Zhang, Qin Xu, Xiuming Liu and Wantao Chen

Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China

Background: Adenoid cystic carcinoma is one of the most common types of salivary gland cancers. The poor long-term prognosis for patients with adenoid cystic carcinoma is mainly due to local recurrence and distant metastasis. Disintegrin and metalloprotease 10 (ADAM 10) is a transmembrane protein associated with metastasis in a number of diverse of cancers. The aim of this study was to analyze the relationship between ADAM 10 and the invasive and metastatic potentials as well as the proliferation capability of adenoid cystic carcinoma cells *in vitro* and *in vivo*.

Methods: Immunohistochemistry and Western blot analysis were applied to detect ADAM 10 expression levels in metastatic cancer tissues, corresponding primary adenoid cystic carcinoma tissues, adenoid cystic carcinoma cell lines with high metastatic potential, and adenoid cystic carcinoma cell lines with low metastatic potential. RNA interference was used to knockdown ADAM 10 expression in adenoid cystic carcinoma cell lines with high metastatic potential. Furthermore, the invasive and metastatic potentials as well as the proliferation capability of the treated cells were observed *in vitro* and *in vivo*.

Results: It was observed that ADAM 10 was expressed at a significantly higher level in metastatic cancer tissues and in adenoid cystic carcinoma cell lines with high metastatic potential than in corresponding primary adenoid cystic carcinomas and adenoid cystic carcinoma cell lines with low metastatic potential. Additionally, silencing of ADAM 10 resulted in inhibition of cell growth and invasion *in vitro* as well as inhibition of cancer metastasis in an experimental murine model of lung metastases *in vivo*.

Conclusions: These studies suggested that ADAM 10 plays an important role in regulating proliferation and metastasis of adenoid cystic carcinoma cells. ADAM 10 is potentially an important therapeutic target for the prevention of tumor metastases in adenoid cystic carcinoma.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Peptide-Targeted Chemotherapy against Breast Cancer

Chin-Tarng Lin

National Taiwan University, College of Medicine, Taiwan

To obtain a better efficacy of chemotherapy we used one nasopharyngeal carcinoma (NPC) line to select a 12-mer specific peptide which can bind specifically to the surface of NPC cells from a phage-displayed random peptide library. This peptide has met several criteria for targeted drug delivery into the NPC solid tumor. In vitro the peptide can bind specifically to the cell surfaces of most NPC cell lines and biopsy specimens; the peptide-linked liposome containing fluorescent substance is capable of binding to and translocation across cell membranes; in vivo, this specific peptide can bind and accumulate in the NPC xenograft in SCID mice, but not in normal organs; similarly, the peptide-linked liposome carried doxorubicin (Dox) not only can cause marked cytotoxicity of NPC cells in vitro, it can also suppress markedly the xenograft growth in SCID mice without systemic side effect. In addition, FITC-labeled L-peptide could also bind to breast cancer cells by FACScan. In MDA-231 breast cancer xenografts, L-peptide-labeled Dox could inhibit not only the in situ xenograft but also the metastatic tumor nodules with minimal adverse effect. The L-peptide linked iron oxide (Fe3O4) nanoparticles could be localized in MDA-231 cultured cells and on the breast cancer surgical specimens. In conclusion, the novel peptide we identified can be used for targeted chemotherapy with high efficacy and without systemic side effect. Apparently, the peptide-targeted chemotherapy is superior then the conventional chemotherapy, and application of this peptide-targeted therapy against breast cancer may let this cancer becomes a controllable disease.

Biography

Dr. Chin-Tarng Lin was awarded his D.D.S. degree from National Taiwan University (NTU), Taipei, Taiwan in 1963 and obtained his Ph. D. degree in 1975 from the Graduate Institute of Texas Medical Branch at Galveston, Texas, U.S.A. He was a Professor in the Institute and Department of Pathology, NTU since 1987 and became an Emeritus Professor in 2009. He has established 10 nasopharyngeal carcinoma (NPC) cell lines, and developed the peptide-targeted chemotherapy method against cancers. He has published more than 87 papers in reputed journals. The published data strongly indicate that peptide-targeted chemotherapy has a great potential for cancer treatment.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Targeting the BCR-ABL Tyrosine Kinase in Chronic Myeloid Leukemia as a model of rational drug design in cancer

Zámečníkova Adriana

Kuwait Cancer Control Center, Department of Hematology, Kuwait

Many biological and clinical features of chronic myeloid leukemia make it as a paradigm of rational drug design in human cancer. Chronic myeloid leukemia was the first malignancy to be linked to a clear genetic anomaly, the Philadelphia chromosome and at present, it is probably the best understood of all human malignancies. Studies of the disease pathology revealed, that the molecular consequence of the Philadelphia translocation is a novel fusion gene, *BCR-ABL,* which encodes a constitutively active tyrosine kinase with wholesale range of biological activities. Animal models have validated the direct role of the BCR-ABL protein in malignant transformation and subsequent research confirmed that the enhanced tyrosine kinase activity of BCR-ABL is essential and sufficient for the leukemogenesis. The very existence of a single genetic abnormality, presented in essentially all patients made it a potential target for molecularly designed therapeutic approaches for the disease. The advent of tyrosine kinase inhibitors, designed specifically to inhibit the tyrosine kinase activity of the BCR-ABL protein represents one of the major innovations in cancer therapy and may serve as a pattern how discoveries of disease pathogenesis may be translated into the development of successful targeted therapies in cancer medicine.

Biography

Dr, Zámečníkova Adriana, PhD has a Masters degree from Clinical Genetics and has completed her Ph.D from Comenius University, Slovakia in 2001. Registered by Health Professions Council, UK, London, as a Clinical Scientist and by Health Practitioners Competence Assurance, New Zealand, as a Medical laboratory Scientist. From 1997 she was appointed as a Head of the Department of Cancer Genetics at National Cancer Institute, Slovakia and from 2001 she is working as a supervisor of Cancer Genetics Laboratory at Kuwait Cancer Control Center, Kuwait. She has published more than 40 papers in reputed journals and participated as a speaker in various meetings and conferences.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Microtubule: A target for withaferin-a induced cell death

Sumita Sengupta[1], Kamalini Ghosh[1], Amlan Das[2], Ansuman Lahiri[1] and Gopal Chakrabarti[2]

[1]Department of Biophysics, University of Calcutta, India
[2]Department of Biotechnology University of Calcutta, India

Background: Withaferin-A effectively induces cell cycle arrest and apoptosis by targeting multiple proteins in variety of carcinomas. WA limits migratory and invasive capabilities of cancer cells by interfering with actin cytoskeleton and intermediate filament protein vimentin, but, heretofore, no evidence has been reported whether it can binds to tubulin directly resulting in inhibiting microtubule assembly.

Methods: MTT assay was done to get the IC-50 value of WA for cancer cells, cell cycle arrest was determined by FACS, apoptosis was found by AnnexinV/ PI staining, immune-cytochemistry was performed to check microtubular network within cells, cellular migratory activity was monitored by wound healing assay. *In vitro* tubulin polymerization was studied by light scattering technique, kinetics of WA-tubulin interaction was monitored by fluorometric assays and probable WA-tubulin interaction site was proposed by molecular modeling method.

Results: WA inhibited proliferation of cancer cells, caused S and G2-M arrest as well as apoptosis, caused significant disruption of interphase and spindle microtubules, inhibited microtubule polymerization of purified tubulin *in vitro*. Direct binding of WA to tubulin altered fluorescence of tubulin tryptophan residues, ANS-tubulin complex. Competition assays showed no binding of WA to colchicine binding site of tubulin. Molecular docking simulations indicated preferential binding site of WA to tubulin which is different from colchicine or vinblastin binding sites.

Conclusion: These findings provide strong evidence that WA suppresses microtubule dynamics within cells by directly binding to tubulin, thereby perturbs cancer progression.

Molecular basis of anti-inflamatory strategies in cancer cachexia

Marilia Seelaender
University of Sao Paulo, Brazil

Cancer cachexia is a paraneoplasic syndrome affecting the large majority of terminally ill cancer patients and is clinically characterized by a number of symptoms which are not overcome by standard nutritional supplementation or by pharmacological therapy. L-Carnitine has been tested in preliminary studies in human cachexia, resulting in improved fatigue and quality of life. Our results show that in experimental cachexia the marked alterations of lipid metabolism are suppressed by L-carnitine supplementation, and associated with increased survival. The anti-inflammatory effects of L-carnitine supplementation seem to be similar to those elicited by chronic physical exercise in cachectic animals and patients. We have shown that the expression of lipid metabolism-related proteins is restored to normal levels in the liver and muscle after exercise training, re-establishing cellular function. These results are associated with decreased local and systemic inflammation, to which the white adipose tissue markedly contributes in cachexia. The molecular basis of the effects of L-carnitine supplementation and of exercise training upon cancer cachexia, with special focus on the relevance of white adipose tissue, will be examined.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Adenovirus Library for Novel Transductional Targeting

Yamamoto Masato
University of Minnesota, USA

Adenovirus (Ad) vector and oncolytic adenovirus has been engineered as therapeutics taking advantage of high in vivo transduction efficiency. However, targeting by selective infection (transductional targeting) and its incorporation to virus-coding sequence has been a nightmare in many vectors including Ad vectors. A lot of targeting peptide-coding sequences have been placed into capsid coding regions but extremely limited number of the targeting moiety successfully worked in Ad capsid, presumably due to structural limitation of the virus structure. Thus, it is natural to screen the peptide presented on adenovirus capsid format from the beginning. However, to date, the library size achievable in Ad system has been low. Conventional system makes few plaques from 1ug viral DNA. The most advanced system with Cre-loxP system yields 10^6 order diversity. Recently, we have developed a novel hyper-efficient Ad vector generation system by overcoming three major bottle necks for Ad vector production by performing the process in fiber complementing producer cell with newly designed shuttle plasmid and rescue virus. We applied this technology for Ad targeting ligand library generation and achieved 10^10 diversity. High throughput screening of the library identified novel targeting motifs which selectively bindto cell surface protein highly expressed in several major cancers including pancreatic cancer. The oncolytic virus with one of these targeting motifs showed selective and potent antitumor effect in vitro and in vivo in the receptor positive cells. In summary, we have developed a new way to identify the adenovirus transductional targeting ligand. Such vectors with preferential distribution and the system to generate them are expected to be beneficial for the development of systemically injectable cancer targeted vector system.

Biography

Dr. Yamamoto, Masato obtained his M.D & Ph.D from Osaka University School of Medicine, Osaka, Japan. He is board-certified gastroenterologist in Japan. He has been working for cancer gene therapy with adenovirus vectors. His lab has developed a series of replication competent adenovirus vectors and is considered to be one of the leading labs for replication competent adenovirus vectors. His group has been a leading lab for the application of oncolytic virus in the field of GI cancers including pancreatic and esophageal cancers. He has rich experience of experiments with clinical materials and evaluation of the oncolytic viruses. He was awarded *John R. Durant Award for Excellence in Cancer research 2001-Junior Faculty Category University of Alabama at Birmingham Comprehensive Cancer Center. The MCMRC Excellence Award at the 14th Intl. Conference on Gene Therapy of Cancer in 2005.*

6(i): Clinical Medicine

Session Chair
Dr. Eugene P. Goldberg
University of Florida, USA

Session Co-Chair
Dr. Sudhakar Akul Yakkanti
Boys Town National Research Hospital, USA

Session Introduction

Title: **Intratumoral chemotherapy (ITC) as adjunct to standard therapy in NSCLC iiia-iv prolongs life**

Dr. Wolfgang Hohenforst-Schmidt, Klinikum Coburg GmbH, Germany

Title: **Endobronchial Intratumoral Chemotherapy (EITC): A new modality for palliation and potential curative therapy of NSC lung cancer**

Dr. Eugene P. Goldberg, University of Florida, USA

Title: **Extra cellular matrix derived endogenous angioinhibitor tumstatin and its mechanism(s) of action**

Dr. Sudhakar Akulapalli, Boys Town National Research Hospital, USA

Title: **The association between Charlson Comorbidity Index(CCI) and the burden of cancer**

Dr. Eun-Jung Kim, Cheju Halla University, Republic of Korea

Title: **Therapeutics and toxicology of lLiposome based anticancer drugs**

Dr. Alberto Gabizon, Shaare Zedek Oncology Institute, Israel

Title: **High-risk human papillomavirus (HPV) screening and detection in normal, healthy patient saliva samples: a pilot cluster randomized study**

Dr. Karl Kingsley, University of Nevada, USA

Title: **Molecular basis of anti-inflamatory strategies in cancer cachexia**

Dr. Martins Thomas, University of Lagos College of Medicine, Nigeria

Title: Nose bleed gone wild: Extramedullary plasmacytoma of the right nasal septum

Dr. Erwin Jannino O. Ybanez, Davao Doctors Hospital, Philippines

Title: Evaluation of dendritic cells and RANTES in patients suffering from ovarian cancer

Dr. Jan Kotarski, Medical University of Lublin, Poland

Title: Sam-Pointed Domain Ets Transcription Factor-1 (SPDEF-1, a.k.a. PDEF-1) is a Tumor Metastasis Suppressor and its Mechanism(s) of Action

Dr. Hari K Koul, University of Colorado School of Medicine, Aurora

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Intratumoral chemotherapy (ITC) as adjunct to standard therapy in NSCLC iiia-iv prolongs life

Wolfgang Hohenforst-Schmidt

Coburg Klinic, Germany

The efficacy of conventional intravenous cancer chemotherapy is severely limited by systemic drug toxicity. Statistics for the past 20 years indicate little progress in reducing cancer mortality except for distinctive genetically defined subtypes. Reported here are studies showing the efficacy of *intratumoral chemotherapy* (ITC) as a debulking tool in central tumors applied worldwide in more than 370 published patients over the last decade. *ITC* has already shown in few observational studies that a surplus of median survival can be achieved if this method is as an adjunct to standard options like reduced intravenous chemotherapy, external or internal radiotherapy even in patients with poor performance status: Cancer drugs are injected directly into the tumor for central tumors or transthoracically for peripheral cancer site and by an EBUS-system for involved mediastinal lymph nodes. In more than 60 published patients (inoperable IIIa – IV) a surplus of up to 77% in median survival (MS) in comparison to expected MS according to UICC 7 data was achieved when ITC was used as an adjunct to standard therapy. Superdoses of cytotoxic drugs may thereby accomplish rapid tumor cell killing without systemic toxic complications but also involved lymph nodes - in many studies the hallmark of local recurrence – could be treated directly and specifically. This new paradigm promises to significantly reduce lung cancer morbidity and mortality without the toxic complications associated with conventional systemic chemotherapy. It maybe not only considered in palliative situations but also as preoperative therapy according to the results in animal studies.

Biography

Dr. Wolfgang Hohenforst-Schmidt works as a senior physician executive in the field of interventional pulmology including chest oncology, interventional cardiology and intensive care medicine since more than one decade. He is author of the national guideline commitee on Pulmonary Hypertension (Dtsch Med Wochenschr 2010; 135: S102-115). In interventional pulmology he published new methods like perthoracical endopulmonary ultrasound to guide peripheral cancer biopsies (49th Congress of the German Society of Pulmology (DGP) 2008, Lübeck, P79) and reported for the first time surprising survival rates in NSCLC-patients following an interventional program that used controlled submaximal physical exercise as adjunct treatment to standard therapy (Medical Tribune 2010; 31/32: S16). On the 16th World Congress of Bronchology in Budapest he presented surprising preliminary data on survival of patients treated with ITC in combination with intravenous chemotherapy (16th WCB 2010, Budapest, A-0190).

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Endobronchial Intratumoral Chemotherapy (EITC): A New Modality for Palliation and Potential Curative Therapy of NSC Lung Cancer

Eugene P. Goldberg[1], Wolfgang Hohenforst-Schmidt[2] and Seyhan Celikoglu[3]

[1]Colleges of Engineering & Medicine, University of Florida, USA
[2]Klinikum Coburg, Germany,
[3]University of Istanbul Medical Center, Turkey

Lung cancer remains the most deadly and most difficult cancer to treat effectively. The standard of care for conventional treatment; radiation, systemic chemotherapy and surgery is relatively ineffective for long term survival. CDC statistics indicate a 75% increase in lung cancer mortality during the past 20 years. New concepts for enhancing quality of life and for prolonged survival are needed. Reported here is progress for a new therapeutic paradigm, intratumoral (IT) chemotherapy, a novel localized treatment modality. The procedure, endobronchial intratumoral chemotherapy (EITC) involves direct intratumoral drug injection via a needle bronchoscope. A superdose of drug is thereby made to perfuse the tumor mass and achieve rapid tumor necrosis and massive tumor cell killing. Because of the localized drug delivery, there are no systemic toxic complications with cisplatin or mitoxantrone that are normally associated with conventional IV chemotherapy. Palliation and prolonged survival have been observed clinically for EITC, especially for patients presenting with significant airways obstruction. Collaborative clinical studies has been conducted with Dr. Celikuglu, who has pioneered EITC in Istanbul, and with Dr. Hohenforst-Schmidt in Germany. Favorable clinical outcomes for EITC have now been observed for hundreds of NSCLC patients. In parallel preclinical IT chemotherapy research in Florida, using a murine Lewis lung carcinoma, mitoxantrone-loaded albumin nanomesospheres afforded prolonged IT tumoricidal activity and evidence for systemic tumor-specific immune response. Additional research indicates that IT neoadjuvant chemotherapy followed by resection of the necrotic tumor mass may afford a curative response. It is reasonable to conclude that IT chemotherapy represents an important new approach to improved lung cancer treatment.

Biography

Dr. Goldberg FAIMBE, FBSE, joined the faculty of the University of Florida as the Biomedical Program of Excellence Professor in 1975. At Florida, as part in the Departments of Chemistry and Materials Science & Engineering, he helped establish intramural graduate programs in Polymer and Biomedical Sciences. He is now also affiliated with the University's Cancer Center and the Departments of Biomedical Engineering, Pulmonology, and Pharmacology & Therapeutics. His biomedical research interests and activities for the past 35 years have been diverse with strong focus on localized chemotherapy by direct intratumoral drug injection. Pioneering cancer therapy studies were initiated in 1976 as a Visiting NIH Scientist and marked by a seminal 1978;38:1311 Lung Cancer paper on IT Chemoimmunotherapy. Subsequent research was devoted to enhancement of intratumoral chemotherapy using drug-loaded albumin and DNA nanomesospheres as reviewed in JPP 2002;54;159-180. Recent clinical research has been focused primarily on bronchoscopic intratumoral injection of chemotherapy with Drs. Seyhan and Firuz Celikoglu and Dr. Wolfang Hohenforst-Schmidt as reported in Cancer Therapy 2008;6:545-552 and JPP 2010;62:287-295. Dr. Goldberg is the senior author of more than 425 published and presented papers and is on the editorial boards of numerous journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Extra cellular matrix derived endogenous angioinhibitor tumstatin and its mechanism(s) of action

Sudhakar Akul

Boys Town National Research Hospital, USA

Cancer is currently one of the most prevalent causes of human deaths in the world. Current therapeutic options aim only to slow the progression of cancer disease. Therefore, a renewed effort must be made to identify relevant endogenous cancer inhibitors that could be exploited as therapeutic drugs. We identified several endogenous anti-cancer molecules, which are released from extracellular matrix (ECM) into the blood circulation of cancer patients. Several of these endogenous circulating molecules were cloned and identified as angioinhibitors of tumor growth. These endogenous angioinhibitory proteins bind to the cell surface integrins and transduce the signalling mechanisms & regulate angiogenesis. Thus, integrins serve as transmembrane linkers between the ECM and cytoskeleton for outside-in signalling. One such endogenous circulating molecule, tumstatin, a 28-kDa protein from the C-terminal non-collagenous (NC1) domain of alpha3 type IV collagen was identified by us as an inhibitor of angiogenesis (Science 2002; PNAS 2003). Tumstatin interacting with alphaVbeta3 integrin and inhibits activation of focal adhesion kinase (FAK), phosphatidylinositol 3-kinase (PI-3K), serine/threonine kinase (Akt/protein kinase B), mammalian target of rapamycin (mTOR) and prevents dissociation of eukaryotic translation initiation factor 4E (eIF4E) from 4E binding protein (4E-BP1) leading to the inhibition of Cap-dependent translation in proliferating endothelial cells. Recently, we also demonstrated that tumstatin inhibits hypoxia induced pro-inflammatory cyclo-oxygenase-2 (COX-2) expression via FAK/Akt/NFkB pathway, leading to decreased tumor angiogenesis and tumor growth in an alpha3beta1 integrin dependent manner (Blood 2007; J Canc Sci Ther 2009). At present my laboratory is studying to understand four such endogenous angioinhibitor molecules derived from type IV collagen that include tumstatin, arresten, combostatin and hexastatin which are involved in cell signalling and the way these proteins control adhesion and migration of endothelial cells in pathological processes including tumor angiogenesis.

Biography

Sudhakar Akulapalli (Akul) is the founder Director of Cell Signaling, Retinal and Tumor Angiogenesis Laboratory at Boys Town National Research Hospital, Associate Professor at Creighton University School of Medicine and University of Nebraska Medical Center, Omaha, NE, USA. He did his postdoctoral training at Harvard Medical School, Boston, MA, USA (2003). He has received Ph.D (2001), M.Phill (1997) and M.Sc (1995) degrees in life sciences from University of Hyderabad; and B.Sc in Biology from Silver Jubilee College (APRDC) Kurnool, SK University (1993) from India. He received President's fellowship (1992), GATE (1996) and CSIR (2007-2000) fellowships from Government of India. He received Mahindra & Mahindra Educational Award (2000) and Young Clinical Scientist Awards from Flight Attendant Medical Research Institute (FAMRI) in 2007 and 2010. He also received Bio-Bio Young Scientist Award from OMICS publishing group; Michael A. O'Connor Young Investigator Award; RO1 grant Award from NIH/NCI and Research Scholar Grant Award from ACS (2010). He is serving as AIBS/NIH-RO1 Grant reviewer for DT study section. He has published more than 35 research articles in several top journals including Science, Cancer Cell, JCI, Blood, PNAS, Gastroenterology, Cancer Research, JBC, IOVS, JCST etc. He is serving as an Executive Editor, Editor and Editorial board member of reputed journals and is serving as a reviewer for 21 scientific journals including JCI, Blood, Circulation, Circulation Research, Cancer research, Clinical Cancer research etc. He was honored by giving a position as Keynote Speaker, Chairman, Co-chairman and organizing committee member for several international conferences including Bio-Bio-2009; Bio-Bio-2010; Anal-Bio2010; Biomarkers & Clinical Research 2010; Diabetes & metabolism 2010 etc.

The association between Charlson Comorbidity Index(CCI) and the burden of cancer

Eun-Jung Kim

Cheju Halla University Department of Nursing, Republic of Korea

This study compared the association of comorbidity related with health outcomes by considering the fatality of cancer. Lastly, it will examine how the association on health outcomes differs according to patterns of associated diseases by types of cancer and will analyze the correlation with health outcomes. This retrospective, non-controlled and non-randomized study was conducted with 287 breast cancer patients, 273 colon cancer patients, 614 stomach cancer patients and 391 lung cancer patients. Using claim data, I measured comorbidity index. I used EDI claim data for calculating medical cost. Multiple regression and logistic regression model were utilized to investigate the effect of comorbidity on health outcomes as a total medical cost. This study controlled demographic characteristics and stage of cancer to estimate the influence of CCI on health outcomes. All statistical analysis was performed with sas 9.1. The effect of CCI measured with the medical records on the medical costs is higher CCI increased the medical cost of stomach cancer patients 1.05 and the cost of colon cancer patients 1.01. The breast cancer patients with COPD paid more medical cost than those without it and the increasing rate got lesser when CCI increased. And the colon cancer patients with DM paid more medical cost when the CCI got 1 point. But the lung cancer patients with COPD and CCI 2 point paid less than other patients. There are some differences according to comorbid diseases due to the characteristics of each cancers. The chronic comorbid were major factor to increasing medical cost and using medical resources. To prevent above mentioned disease, we must focused to check metabolic syndromes then preserve insurance financial health.

Biography

Eun-Jung Kim has completed her Ph.D at the age of 30 years from Korea University. She is the assist professor of Cheju Halla University. She has published more than 5 papers in reputed journals and serving as a member of repute.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Therapeutics and Toxicology of Liposome-Based Anticancer Drugs

Alberto A. Gabizon

Shaare Zedek Medical Center and Hebrew University-School of Medicine, ISRAEL

Most of the currently used anti-tumor agents have problematic toxicities compromising efficacy, and often resulting in life-threatening events. Liposomes can provide effective control of the release rate and of the tissue distribution of many of these agents. These pharmacokinetic changes often have a major pharmacodynamic impact with attenuation of toxic effects and protection of sensitive tissues from dangerous and unwanted drug exposure. Polyethylene-glycol (PEG) coating of liposomes results in inhibition of liposome uptake by the reticulo-endothelial system and significant prolongation of liposome residence time in the blood stream. A hallmark of these long-circulating liposomal drug carriers is their enhanced accumulation in tumors. The mechanism underlying this passive targeting effect is the phenomenon known as enhanced permeability and retention (EPR) which has been described in a broad variety of experimental tumor types, and appears also to be a relevant phenomenon in human cancer. Developments in drug loading technology have improved the efficiency and stability of drug entrapment in liposomes, particularly with regard to anthracyclines, vinca alkaloids, and camptothecin analogs. Coupling the advances in liposome engineering such as pegylation with highly efficient drug remote loading techniques has resulted in robust formulations with great improvements in pharmacokinetics and pharmacodynamics over the conventional administration of cytotoxic drugs.

An example of liposome formulation with demonstrated clinical added value is pegylated liposomal doxorubicin (PLD), which has demonstrated clinically a favorable safety profile and proven efficacy against various malignancies and can be considered as the first anti-cancer nanomedicine approved for clinical use. The clinical pharmacokinetic profile of PLD is characterized by slow plasma clearance and small volume of distribution with drastic shifts (~1000-fold) from free doxorubicin. Based on preclinical studies, other formulations such as pegylated liposomal irinotecan hold promise to offer an important clinical edge in cancer chemotherapy. Another type of approach applicable to liposomal drug delivery combines the concept design of a stable and long-circulating liposome with chemical modification of a drug to provide a lipophilic prodrug with strong association to the liposomal bilayer. This is the case of a prodrug of mitomycin-C activated by thiolytic cleavage. Thiolytic cleavage takes place in the tissue micro-environment with negligible activation in plasma thus preventing drug activation and drug leakage in the blood stream and resulting in 3-fold decrease in toxicity when compared to treatment with free mitomycin-C.

Further to the passive targeting effect, the liposome drug delivery platform offers the possibility of grafting tumor-specific ligands on the liposome membrane for active targeting to tumor cells, and potentially intracellular drug delivery. Ligand-specific targeting may enhance tumor drug accumulation and reduce further the toxicity of liposome-delivered drugs in comparison to passively targeted systems.

Liposome-based systems offer a vast array of potential applications in the delivery of cancer chemotherapeutic agents. Provided liposome composition and drug entrapment are properly engineered, major changes in the pharmacokinetics and biodistribution can be obtained. Pharmacodynamic changes may result in a substantial improvement of the toxicity profile and in a significant enhancement of the therapeutic index of the entrapped drug. Although liposomal doxorubicin has already found a place in routine clinical use, the potential of liposomal drug delivery remains so far under-exploited.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

High-risk human papillomavirus (HPV) screening and detection in normal, healthy patient saliva samples: a pilot cluster randomized study

Karl Kingsley and Deidre Turner

University of Nevada, School of Dental Medicine, USA

Human papillomavirus (HPV) is the primary etiological factor that transforms cervical epithelia into cancer. The presence of HPV in oral cancers suggests that HPV may play a similar role in transforming the oral epithelia. In addition to Epstein-Barr and Cytomegalovirus, new evidence has also revealed the frequent presence of high-risk HPV strains in breast carcinoma biopsies. Although epidemiologic studies suggest tobacco and alcohol use, and genetic predisposition are likely responsible for oral and breast carcinogenesis, concomitant HPV infection may be a significant factor that mediates growth and development. Although HPV may be transmitted from the oral cavity to the breast through direct contact, little evidence to date regarding oral HPV prevalence among health adults in the United States is available. The current study involved a non-invasive HPV screening of normal healthy adults at a US dental school, randomly selected to participate in a clustered pilot study. DNA was isolated from saliva samples and screened for HPV16 using qPCR. Chi-square analysis revealed the random patient sample was representative of the general clinic population with respect to gender, race and age ($p < 0.05$). Four patient samples were found to harbor HPV16 DNA, representing 3.9% of the total ($n = 102$); all four were female and Hispanic. This provides new information about oral HPV status, which may help to contextualize results from other studies demonstrating increasing oral cancer rates among females and minorities and in some geographic areas that may be associated with risk factors in addition to tobacco and alcohol use.

Biography

Karl Kingsley completed his PhD in 2001 and subsequently pursued postdoctoral studies at Stanford University in the School of Medicine, Division of Hematology. Dr. Kingsley is currently an Associate Professor of Biomedical Sciences at the UNLV School of Dental Medicine, where he teaches and directs an oral cancer research laboratory, specifically investigating high-risk HPV infection. He recently earned a Master of Public Health (MPH) in Occupational and Environmental Health and has published more than 25 papers in peer-reviewed journals. In addition, Dr. Kingsley is an avid supporter of the American Cancer Society in Las Vegas, Nevada.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Molecular basis of anti-inflamatory strategies in cancer cachexia

Martins Thomas
Cardiothoracic Surgery Unit, College of Medicine of University of Lagos, Nigeria

Background: There are newer diagnostic and therapeutic armamentaria for pri mary lung cancer. Application of molecular genetics in lung cancer management is evolving rapidly. However, the traditional knowledge and practices that were applicable before the 1980s still hold sway in most developing countries.

Aims and Objectives: This research was conducted to highlight the staggeri ng gap in the current aetiopathology and management profile of primary lung cancers and to assess the readiness of developing world for the chal lenges of lung cancer management in the new decade.

Methods: We studied the patients referred to Lagos University Teaching Hospital with suspicion of primary lung cancer. We noted their bio-dat a, predisposing factors and final diagnosis on completion of investigations. We also noted the therapeutic modalities that were applied - especially the type of operation that was done for each of the patients.

Results: The research lasted 99 months beginni ng in October 1999 and 267 patients were enlisted. There were 148 males (55.4%) and 119 females (44.5%). Stage IV patients were 183 (68.5%) while only 3 patients were found at stage I. Histology showed squamous cell carcinoma in 27.7% of cases while adenocarcinoma constituted 64.0%. Curative surgery was performed for 13.1% while non curative surgery was performed for 16.5%. Correlation between smoking and malignancy was stronger among the males than the female patients.

Discusion and Conclusion: There is increasing incidence of primary lung cancers among non-smoking females.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Nose bleed gone wild: Extramedullary plasmacytoma of the right nasal septum

Erwin Jannino O. Ybanez
Davao Doctors Hospital, Philippines

This is a rare case of extramedullary plasmacytoma (EMP) of the right nasal septum in a 25-year-old, Filipino, woman. She presented with recurrent episode of epistaxis and a mass in the right nasal cavity. Nasal endoscopy revealed a friable mass occupying the right anterior nasal cavity originating from the right lateral nasal wall superior and anterior to the inferior turbinate. Computed tomography of the paranasal sinuses showed a nipple-like structure projecting to the side of the nasal septum compatible with a vascularized polyp. The mass was completely removed endoscopically and histopathologic examination showed a densely packed tumor cells showing ovoid polygonal polychromatic and vesicular nuclei with moderate eosinophilic cytoplasm. Immunohistochemical staining showed positive for kappa and lambda light chains and negative for cytokeratin (CK) and leukocyte common antigen (LCA). Biopsy specimen was strongly immunoreactive to CD79a, MUM-1 and Ki67, consistent with EMP. Three months after initial polypectomy, the patient noticed recurrence of right nasal obstruction. A repeat CT scan of paranasal sinuses revealed right nasal mass almost entirely occupying the nasal cavity. Polypectomy and histopathologic examination of the specimen was still consistent with plasmacytoma. All diagnostic evaluation in this patient didn't show evidence of multiple myeloma. After removal of nasal mass, she received postoperative radiotherapy with total dose of 4500cGY to tumor bed. She remains disease free after six months. EMP of the nasal septum should be one of the differential diagnoses for nasal mass with history of recurrent epistaxis and nasal obstruction.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Evaluation of dendritic cells and RANTES in patients suffering from ovarian cancer

Jan Kotarski, Iwona Wertel and Wanda Rogowska

Medical University, Department of Oncological Gynaecology and Gynaecology, Lublin

The study was undertaken to evaluate Regulated on Activation, Normal T-cell Expressed and Secreted (RANTES) levels in the peritoneal fluid (PF) and plasma of patients with different stage, grade and histological type of ovarian cancer (n=73) or serous cystadenoma (n=32) in relation to PF and peripheral blood (PB) myeloid and lymphoid dendritic cells (DCs). The PF and plasma level of RANTES was detected using ELISA assay. DCs were estimated using flow cytometry. The following directly conjugated mAbs were used: anti-BDCA-1 (CD1c) FITC, anti-BDCA-2 (CD303) FITC and anti-CD19 CyChrome, anti-CD123 PE.

The percentage of myeloid DCs was significantly lower in the PF of patients with ovarian cancer (0.64%) than in women with benign tumors (7.76%). In contrary, the percentage of lymphoid DCs was higher in the PF of patients with malignant disease (0.66%) than in the reference group (0.20%).

The PF and plasma RANTES concentrations were significantly elevated in the ovarian cancer patients compared to the group of non-malignant ovarian tumors.

There were no significant differences in the plasma RANTES levels based on tumor stage, grade or histology.

Women with serous cystadenocarcinoma, clear cell carcinoma and endometrioid cystadenocarcinoma had significantly higher PF RANTES levels than patients with undifferentiated carcinoma. Women with clear cell carcinoma and patients with endometrioid cystadenocarcinoma had higher PF RANTES levels than women with mucinous cystadenocarcinoma.

We concluded that RANTES production in the peritoneal cavities of ovarian cancer patients depends on the histological type of the tumor cells.

The study was supported by the Grant KBN NN 407 114036 and KBN NN 407 038537.

Biography

Professor Jan Kotarski since 1999 is the Head of the 1st Department of Oncological Gynaecology and Gynaecology, Medical University of Lublin. He is one of the world's leading experts in gynaecologic oncology. He served as a President of Polish Gynaecological Society from 2006 to 2009. Currently he is a member of New York Academy of Science, European Society of Gynaecologic Endoscopy, European Society of Gynaecologic Oncology, Professor Kotarski's latest interests and research focus on clinical and experimental immunology and immunotherapy of gynaecological malignancies. He is one of the pioneers of dendritic cell vaccination use in the treatment of ovarian cancer.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Sam-Pointed Domain Ets Transcription Factor-1 (SPDEF-1, a.k.a. PDEF-1) is a Tumor Metastasis Suppressor and its Mechanism(s) of Action

Hari K Koul

University of Colorado School of Medicine, Aurora

Conventional therapies produce a high rate of cure for many patients with cancer, but there is, at present, limited effective treatments for intervention in metastatic cancer. Therefore, at present there is an urgent and unmet need for identifying new targets that could be exploited for intervention in metastatic disease. Progression of cancer from focal to metastatic cancer requires deregulation of growth control, invasiveness and cell motility. SPDEF/PDEF is the latest family member of the ETS transcription factor family, although it is unique in many aspects. PDEF was first discovered as an mRNA transcript highly expressed in prostate tumor cells where it regulates prostate-specific antigen (PSA) gene expression and is an androgen receptor co-regulator. SPDEF/PDEF expression is highly restricted to epithelial cells and has been found in prostate, breast, colon, ovary, stomach, and airway epithelium. Our recent studies demonstrated that SPDEF/PDEF is lost in a graded fashion as prostate cancer cells advance to aggressive stage (Molecular Cancer, 2010). Strong preclinical evidence is emerging that SPDEF/PDEF is a negative regulator of tumor progression and metastasis. PDEF expression is often lost in late-stage, advanced tumors. The induction of tumor aggressiveness in response to the loss of PDEF is thought to be due to the plethora of PDEF-regulated gene targets, many of which are known players in tumor progression including tumor cell invasion and metastasis (Cancer Letters 2011). Specifically our studies point to the direct regulation of MMP-9, a tumor progression associated MMP that is associated with cancer metastasis, by PDEF. These data lead us to the hypothesis that PDEF is a tumor metastasis suppressor protein. Current studies in our lab are aimed at understanding molecular mechanism/s involved in regulation of cancer cell metastasis by SPDEF/PDEF as well as mechanisms of SPDEF/PDEF silencing during cancer progression form indolent to aggressive metastatic phenotype.

Biography

Professor Hari K Koul is the founder Program Director of Urosciences Program and Cell Signaling and Molecular Urology Laboratory; Professor (with Tenure) and Director of Research, Department of Surgery-Division of Urology at The University of Colorado School of Medicine, Anschutz Medical Campus-Aurora-CO-USA; Research Biologist the Department of Veterans Administration Health Center-Denver-CO-USA; Professor Department of Bioengineering, and Program in reproductive Sciences; and Professor/ full member of the Developmental Therapeutics program at The University of Colorado Comprehensive Cancer Center Anschutz Medical Campus-Aurora-CO-USA. He is an internationally recognized researcher and over past two decades, Dr. Koul has greatly contributed to our understanding of molecular mechanisms, specifically signal transduction pathways in genitor-urinary disorders including prostate and bladder cancer. Dr. Koul's research is currently focused in understanding the role of Hypoxia/ re-oxygenation and the resulting ROS in mediating aggressive phenotypes in solid tumors in general and prostate, bladder and kidney cancer in particular. In addition his laboratory is engaged in deciphering the molecular signatures of aggressive renal and prostate tumors; and has recently identified MMP9 as a downstream target of Prostate Derived Ets transcription Factor (PDEF). Dr. Koul has been elected Fellow of the American Society of Nephrology (FASN: since 2004), and A Fellow of the American College of Nutrition (FACN; since 2002). Dr. Koul earned M.Sc. (Biochemistry-1986) from Kashmir University-Srinagar, J&K-India and Ph.D. (Biochemistry-1990) from PGI, Chandigarh, India. As a graduate student Dr. Koul was a recipient of prestigious fellowships from CSIR-India. Dr. Koul came to USA in 1991 on a NIH-post-doctoral fellowship and worked as a post-doctoral fellow (1991-1994) at the University of Massachusetts Medical School, in Worcester, MA. He was promoted to Jr. Faculty position at UMASS Medical School and continued to work there until 1996. Dr. Koul served as Sr. Staff Scientist and founding member of Urology Research team at Henry Ford Health Sciences Center/ Case Western University, Detroit MI from 1996-2003, when Dr. Koul was recruited to head the Urology Research Program at the University of Colorado Denver, School of Medicine.

6(ii): Targeting anti cancer drug

Session Chair
Dr. Takahiro Ochiya
National Cancer Center Research Institute, Japan

Session Co-Chair
Dr. Chulso Moon
Johns Hopkins University School of Medicine, USA

Session Introduction

Title: **Cancer-relevant functions of the plasma membrane receptor for thyroid hormone analogues**

Dr. Paul J. Davis, Albany Medical College, USA

Title: **Ribophorin II (RPN2) as a novel therapeutic target for cancer stem cells**

Dr. Takahiro Ochiya, National Cancer Center Research Institute, Japan

Title: **Aquaporin 5 (AQP5) activates the epidermal growth factor receptor (EGFR) and Src, potentially through its novel kinase activity, and may be involved in Iressa resistance**

Dr. Chulso Moon, Johns Hopkins University School of Medicine, USA

Title: **Analysis of miR-195 and miR-497 expression, regulation and role in breast cancer**

Dr. Lihui Lai, East China Normal University, China

Title: **Cucurbitacin B enhances the cytotoxicity of doxorubicin by increasing intracellular drug accumulation**

Dr. Meixia Zhang, China Medical University, China

Title: **Multifunctional nanoparticles for targeted drug delivery and MRI contrast agent**

Dr. Panchanan Pramanik, Indian Institute of Technology-Kharagpur, India

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Cancer-Relevant Functions of the Plasma Membrane Receptor for Thyroid Hormone Analogues

Paul J. Davis, Hung-Yun Lin, Vivian Cody, Faith B. Davis, Aleck Hercbergs and Shaker A. Mousa

Ordway Research Institute and Albany College of Pharmacy and Health Sciences, USA

Integrin αvβ3 is a heterodimeric structural protein of the plasma membrane that contains a high affinity receptor for thyroid hormone. Functions of this receptor are wholly distinct from those of the classical nuclear receptor (TR) for thyroid hormone. The hormone receptor on αvβ3 enables L-thyroxine (T_4) and 3, 5, 3'-triiodo-L-thyronine (T_3) to stimulate cancer cell proliferation and angiogenesis. A deaminated derivative of T_4, tetraiodothyroacetic acid (tetrac), blocks binding and proliferative actions of T_4 and T_3 at the αvβ3 receptor; tetrac also has anti-proliferative actions at the thyroid hormone receptor in the absence of T_4 and T_3. Structure-activity relationships of hormone analogues at the receptor have been computer-modeled and indicate the receptor includes a site (S1) that binds T_3 and a site (S2) for which both T_4 and T_3 are ligands. Tetrac acts at both S1 and S2. Cell proliferation is modulated from the S2 site. Tetrac has been re-formulated as a nanoparticle (nanotetrac) that acts exclusively at the αvβ3 receptor and does not enter cells. Nanotetrac 1) disorders expression of genes in multiple cancer cell survival pathways 2) blocks human cancer cell proliferation *in vitro* and in tumor xenografts and 3) inhibits the pro-angiogenic actions *in vitro* of VEGF, bFGF and other growth factors. Nanotetrac radiosensitizes cancer cells by inhibiting repair of double-strand DNA breaks. Thus, the receptor described on integrin αvβ3 for T_4 and T_3 provides insight into tumor cell and vascular cell biology and tetrac formulations offer a novel, disabling effects on multiple cancer cell defense pathways.

Biography

Paul J. Davis obtained his M.D. at Harvard Medical School and his clinical training at Albert Einstein College of Medicine and the NIH. He is Senior Associate Dean for Clinical Research at Albany Medical College and a senior faculty at Albany College of Pharmacy and Health Sciences. He was a founder of Ordway Research Institute, a nonprofit translational biomedical research company. He is a basic science endocrinologist, is co-author of more than 200 original papers and 25 textbook chapters and is an Associate Editor of two medical journals.

Ribophorin II (RPN2) as a novel therapeutic target for cancer stem cells

Takahiro Ochiya

National Cancer Center Research Institute, Japan

The survival rate for women with advanced, metastatic breast cancer has not changed significantly for decades. Regardless of effective therapies, many women still experience recurrences of breast cancer after treatment. Docetaxel has been shown to be beneficial in the treatment of breast cancer; however, almost half of treated patients do not respond to it and many tumors develop resistance. At present no method exists to predict response to docetaxel or to detect resistance. Moreover, target molecules to increase the efficacy of chemotherapy have not yet been identified. Here we found that inhibition of the ribophorin II (*RPN2*), a part of oligosaccharyltransferase (OST) complex, promoted docetaxel-dependent apoptosis and inhibited cell growth in a docetaxel-resistant human breast cancer cell line. Silencing of *RPN2* resulted in decreased glycosylation and membrane localization of the P-glycoprotein efflux pump, which caused increased sensitization of drug resistant cells to docetaxel (Nat Med, 2008). We also currently found that RPN2 is highly expressed in breast cancer stem cells. Knockdown of RN2 in cancer stem cells by shRPN2 vector system allowed a significant inhibition of cancer growth and lymph node metastasis in vivo. We also found that small non-coding RNA tightly regulates *RPN2* gene expression. *RPN2* could, therefore, have clinical applications as a target for micromanaging cancer stem cells.

Biography

Dr. Takahiro Ochiya is Chief of Division of Molecular and Cellular Medicine at the National Cancer Center Research Institute, Tokyo and he is also appointed as a invited professor of Waseda University (since 2004) and Tokyo Institute of Technology (since 2008). After he got Ph.D. in 1988 in Osaka University and then went to do a post-doc at La Jolla Cancer Research (Burnham Institute for Medical Research), CA, USA. Dr. Ochiya's lab focuses the development of novel animal models, methods, and strategies to study cancer development and metastasis. Especially, current focus are siRNA- and microRNA-based therapy against cancer stem cells.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Aquaporin 5 (AQP5) activates the epidermal growth factor receptor (EGFR) and Src, potentially through its novel kinase activity, and may be involved in Iressa resistance

Chulso Moon

Johns Hopkins University School of Medicine, USA

The role of aquaporin water channels in human carcinogenesis (AQPs) recently has become an area of great interest. We have previously demonstrated that AQP5 can promote cell proliferation leading to tumorigenesis by activation ERK1/2 pathways and that the expression of AQP5 is associated with prognosis of lung cancer, colon cancer and CML. Here, we provide evidences that these phenomenon may be mediated by activation of EGFR and/or Src, upstream signal for ERK1/2. Cellular hyperplasia and activation of ERK1/2 in transgenic mice carrying human AQP5 over-expression construct confirms our prior findings *in vivo*. Expression of AQP5 activate EGFR and Src in BEAS cells and HCT116 cells by increasing phosphorylation of both EGFR and Src, and inhibition of AQP5 expression lead to decreased phosphorylation of both molecules with decreased ERK1/2 activation. The association of AQP5 with EGFR and Src are demonstrated by immnoprecipitation and immnofloursecnce examinations in BEAS cells and such interaction is inhibited by mutation in PKA site in AQP5. Furthermore, by using baculovirus system, recombinant hAQP5 (rAQP5) was purified, which shows a unique kinase activity *in vitro* and that rAQP5 can synergistically increase overall kinase activity when combined with EGFR and Src. Based on these findings, we demonstrate that AQP5 may be involved in the development of Iressa (a small molecular inhibitor for EGFR) resistances, possibly through modulating phosphorylation of EGFR. While these observations provide several novel findings, studies for the detailed mechanistics leading to activation of EGFR and Src by AQP5 are warranted in the future.

Biography

Dr. Chulso Moon MD, PhD is a board certified medical oncologist in US and has been working in Johns Hopkins University (JHU) since 2001 as tenure track faculty, attending physician in the department of otolaryngology/oncology and JHU Cancer Center. Presently, he is actively participating in the cancer research as adjunct professorship in JHU and also mentoring graduate student in human genetics program in Johns Hopkins Medical School. He is an MD, PhD physician scientist participating both academic research and patient care. He obtained his PhD in human genetics from JHU under Dr. Peter Agre (2003 Novel Laureate) and finished his medicine and oncology training in MD Anderson Cancer Center. He played a key role in characterizing the role of AQPs in human cancer by providing the first model of AQP5 as a novel therapeutic target. Additionally, he has published several key review articles in clinical oncology focused on head and neck and prostate cancer.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Analysis of miR-195 and miR-497 expression, regulation and role in breast cancer

Dan Li[1], Yulan Zhao[1], Changxing Liu[3], Xiaona Chen[1], Yanting Qi[2], Yue Jiang[2,1], Chao Zou[1], Xiaolong Zhang[1], Shunying Liu[1], Xuejing Wang[4], Chuan-Xiu Bian[2], Dan Zhao[1], Qiang Sun[4], Zhenbing Zeng[7], Andreas Dress[7], Marie C. Lin[6,1], Hsiang-Fu Kung[5,1], Feng Mao[4], Bing-Hua Jiang[2,1] and Lihui Lai[1]

[1]Institute of Molecular and Chemical Biology, East China Normal University, Shanghai, China
[2]Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA
[3]Department of General Surgery, Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai, China
[4]Department of Breast Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China
[5]Faculty of Medicine, The Chinese University of Hong Kong, HK, SAR, China
[6]Brain Tumor Center, Neurosurgery Division, Faculty of Medicine, PWH, The Chinese University of Hong Kong, Shatin, Hong Kong, China
[7]CAS-MPG Partner Institute and Key Lab for Computational Biology, SIBS, CAS, Shanghai, China

Purpose: To investigate expression, regulation, potential role and targets of miR-195 and miR-497 in breast cancer.

Experimental design: The expression patterns of miR-195 and miR-497 were initially examined in breast cancer tissues and cell lines by Deep sequencing: Northern blotting and quantitative real-time PCR. Combined bisulfite restriction analysis and bisulfite sequencing were carried out to study the DNA methylation status of miR-195 and miR-497 genes. Breast cancer cells stably expressing miR-195 and miR-497 were established to study their role and targets. Finally, normal, fibroadenoma and breast cancer tissues were employed to analyze the correlation between miR-195/497 levels and malignant stages of breast tumor samples.

Results: MiR-195 and miR-497 were significantly down-regulated in breast cancer. The methylation state of CpG islands upstream of the miR-195/497 gene was found to be responsible for the down-regulation of both miRNAs. Forced expression of miR-195 or miR-497 suppressed breast cancer cell proliferation and invasion. Raf-1 was identified as a novel direct target of miR-195 and miR-497. miR-195/497 expression levels in clinical specimens were found to be correlated inversely with malignancy of breast cancer.

Conclusion: Our data imply that both miR-195 and miR-497 play important inhibitory roles in breast cancer malignancy and may be the potential therapeutic and diagnostic targets.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Cucurbitacin B enhances the cytotoxicity of doxorubicin by increasing intracellular drug accumulation

Meixia Zhang[1], Jiao Yang[1,2], Xueying Zhou[1], Yanli Wang[1], Wen Li[1], Jesse Li-Ling[3] and Yihui Deng[4]

[1]Department of Clinical Pharmacology, China Medical University, China
[2]Department of Pharmacy, The General Hospital of Daqing Oilfield, China
[3]Department of Medical Genetics, China Medical University, China
[4]Department of Pharmacy, Shenyang Pharmaceutical University, China

Purpose: To assess the effect of cucurbitacin B (CuB) on the cytotoxicity of doxorubicin (Dox) in human hepatocellular carcinoma cells and to explore the potential mechanisms.

Methods: The cytotoxicity of combined CuB and Dox in human hepatocellular carcinoma cell line (HepG2) was investigated with a 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay. The effect of CuB on Dox concentration in HepG2 cells was determined by evaluating the influx of Dox and the efflux of Dox from such cells. *In vivo* effect of combined CuB and Dox on the growth of murine H22 cells was also determined.

Results: Our data demonstrated that the cytotoxicity by CuB and Dox was additive in HepG2 cells. CuB has significantly increased Dox concentration in tumor cells by promoting Dox influx and suppressing Dox efflux. *In vivo* anti-tumor activity assay also showed that the combination of two drugs can result in more significant tumor regression compared with single drug usage.

Conclusion: Our results suggested that combined CuB and Dox may be an effective regime for the chemotherapy of HCC.

Multifunctional nanoparticles for targeted drug delivery and mri contrast agent

P. Pramanik

Nanomaterials Laboratory, Indian Institute of Technology-Kharagpur, India

Superparamagnetic iron oxide nanoparticles offer a unique carrier system, whose surface can be modified with multiple diagnostic and therapeutic entities to serve as both targeting contrasts and drug carriers simultaneously, allowing for real time monitoring of response from tumor to drug treatment. An effective approach towards improving the targeting capability and drug release efficiency of magnetic nanoparticles is to conjugate the nanoparticles with low molecular targeting agent, such as folic acid and small bio-molecule those have strong affinities for target cells and high efficiency for internalization of nanoparticle . Recently we have developed a series of novel technique to synthesize highly stable folic acid conjugated magnetite (Fe_3O_4) nanoparticles for targeting cancer cells, using derivatives of phosphonic acid and chitosan as vehicle . 2, 2'-(ethylenedioxy)-bis-ethylamine, a non-polymeric hydrophilic linker has been used as surface-coupling agent .These iron-oxide folate nano-conjugates are non-cytotoxic and shows high site-specific intracellular uptake against folate receptors over expressed onto cancer cells.

In our constant endeavor to design nanoparticles for site-specific drug targeting, "smart" superparamagnetic nanodevice has been developed which combines magnetic targeting, fluorescent-imaging, receptor-specific targeted delivery and pH responsive drug release into one system. The device has been synthesized by covalently grafting the widely used targeting agent folic acid, chemotherapeutic anticancer drugs and fluorochrome rhodamine isothiocyanate onto the surface of supeparamagnetic magnetite nanoparticles, functionalized with surface anchoring agent. The decorated magnetite nanoparticles serve as the core material to allow magnetically guided drug delivery and helps to enhance contrast due to T2-weighted magnetic resonance .Magnetically activated cell-sorting and confocal microscopy clearly establish that cells with over expressed with human folate receptors internalize efficiently the drug modified with nanoparticles than normal cells.

Biography

Prof P.Pramanik completed M.Sc and Ph.D from Indian Institute of Technology (IIT), Kharagpur, India . He is professor since 1993 in IIT, Kharagpur. His research interest is material chemistry and nano-biotechnology .He has publishes about 200 papers in international journals. He is member of many advisory board of government of India. He is key member of task force for nano-biotechnology of government of India.

Track 6(iii) 6(iv)

6(iii): Therapeutic Targets in Cancer

6(iv): Clinical Research in Cancer Immunology

Session Chair
Dr. Mahin Khatami
National Cancer Institute, USA

Session Co-Chair
Dr. Roman Kischel
Micromet AG, Germany

Session Introduction

Title: Targeting superoxide dismutase 1 for chemosensitization of platinum resistant ovarian cancer cells

Dr. Mu Wang, Indiana University School of Medicine, USA

Title: Unresolved Inflammation: Immune dynamics of aging process and tumorigenesis

Dr. Mahin Khatami, National Cancer Institute, USA

Title: IPMN of the pancreas - evaluation of pathohistological subtypes and clinical outcome

Dr. Marius Distler, University hospital Carl Gustav Carus, Germany

Title: Using GlycoExpress for production of highly active antibodies directed against novel and existing targets

Dr. Steffen Goletz, Glycotope GmbH, Germany

Title: BiTE antibodies for cancer therapy

Dr. Roman Kischel, Micromet AG, Germany

Title: Lactobacillus casei ssp.casei could induce the Th1 cytokine production and Natural Killer cells activity in BALB/c mice bearing invasive ductal carcinoma

Dr. Mohammad Hossein Yazdi, University of Medical Sciences, Iran

Title: Clinical pharmacokinetics of cisplatin in patients with malignant tumor of limb (mal) by Hyperthermic Antiblastic Perfusion (HAP) treatment

Dr. Jianshi Lou, Tianjin Medical University P. R. China

Title: Impaired cytolytic function of natural killer (NK) cells obtained from patients with head and neck cancer can be partially restored by the triggering of toll-like receptor 3 (TLR3) expressed on NK cells

Dr. Miroslaw J. Szczepanski, Poznan University of Medical Sciences, Poland

Title: Targeted and image-guided cancer treatment using Theranostic nanoparticles

Dr. Lily Yang, Emory University, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Targeting superoxide dismutase 1 for chemosensitization of platinum resistant ovarian cancer cells

Mu Wang

Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, USA

Platinum-based chemotherapy, such as cisplatin, is the primary treatment for ovarian cancer. However, drug resistance has become a major impediment to the successful treatment of ovarian cancer. To date, the molecular mechanisms of resistance to platinum-based chemotherapy remain unclear. In our previous study using a proteomic approach, more than 90 proteins showed significant expression changes when two pairs of ovarian cancer cell lines, A2780/A2780-CP (cisplatin-sensitive/cisplatin-resistant) and 2008/2008-C13*5.25 (cisplatin-sensitive/cisplatin-resistant), were compared. Bioinformatics analysis suggested several potential pathways that may be involved in platinum resistance. Among these potential pathways, a redox regulated pathway involving superoxide dismutase 1 (SOD1) was targeted in order to further explore its involvement in drug resistance. Inhibition of SOD1 activity in the resistant cells by either small-molecule inhibitors or siRNA enabled partial reversal of platinum resistance. Our data suggest that targeting SOD1 can potentially lead to sensitization of platinum-resistant ovarian cancer cells, and SOD1 may be used as a therapeutic target for chemosensitization of ovarian cancer.

Biography

Dr. Wang is the Director of Proteomics and Associate Professor of Biochemistry and Molecular Biology at Indiana University School of Medicine. He received his PhD in Bio-organic Chemistry from Washington University in St. Louis, Missouri, USA and was an NIH postdoctoral fellow studying mechanism of DNA repair in mammalian system. He has published more than 60 peer-reviewed articles in biochemistry and proteomics related journals. His own research involves mechanistic study of drug resistance in ovarian cancer and DNA repair mechanisms in mammalian systems in response to genomic stresses. In his recent study in searching for biomarkers of cisplatin resistance in human ovarian cancer using a proteomic approach, he identified multiple pathways that are involved in cisplatin resistance. His preliminary data suggests that SOD1 is a key determinant of drug resistance. Through inhibition of SOD1 activity, the cisplatin resistant ovarian cancer cells can be sensitized. He is in the process of developing a chemosensitizer to overcome platinum resistance in ovarian cancer. Dr. Wang was a recipient of the HUPO (Human Proteome Organization) 2004 Young Investigator Award.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Unresolved inflammation: Immune dynamics of aging process and tumorigenesis

Mahin Khatami
National Cancer Institute (NCI), National Institutes of Health (Retired)

For over 150 years increasing publications reported on circumstantial association between injuries/inflammation and cancer. However, until recently no data were available on a direct link between inflammation and tumor development. In 1980's, we established experimental models of acute and chronic inflammatory diseases in conjunctival associated lymphoid tissues (CALTs) in guinea pigs by topical application of fluoresceinyl ovalbumin (FLOA) for up to 30 months. Analyses of series of clinical and immunopathological findings demonstrated at least three distinct developmental phases of immune responses: a) Acute phase, involving IgE-Fc receptor aggregation and mast cell degranulation, histamine and prostaglandin release and vascular hyperpermeability; b) Intermediate phase, involving desensitization phenomenon, loss/exhaustion of mast cells function, infiltration of inflammatory cells (e.g., eosinophils) into subepithelium and goblet cells and neovascularization; c) Chronic phase, induction of massive lymphoid hyperplasia, follicular formation with germinal centers, increased swollen goblet cells, increased degranulation of mast cells ('leaky'), increased activity of macrophages, extensive epithelial thickening and thinning, changes in local antibody profiles (IgG1/IgG2 ratios) and angiogenesis.

The results are suggestive of a first evidence for direct association between inflammation and development of tumor-like lesions in lymphoid tissues, extensive changes in adjacent epithelium and angiogenesis. Mast cells are effector cells within innate immunity and play important roles, being 'tumoricidal' in their granulated (mature-resting) status during acute inflammation, while they possess 'tumorigenic' properties when partially granulated ('leaky') under persistent inflammation.

Designs of Clinical Trials and Drug Development: Unresolved inflammation is loss of balance between 'tumoricidal' vs. 'tumorigenic' (pleiotropy or 'Yin' and 'Yang') properties of acute inflammation. Promotion of innate and adaptive immune cells plays key roles in tumor surveillance ability of host tissues. Designs of suitable clinical trials and drug development will be discussed based on a concept that chronic inflammation is a common denominator in the genesis and progression of nearly all age-associated chronic diseases including cancer.

Recent Selected References:

Khatami, M: Developmental phases of inflammation-induced massive lymphoid hyperplasia and extensive changes in epithelium in an experimental model of allergy: Implications for a direct link between inflammation and carcinogenesis. Am. J. Ther. 12: 117-120, 2005.

Khatami, M: 'Yin' and 'Yang' in inflammation: duality in innate immune cell function and Tumorigenesis. Exp. Opin Biol. Ther. 8: 1461-1472, 2008.

Khatami, M: Inflammation, aging, and cancer: Tumoricidal versus Tumorigenesis of immunity. Cell Biochem Biophys. 55: 55-79, 2009.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

IPMN of the pancreas - Evaluation of pathohistological subtypes and clinical outcome

Marius Distler

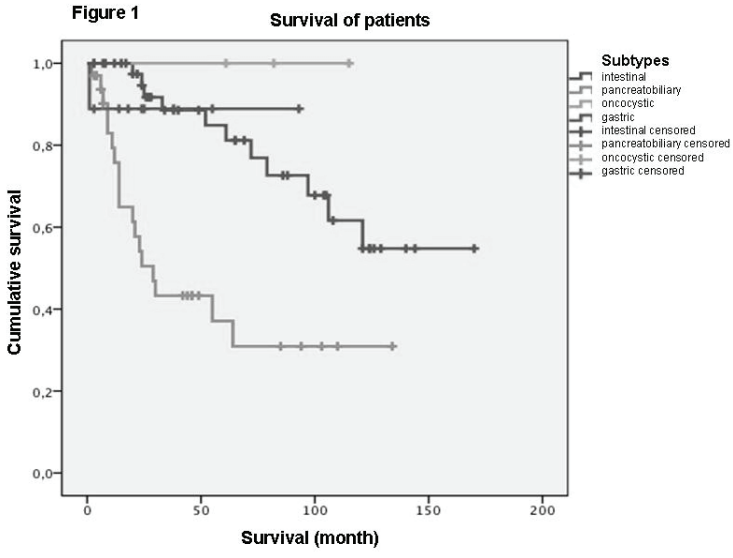
Department of General-, Thoracic- and Vascular Surgery, University hospital Carl Gustav Carus, Germany

In recent years papillary mucinous neoplasms of the pancreas (IPMN) have been increasingly recognized in clinical practice. IPMNs are estimated to have a better prognosis than pancreatic ductal adenocarcinomas. In addition to the different growth types (main duct vs. branch duct), the histological subtypes of IPMN (intestinal, pancreatobiliary, gastric and oncocystic type) became prognostically relevant. These subtypes can be characterized by different expression patterns of MUC using immunohistochemistry. In this study we analyzed the IPMNs of two pancreatic centers regarding to MUC expression and subtypes as well as the clinical outcome.

Over a period of 10 years we revaluated all pancreatic resections due to a cystic tumor in two German university hospitals. Cases with IPMN were screened and subtypes were defined by histopathological analysis including immunohistochemical analysis of MUC ($MUC1^+$, $MUC1^-$, $MUC2^-$, $MUC5AC^+$) expression. Furthermore we determined clinical and follow up data as well as patients outcome.

A total of 128 IPMN were detected. In 98 cases histopathological subtype classification was possible: intestinal type n=45 (46%), pancreatobiliary type n=38 (39%), gastric type n=11 (11%) and oncocystic type n=4 (4%). We performed the following types of resections: pancreatic head resections in 76.4%, left resections in 14.2%, total pancreatectomies in 5.5% and pancreatic segment resections in 4% of the cases. Median survival of intestinal IPMN is significantly better than pancreatobiliary IPMN (60 vs. 21 month) (Figure 1). Clinical data of the IPMN subtypes showed no differences. Common preoperative clinical symptoms were dorsalgia, abdominal pain and obstructive jaundice.

Figure 1



Evaluation of IPMN subtypes supports the postoperative prediction of the patient's prognosis. Therefore, it could lead to improvement in clinical management. Potentially identification of subgroups with the need for adjuvant therapy is possible.

Biography

M. Distler started to study medicine at LMU Munich, Germany and earned his medical degree in 2004 at TU-Dresden, Germany. Till 2004 he works as a general surgeon at the department of general-, thoracic- and vascular surgery at the university hospital of Dresden, Germany. His research activity is focused on carcinogenesis and treatment of pancreatic cancer. He presented and published research results on several national and international meetings or journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Using GlycoExpress for production of highly active antibodies directed against novel and existing targets

Steffen Goletz
Glycotope GmbH, Germany

Glycosylation is the major post-translational modifications of biotherapeutics that depends on the cell line used for production. By establishment of the GlycoExpress Toolbox we have generated a set of glycoengineered human cell lines to optimize the human glycosylation of biotherapeutics. PankoMab-GEX™ is a novel glycooptimized humanized monoclonal antibody produced in GlycoExpress. It recognizes a unique carbohydrate-induced conformational epitope (TA-MUC1). This epitope is tumor-distinctive and is present in the majority of cases of a variety of carcinomas. PankoMab-GEX™ is currently in late Phase I trial. Tumors carrying target molecules like Her2/neu, EGFR, CD20 and others are currently challenged by antibody therapeutics like Herceptin, Erbitux and Rituxan. However, clinical data shows that the success of the therapy depends on the Fc RIIIa allotype present within the treated patient. By Using GlycoExpress existing antibodies can be optimized in respect to manifold improvement of anti-cancer activity enabling clinicians to treat patients carrying the low affinity Fc RIIIa allotype and thus broadening the patient spectra. The activity of the antibodies was improved several hundred fold when measured by means of an ADCC assay. Furthermore the antibodies are improved with respect to half-life elongation and removal of immunogenic components. Two biobetter antibodies are currently in Phase I clinical trials.

Biography

Dr. Steffen Goletz, CEO, CSO and founder of the biotech company GLYCOTOPE, studied biology, biochemistry and molecular biology at the universities in Heidelberg, Kaiserslautern, Manchester (UK) and Berlin and holds a Ph.D. in biochemistry. During his research, Dr. Goletz has focused on glycobiology, tumor immunology, antibody engineering and cellular engineering. As CSO, Steffen is responsible for the development of GLYCOTOPEs product pipeline of glycooptimized biotherapeutics with four products currently in clinical trials.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

BiTE Antibodies for Cancer Therapy

Patrick A. Baeuerle and Roman Kischel
Micromet Inc., USA

Bispecific antibodies can transiently link tumor cells with otherwise inactive cytotoxic T cells in patients for induction of potent redirected lysis of tumor cells. One example is blinatumomab (MT103), a CD19/-CD3-bispecific BiTE for the treatment of human B cell-derived malignancies. Blinatumomab and other BiTE antibodies were shown to activate T cells in a highly conditional manner that is strictly dependent on the presence of target cells. Blinatumomab has commenced a pivotal study for the treatment of adult patients with therapy-refractory acute lymphocytic leukemia (ALL). A phase 2 study in ALL patients has shown an 80% complete molecular response rate at a dose level of 15 micrograms/squaremeter per day. Blinatumomab has also shown high response rates in non-Hodgkin's lymphoma (NHL) patients with follicular and mantle cell lymphoma, and first signs of efficacy in patients with diffuse large B cell lymphoma. Centrally confirmed complete and partial responses according to Cheson criteria were seen in NHL patients treated at a dose of 60 micrograms/squaremeter/day. The presentation will update on the clinical development of blinatumomab in leukemia and lymphoma.

MT110 is a novel BiTE antibody recognizing the pan-carcinoma antigen EpCAM (CD326), which is expressed on a large variety of human adenocarcinoma, and on cancer-initiating or stem cells derived thereof. MT110 is a in phase 1 study with gastrointestinal, lung, breast, prostate, ovarian, and esophageal cancer patients. A murine EpCAM/CD3-specific version of the BiTE antibody, called muS110, has shown a robust therapeutic window in mice with no damage to EpCAM-expressing normal epithelia. A series of new BiTE antibodies for solid tumor treatment are being developed in collaboration with large biopharma partners, including MedImmune/AstraZeneca, Bayer Schering Pharma, Boehringer Ingelheim and Sanfi-aventis.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Lactobacillus casei ssp.casei could induce the Th1 cytokine production and Natural Killer cells activity in BALB/c mice bearing invasive ductal carcinoma

Mohammad Mehdi Soltan Dallal[1], Mohammad Hossein Yazdi[1], Marzieh Holakuyee[2], Zuhair Mohammad Hassan[3], Abbas Mirshafiey[1] and Mehdi Mahdavi[3]

[1]Faculty of public health, Tehran University of medical science, Iran
[2]Department of immunology, Pasteur Institute of Iran, Tehran, Iran
[3]Faculty of medical sciences, Tarbiat Modares University, Iran

Lactic acid bacteria used as probiotics have ability to modulate immune responses. They have also been shown to affect the immune responses against solid tumors. In the present work, we proposed to study the effects of oral administration of *L.cacesi ssp casei* on the NK cytotoxicity and production of cytokines in spleen cells culture of BALB/c mice bearing invasive ductal carcinoma. Tow groups of female mice as test and control each containing 15 mice were used. 2 weeks before tumour transplantation test mice were orally administered by 0.5 ml of PBS containing 2.7×10^8 CFU/ml of *L.casei.* Administration was followed 3 weeks after transplantation with 3 days interval. Control mice received an equal volume of PBS in a same manner. Results showed that *L. casei* significantly increased the production of IL-12 and IFN-γ and increased the NK cytotoxicity. The growth rate of tumor in the test mice was decreased and survival rate of them significantly raised in comparison to the controls. Our findings suggested that daily intake of *L.casei* can improve the production of IL-12 and IFN-γ and motivate the NK cytotoxicity, but further studies are needed to investigate the other mechanisms of these effects.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Clinical Pharmacokinetics of Cisplatin in Patients with Malignant Tumor of Limb (MAL) by Hyperthermic Antiblastic Perfusion (HAP) Treatment

Jianshi Lou, Jing Zhu and Zhiqing Cui

Dept. of Pharmacology, Tianjin Medical University, Tianjin 300070, P. R. China

Objective: To study the pharmacokinetics of cisplatin in MAL patients by the treatment of HAP, a quick and sensitive UV spectrometry was used to determine the cisplatin concentrations in plasma.

Methods: The patients were divided into 3 groups. I: The systemic blood cisplatin concentrations (SBCC) were determined after cisplatin (2mg/kg) iv gtt. II: The local and the SBCC were determined during HAP (3mg/kg). 200ml blood was discarded after HAP. The SBCC were determined for 72 hours. III: 200ml blood returned to systemic circulation after HAP. Other performances were same as II.

Results: During HAP the cisplatin concentrations in local blood were 3-15 folds higher than that in systemic blood at the same time. After HAP SBCC of III were close to that of II at the same time. After HAP of 72 hours SBCC was still higher than that of 50% inhibiting cancer concentration in vitro. There was no significant deference in pharmacokinetic parameters within 3 groups. The toxicity in III was not increased.

Conclusion: The method without discarding blood after HAP is confirmed useful in clinic.

Biography

Prof. Jianshi Lou is the director of Dept. of Pharmacology, guided about 10 Ph D students and 40 MM students in his Lab. He has published more than 100 papers in repute journals and Chinese journals. Now he served as Vice-Chairmen of The Tianjin Pharmacological Society; Vice-Chairmen of The Tianjin Pharmaceutical Society; Vice-Chairmen, Branch of Mathematics Pharmacology, Chinese Pharmacological Society.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Impaired cytolytic function of natural killer (NK) cells obtained from patients with head and neck cancer can be partially restored by the triggering of toll-like receptor 3 (TLR3) expressed on NK cells

Miroslaw J. Szczepanski
Poznan University of Medical Sciences, Poland

Background: Human natural killer (NK) cells play a critical role in innate immunity through their capacity to lyse malignant cells without prior antigen-specific priming. TLRs are expressed on inflammatory cells, including NK cells, and provide protection against infections benefiting the host. NK-cell function is impaired in patients with cancer. TLR3 is expressed on NK cells, but little is known about its role in NK-cell mediated activity in cancers. The aims of the study were: a) to analyze the frequency, phenotype and function of peripheral blood NK cells in patients with head and neck cancers (HNC) and b) to evaluate effects of TLR3 triggering on NK cell phenotype and function in these patients.

Materials and Methods: RT-PCR was used to evaluate the expression of TLR3 in NK cells TLR3 expression in NK cells was studied by RT-PCR. Multiparameter flow cytometry was used to evaluate the frequency of NK cells and expression of NK-cell activating receptors (NKp30, NKp46, NKG2D), CD69, interferon gamma, granzyme B, perforin, on NK cells isolated from the PBMC of normal controls (NC, n=10) and HNC (n=14). Lytic activity of NK cells stimulated or not with poly I:C, a ligand of TLR3, (50µg/mL) -/+ a constant dose of IL-2 (50 IU/mL) for 24h was tested in 51Cr-release assays against K562 targets. NF-kappaB translocation to nuclei and formation of conjugates with K562 cells after triggering of TLR3 was studied by confocal microscopy following immunostaining for a p65 subunit.

Results: Expression of CD69, activating receptors, granzyme B and perforin measured as mean fluorescence intensity (MFI) was significantly lower in NK cells of HNC patients vs NC ($p < 0.05$ for all) and correlated with the decreased function of NK cells (1170 vs. 1890 lytic units). TLR3 triggering on NK cell in HNC induced translocation of NF-kappaB, significantly increased lytic activity function and up-regulated expression of CD69 as well as IFN-gamma. However, it had no effect on the expression of activating receptors.

Conclusion: TLR3 expressed on NK cells is involved in the regulation of NK cell activity, and the impaired function of NK cells in HNC can be partially restored via TLR3 signaling using poly I:C.

Biography

Miroslaw J. Szczepanski, MD PhD graduated from Poznan University of Medical Sciences in Poznan, Poland in 2001 and completed his PhD in head and neck cancer immunology in 2010. He was a postdoctoral fellow at the University of Pittsburgh Cancer Institute from 2006-2009. After finishing his training in Pittsburgh he came back to Poland to complete his residency in Otolaryngology at the Department of Otolaryngology in Poznan. He has published 22 papers in reputed journal and has served as a reviewer for two scientific journals. His research interests are focused on cancer stem cells and on the role of toll-like receptors in head and neck cancer. He is also a principal investigator of two Polish Ministry of Sciences and Higher Education and Foundation for Polish Sciences grants on head and neck cancers.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Targeted and image-guided cancer treatment using Theranostic nanoparticles

Lily Yang

Department of Surgery and Winship Cancer Institute, Emory University, USA

Recent advances in nanotechnology have opened an exciting frontier in developing and applying novel approaches for the detection and treatment of human cancer. The major challenges in clinical oncology are the selective delivery of large amounts of therapeutic agents into tumor cells, accurate evaluation of the drug delivery, timely assessment of the therapeutic response and effective treatment of drug resistant cancers. Nanomaterial is playing a pivotal role in cancer diagnostics and therapeutics due to their unique optical, electronic, and magnetic properties. Theranostic nanoparticles with the abilities to target tumors, carry therapeutic agents, and produce contrasts for tumor imaging offer a promising means for novel treatments of cancer patients. We have developed a multifunctional theranostic magnetic iron oxide nanoparticle (IONP) platform that utilizes receptor-targeted IONPs to carry single or multiple therapeutic agents for drug delivery and optical and magnetic resonance imaging (MRI). Our theranostic nanoparticles are designed to overcome physical and intrinsic barriers that reduce efficiency of drug delivery and confer drug resistance in human cancers. By targeting to cellular receptors that are highly expressed in tumor cells, angiogenic endothelial cells, and active tumor stromal cells, these IONPs allow the drug to overcome the physical barrier in stroma-rich tumors, such as pancreatic cancer and triple negative breast cancer (TNBC), by serving as carrier vehicles for passage through the tumor endothelial cell layer and stromal fibroblasts, thereby increasing the efficiency of delivery into tumors but not into normal tissues. Based on the surface functionalization of the IONPs and chemical properties of drug molecules, we developed approaches for encapsulating or conjugating drugs to the IONPs, resulting in theranostic IONPs which carry one or multiple therapeutic agents. Targeted delivery, drug release, tumor growth inhibition, and MRI of drug delivery and response have been demonstrated in orthotopic breast and pancreatic cancer animal models. Conjugation of a new near infrared dye with a lasting-signal to the theranostic nanoparticles provides an optical imaging modality that allows identifying and removal drug resistant residual tumors by image-guided surgery. Therefore, our theranostic IONPs have the potential to significantly improve the efficiency of cancer treatment, Current preclinical studies focus on the development of an integrated protocol for the treatment of locally advanced pancreatic and triple negative breast cancers using targeted neoadjuvant nanotherapy and image-guided surgery.

Biography

Dr. Yang is an Associate Professor of Surgery and Radiology and Nancy Panoz Chair of Surgery in Cancer Research at Emory University. Dr. Yang received her medical training in China at West China University of Medical Sciences and then in the Chinese Academy of Preventive Medicine. She received her PhD degree in Molecular and Cellular Biology at Brown University. She was a research fellow in gene therapy at the University of Southern California and Emory University before joining the Department of Surgery at Emory as an Assistant Professor. Dr. Yang's research has concerned liver stem cells and cancer, gene therapy, apoptosis, molecular targeted therapy, biomarker targeted drug delivery, and cancer nanotechnology. During the last several years, she leads a research team to develop targeted optical and magnetic resonance imaging (MRI) nanoparticle probes for early detection of breast and pancreatic cancers and for image-guided therapy and surgery. Her group has developed a theranostic magnetic iron oxide nanoparticle (IONP) platform that utilizes receptor-targeted IONPs to carry single or multiple therapeutic agents for drug delivery and multi-modality tumor imaging. Her current research also focuses on molecular targets and signal pathways that confer aggressive behavior, invasiveness and resistance to apoptosis in triple negative breast cancer. Dr. Yang is the PI of several research projects supported by NIH R01, NIH P50 Emory Molecular Imaging Center, and NIH U01 Cancer Nanotechnology Platform Partnership grants. Her research has resulted in several patent applications. Dr. Yang is a member of the editorial boards of Apoptosis and Breast Cancer-Targets and Therapy. She is a member of the NIH Developmental Therapeutics study section and has served in many other NIH study sections.

7: Carcinogenesis & Mutagenesis

7(i): Metabolism of Carcinogens

7(iii): Biological & External Factors for Carcinogenesis

Session Chair

Dr. Carol Bernstein

University of Arizona College of Medicine, USA

Session Co-Chair

Dr. Jeffrey Field

University of Pennsylvania, USA

Session Introduction

Title: **A high fat diet may increase colon cancer risk through the action of Deoxycholate, A carcinogenic secondary bile acid**

Dr. Carol Bernstein, University of Arizona College of Medicine, USA

Title: **Mutagenesis of p53 by reactive PAH and ROS**

Dr. Jeffrey Field, University of Pennsylvania, USA

Title: **Variability in carcinogen metabolism**

Dr. Mohamadi Sarkar, Altria Client Services, USA

Title: **T regulatory cells (T-regs) and vascular endothelial growth factor (VEGF): Their relation with estrogen (E2) in premenopausal breast cancer (BC)**

Dr. Francesco Recchia, Civilian Hospital, Avezzano and University of L'Aquila, Italy

Title: **Mutagenesis as a biomarker of risk areas for carcinogens: Human biomonitoring**

Dr. Vera Maria Ferrao, Vargas Fundacao Estadual de Protecao Ambiental- FEPAM, Brazil

Title: **Carcinogenic Human PapillomaVirus (HPV) in suburban U.S. female population**

Dr. Lee Sin Hang, Milford Hospital, USA

Title: **The 'tether drop' hypothesis for the mechanism of chromosomal aberrations**

Dr. Leon P Bignold, Institute of Medical and Veterinary Science, Australia

Title: **The autophagic tumor stroma model of cancer: Role of oxidative stress and ketone production in fueling tumor cell metabolism**

Dr. Stephanos Pavlides, Paterson Institute for Cancer Research, UK

Title: Helicobacter pylori promotes angiogenesis in gastric cancer cells depending on cyclooxygenase-2-mediated vascular endothelial growth factor via p38MAPK/ATF-2 pathway

Dr. Qi Li, Shanghai University of Traditional Chinese Medicine, China

Title: Over expression of 17beta hydroxysteroid dehydrogenase type 12 (HSD17B12) correlates with poor prognosis in ovarian cancer

Dr. Marta Szajnik, Poznan University of Medical Sciences, Poland

Title: The mechanism & causes of carcinogenesis and mutagenesis in eukaryotes

Dr. Shaukat Iqbal Malik, Mohammad Ali Jinnah University, Pakistan

A high fat diet may increase colon cancer risk through the action of deoxycholate, a carcinogenic secondary bile acid

Carol Bernstein
University of Arizona College of Medicine, USA

Dietary fat causes bile acid secretion into the gastrointestinal tract. Among individuals in the United States, a relatively high fat diet (based on increased levels of milk fat and beef fat) doubles the level of bile acids in the colon. High fat Western diets increase the risk of colon cancer.

The bile acid deoxycholic acid (DOC) is likely important in colon cancer etiology. Exposure of colon cells to DOC induces reactive oxygen and nitrogen species, and DNA damage. Long-term exposure to DOC causes selection of apoptosis resistant colonic epithelial cells. We showed that DOC causes aneuploidy and micronuclei formation, indicators of genomic instability, in colon epithelial cells.

We tested DOC as a potential colon carcinogen in mice. Adding 0.2% DOC to the diet of wild-type mice resulted in fecal DOC of about 4.6 mg/g dry weight, comparable to DOC in feces of humans on a high fat diet of about 6.4 mg/g dry weight. Feeding a DOC-supplemented diet to 18 wild-type mice for 8 to 10 months caused colonic tumors in 17 mice, where 10 of the mice developed at least one colon cancer while 7 of the 8 remaining mice developed one or more serrated sessile adenomas.

Addition of the antioxidant chlorogenic acid at 0.007% to the DOC-supplemented diet significantly reduced tumor formation in the mice. These results suggest that a high fat diet in humans increase the risk of colon cancer through the mediation of bile acids, and that some dietary anti-oxidants may ameliorate this carcinogenicity.

Biography

Carol Bernstein, PhD, is a faculty member in the Dept. of Cell Biology and Immunology and has published more than 100 refereed papers, of which 45 have been in the areas of bile acids, DNA damage and cancer. Her other areas of interest are in the central importance of DNA damage and DNA repair both in aging and in the selective advantage of sex (why sex exists).

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Mutagenesis of p53 by reactive PAH and ROS

Jeffrey Field
University of Pennsylvania School of Medicine, USA

PAHs (polycyclic aromatic hydrocarbons) are products combustion found in tobacco smoke and other lung cancer carcinogens, but they must be metabolically converted into DNA-reactive metabolites. P4501A1/P4501B1 plus epoxide hydrolase activate PAH to (±) *anti*-benzo[*a*]pyrene diol epoxide ((±)-*anti*-BPDE) which causes bulky DNA adducts. Alternatively, Aldo-Keto Reductases (AKRs) convert intermediate PAH *trans*-dihydrodiols to *o*-quinones, which cause DNA damage by generating reactive oxygen species (ROS). In lung cancer, the types or *pattern* of mutations in *p53* are predominantly G to T transversions. The locations of these mutations form a distinct *spectrum* characterized by single point mutations in a number of hotspots located in the DNA binding domain. One route to the G to T transversions is via oxidative DNA damage. In a yeast model system for p53 mutagenesis, mutations observed with PAH *o*-quinones were predominately G to T transversions and those observed with (±)-*anti*-BPDE are predominately G to C transversions. The mutations observed with either PAH-treatment occurred randomly through the DNA-binding domain of *p53*. However, when the mutants were screened for dominance, the dominant mutations clustered at or near hotspots primarily at the protein—DNA interface, while the recessive mutations are scattered throughout the DNA binding domain, without resembling the spectra observed in cancer. We conclude that mutagenesis can drive the pattern of mutations, but that biological selection for dominant mutations drives the spectrum of mutations observed in *p53* in lung cancer. Studies will be presented suggesting that AKRs protect from acute toxic effects of PAH at the expense of increasing the burden of oxidative stress on cells.

Biography

Dr. Jeffrey Field is professor of Pharmacology at the University of Pennsylvania School of Medicine. He earned a BA in biology from Columbia University and a PhD from the Albert Einstein College of Medicine with Dr. Jerard Hurwitz. During postdoctoral studies with Dr. Michael Wigler at the Cold Spring Harbor Laboratories, he isolated the first known Ras effector, the yeast adenylyl cyclase by developing the technology of epitope tagging. In his own lab at the University of Pennsylvania he established the central role of Pak kinases in Ras signaling and cell transformation. His current work centers on the role of the cytoskeleton in transformation and survival as well as mechanisms of smoking carcinogenesis.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Variability in carcinogen metabolism

Mohamadi Sarkar
Altria Client Services, USA

Cigarette smoke consists of thousands of constituents. Some of these e.g. 4-aminobiphenyl and 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) have been identified by the International Agency for Research on Cancer (IARC) as human carcinogens (IARC Group 1 carcinogens). Exposure to cigarette smoke constituents can occur through many other sources in addition to cigarette smoke. The systemic exposure for these constituents depends primarily on their absorption, distribution, metabolism and excretion (ADME). Of the ADME processes, metabolic activation and detoxification plays a significant role in determining the systemic exposure. A substantial proportion of the differences in metabolism can be accounted by induction or inhibition as well as genetic polymorphisms of the metabolic enzymes. There is abundant evidence on the allelic variants for the different enzymes involved in the metabolism of these carcinogens. The tobacco specific nitrosamine, NNK undergoes carbonyl reduction to NNAL (4-methylnitrosamino-1-(3-pyridyl)-1-butanol) by the CYP450 enzyme, CYP2A6, that exhibits genetic polymorphisms. NNAL undergoes subsequent glucuronidation through the glucuronyl transferases, UGT1A4 and UGT2B10. The UGT2B10 Asp67Tyr allele has been linked to a haplotype associated with decreased N-glucuronidation of NNAL. Similarly, allelic differences in CYP1A2 and N-acetyltransferase enzymes have also been attributed to variations in 4-aminobiphenyl metabolism. The composite effect of the phenotypic outcome of the individual genotypic differences and its subsequent impact on systemic exposure has not been methodically characterized. Such an assessment is possible by determining the metabolite ratios as well as measuring the overall exposure as estimated from urinary excretion. Data from a stratified, multi-center, cross-sectional study of 3,585 adult smokers and 1,077 non-smokers were analyzed to characterize the variability in carcinogen metabolism. The different sources of variability in carcinogen exposure will be discussed in this presentation.

Biography

Mohamadi Sarkar, M.Pharm., Ph.D., FCCP, serves as Senior Principal Research Scientist for Altria Client Services in Richmond, Virginia, since August 2002. He has authored more than 100 scientific peer-reviewed publications and presentations at scientific meetings. Dr. Sarkar has also participated in several invited seminar presentations and authored a variety of scientific book chapters related to his areas of expertise and won several research and teaching awards. He has held various academic appointments in Clinical Pharmacology at the School of Pharmacy in Virginia Commonwealth University (VCU) as well as West Virginia University. He continues to serve as Affiliate Associate Professor and teach Clinical Pharmacology at VCU.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

T regulatory cells (T-regs) and vascular endothelial growth factor (VEGF): Their relation with estrogen (E2) in premenopausal breast cancer (BC).

Francesco Recchia

Civilian Hospital, Avezzano and University of L'Aquila, Italy

Reproductive function and BC share developmental pathways that are mediated by E2: Modulation of VEGF expression and T-regs proliferation. Both functions are important for embryo implantation, pregnancy maintenance and breast cancer progression. Objective of this study was to evaluate wether E2 suppression with an LH-RH analog was able to down regulate VEGF expression, and to decrease the number of circulating T-regs in premenopausal BC patients with high-risk estrogen receptor positive (ER+) and negative (ER-) early BC. From 04-2003 to 10-2008, 100 premenopausal early BC patients were entered into the study. At baseline, after surgery, and every six months, plasma VEGF and T-regs were measured. Treatment consisted of LH-RH analogue for 5 years, tailored chemotherapy, radiation therapy, and 5-year hormonal therapy in ER+ tumors. Primary end-point was the evaluation of VEGF and T-regs. Secondary end-points were progression-free survival (PFS) and overall survival (OS). Median age 43 years; mean number of positive axillary nodes 3.3; 83% ER+, 17% ER - and PGR-, 20% Herb-2 +; Median KI-67, 33%. After 1 and 5 years, 94% of patients, both ER+ and ER-, were disease-free and had a statistically significant decrease of VEGF ($p<0.001$) and T-regs ($p<0.001$). 6% had a disease relapse with VEGF and T-regs increase with respect to baseline values ($p<0.001$). No unexpected toxicity of chemotherapy was observed, while hot flashes and G1 osteopenia were mild. After a median follow-up of 50 months (range 24-90), 5-year PFS and OS were 94% and 100%, respectively. E2 deprivation with an LH-RH analogue is able to decrease plasma VEGF levels and T-regs in premenopausal high risk ER+ and ER- BC patients. These data show how estrogens, through VEGF modulation and T-Regs proliferation, may be responsible for the worst prognosis that is observed in premenopausal BC patients.

Biography

Francesco Recchia MD has completed his M.D at the age of 24 years from Rome University and postdoctoral studies from University of Texas, MD Anderson Hospital. He is the director of Medical Oncology at The Civilian Hospital Avezzano, affiliated with the University pf L'Aquila, Italy. He has published 247 papers in reputed journals and he is serving as an editorial board member in several Oncology journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Mutagenesis as a biomarker of risk areas for carcinogens: Human biomonitoring

Vargas V M F[1,2], Coronas M V[1,2], Pereira T S[1,2], Rocha J V[1], Rodrigues ML[1], Fachel J[3], Faccini L S[4], Thiesen F[5], Nussbaumer L[6], Oliveira S[6] Dapper V[6] and Salvadori D M F[7]

[1]Fundação Estadual de Proteção Ambiental, FEPAM. Avenida Salvador França, Brazil.
[2]Curso pós-graduação Ecologia, UFRGS.
[3]Instituto Matemática e Estatística, UFRGS.
[4]Depto Genética, UFRGS.
[5]Instituto de Toxicologia, PUCRS.
[6]Secretaria Saúde RS,
[7]Depto Patologia, UNESP, SP.

Chemical dispersions of hazardous waste in the environment form complex mixtures containing toxic, genotoxic and carcinogenic agents. Dispersion modifies ecosystems distant from the sources exposing the population to greater risks. Epidemiological studies have associated health problems, especially cancer, acute or chronic cardiorespiratory diseases exposed to genotoxins. FEPAM/RS has implemented strategies to assess environmental genotoxins using biomarkers as early parameters to prevent contamination risks. Studies looked at exposure routes physically characterizing areas, definition and dispersion of contaminants in environmental compartments and early toxic or genotoxic biomarkers. *Salmonella*/microsome assay responses were markers assessing atmospheric compounds associated with wind distributions indicating chronic exposure. Comet assays in peripheral blood lymphocytes and micronuclei of oral mucosa cells were genetic markers for biomonitoring urban populations exposed to different industrial activities at an oil refinery (Site 02), industrial complex (Site 03), site with contaminated soil (Site 04) and reference (Site 01 far from main industrial districts, with restricted urban traffic). PAH, nitro-PAHs, aromatic amines, pentachlorphenol, dioxins/furanes and heavy metals were the main stressors. At Site 04 a significant incidence of neoplasms was identified, especially in first degree relatives. The Comet assay in peripheral blood lymphocytes and micronuclei of oral mucosa cells was sensitive to exposure to human environmental mutagenic compounds. Mutagenesis quantification per unit of sample in different compartments allowed comparing results in different areas. Diagnostic strategies allow selecting genetic damage biomarkers as early indicators for assessing environmental release of hazardous wastes in ecosystems and for preventing risk effects on life quality of the general population. EcoRISCO-SAÚDE/INAGEMP/CNPq/CAPES/FAPERGS.

Biography

Vera Maria Ferrão Vargas completed her Ph.D in 1992 at Universidade Federal do Rio Grande do Sul (UFRGS), Brazil. She is the coordinator of the Research Program at FEPAM, the Rio Grande do Sul state environmental protection agency, a Professor in the Graduate Program of Ecology at UFRGS and Specialization Course of Toxicology at the Pontificia Universidade Católica do Rio Grande do Sul (PUCRS), a research fellow in the National Council of Science and Technology(CNPq) and vice-president of the Latin American Mutagen Society. She has published over 40 papers in refereed journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Carcinogenic human papillomavirus (HPV) in suburban U.S. female population

Sin Hang Lee
Milford Hospital, USA

Persistent infection by "carcinogenic" HPV is a tumor promoter in cervical cancer induction. However, the issues of persistence of an HPV infection can be adequately studied only when sensitive genotype-specific methods are available to the clinical laboratories which perform routine HPV tests for patient management. As cellular pathology advances from a low-grade intraepithelial lesion (LSIL) to a high-grade intraepithelial lesion (HSIL) and cancer, the viral load per abnormal cell tends to decrease. We have established a highly sensitive nested polymerase chain reaction (PCR) followed by direct automated DNA sequencing of the hypervariable region of the L1 gene for detection and genotyping of HPV in cervicovaginal cell suspensions from a suburban U.S. female population under the care of private gynecologists. Persistent HPV infection is defined as isolation of the same genotype of HPV on repeated testing over a period of 6 months to 3 years. The results of the HPV genotyping were correlated with those of companion Pap cytology tests, and follow-up biopsies. We found that all specimens with LSIL or HSIL cytology test results were associated with an HPV infection. However, the overwhelming majority of clinical specimens which were found to contain "carcinogenic" HPV, even classified as "persistent infection" on repeated testing, were negative in Pap cytology test, or did not progress to HSIL which would indicate a need for immediate colposcopic biopsy. Our findings suggest that "carcinogenic" HPV infection is a weak tumor promoter in cervical cancer induction among women under the health care provided by private gynecologists.

Biography

Sin Hang Lee, M.D. graduated from Wuhan Medical College, China, and is qualified to practice medicine in the United States, Canada and the United Kingdom. He was certified by the American Board of Pathology, and obtained the F.R.C.P.(C) degree by examination in 1966. Dr. Lee has been practicing pathology in New Haven, Connecticut, since 1971. Dr. Lee's most recent research is on DNA sequencing-based genotyping of human papillomavirus from clinical specimens, and sequencing-based molecular diagnosis of Chlamydia trachomatis, Neisseria gonorrhoeae and Borrelia burgdorferi infections. Dr. Lee is currently a pathologist at Milford Hospital, and the director of Milford Medical Laboratory.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The 'tether drop' hypothesis for the mechanism of chromosomal aberrations

Leon P. Bignold
Institute of Medical and Veterinary Science, Australia

Chromosomal aberrations involve not only breaks in double strands of DNA, but also inappropriate rejoinings of broken ends of DNA. These abnormalities can be induced by a variety of chemical agents and also by ionizing radiations. Most theories of the mechanisms of chromosomal aberrations involve these agents directly causing double strand breaks in DNA. However, numerous observations are inconsistent with this idea. Almost no chemicals are able to break DNA strands in aqueous solutions, and the doses of radiations required to produce double strand breaks in water are much higher than are needed to produce chromosomal aberrations in living cells. Many chemicals, such as caffeine and acridines do not react covalently with DNA. Certain drugs which cause chromosomal aberrations, especially the etoposides do not react with DNA. These are known to act on enzymes (topoisomerases) which create breaks in DNA strands as part of physiological unraveling of DNA. Current theories also offer no clear explanation of in rejoinings of DNA strands.

Here it is suggested that chromosomal aberration-inducing agents act on the 'tether' component of the enzyme complexes which break DNA *in vivo* – mainly the enzymes of unraveling, synthesis, repair and transcription of DNA. During the period of time in which these complexes carry out their primary action, a component of each complex must tether the broken ends of the DNA strand in place until the last phase of the process – ligation – occurs. Thus if the tether function (often carried out by accessory proteins) of a complex were to fail while the strand-breaking site on the enzyme was acting, then broken ends of DNA could become free in the nuclear space. In relation to re-joining, if additional undamaged accessory proteins and other broken ends were also present in the same space, then the broken strands of DNA could be brought together and acted on by the ligase. All of the known forms of chromosomal aberrations, including ring forms and tri-radials, as well as deletions and amplifications, can be explained by this mechanism acting in the various phases of the cell cycle. Moreover, mutation(s) of 'tether' protein genes may contribute to the unstable aneuploidy ('karyo-unstable phenotype') in cancer cell populations.

Reference: Bignold LP (2009) Mutation Research, 681: 271-298.

Biography

Leon Bignold graduated in medicine from the University of Western Australia in 1971, completed a research doctorate 1978, qualified as a histopathologist in 1980 and has been worked in academic and diagnostic pathology ever since. He has published over 70 papers and edited vol 96 of EXS (Cancer: Cell Structures, Carcinogenesis and Genomic Instability, 2006). With colleagues, he has published a volume (2007) on David Paul Hansemann (1858-1920), who was the first to suggest a chromosomal theory of cancer. Dr Bignold is currently completing a volume on genomic models for complex clinical, pathological and therapeutic aspects of tumors.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The autophagic tumor stroma model of cancer: Role of oxidative stress and ketone production in fueling tumor cell metabolism

Stephanos Pavlides
University of Manchester, Paterson Institute for Cancer Research, USA

A loss of stromal caveolin-1 (Cav-1) in the tumor fibroblast compartment is associated with early tumor recurrence, lymphnode metastasis and tamoxifen-resistance, resulting in poor clinical outcome in breast cancer patients. Here, we have used Cav-1 (-/-) null mice as a pre-clinical model for this "lethal tumor micro-environment". Metabolic profiling of Cav-1 (-/-) mammary fat pads revealed the upregulation of numerous metabolites (nearly 100), indicative of a major catabolic phenotype. Our results are consistent with the induction of oxidative stress, mitochondrial dysfunction and autophagy/mitophagy. The two most prominent metabolites that emerged from this analysis were ADMA (asymmetric dimethyl arginine) and BHB (beta-hydroxybutyrate; a ketone body), which are markers of oxidative stress and mitochondrial dysfunction, respectively. Transcriptional profiling of Cav-1 (-/-) stromal cells and human tumor stroma from breast cancer patients directly supported an association with oxidative stress, mitochondrial dysfunction and autophagy/mitophagy, as well as ADMA and ketone production. MircoRNA profiling of Cav-1 (-/-) stromal cells revealed the upregulation of two key cancer-related miR's, namely miR-31 and miR-34c. Consistent with our metabolic findings, these miR's are associated with oxidative stress (miR-34c) or activation of the hypoxic response/HIF1a (miR-31), which is sufficient to drive authophagy/mitophagy. Thus, via an unbiased comprehensive analysis of a lethal tumor micro-environment, we have identified a number of candidate biomarkers (ADMA, ketones and miR-31/34c) that could be used to identify high-risk cancer patients at diagnosis, for treatment stratification and/or for evaluating therapeutic efficacy during anti-cancer therapy. We propose that the levels of these key biomarkers (ADMA, ketones/BHB, miR-31 and miR-34c) could be (i) assayed using serum or plasma from cancer patients or (ii) performed directly on excised tumor tissue. Importantly, induction of oxidative stress and autophagy/mitophagy in the tumor stromal compartment provides a means by which epithelial cancer cells can directly "feed off" of stromal-derived essential nutrients, chemical building blocks (amino acids, nucleotides) and energy-rich metabolites (glutamine, pyruvate, ketones/BHB), driving tumor progression and metastasis. Essentially, aggressive cancer cells are "eating" the cancer-associated fibroblasts via autophagy/mitophagy in the tumor micro-environment. Lastly, we discuss that this "Autophagic Tumor Stroma Model of Cancer Metabolism" provides a viable solution to the "Autophagy Paradox" in cancer etiology and chemo-therapy.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Helicobacter pylori promotes angiogenesis in gastric cancer cells depending on cyclooxygenase-2-mediated vascular endothelial growth factor via p38MAPK/ATF-2 pathway

Qi Li

Putuo Hospital, Shanghai University of Traditional Chinese Medicine, China

Angiogenesis, the growth of new blood vessels, is closely related with the incidence and development of gastric cancer, but the pathogenesis of angiogenesis is still unknown in *Helicobacter pylori* (*H. pylori*) -induced gastric cancer. Previously, we reported that *H. pylori* could increase the expression of COX-2 via p38MAPK in vitro. In this study, we established a mice model of *H. pylori* infection to define the exact role of *H. pylori* infection in gastric carcinogenesis. Microvessel density (MVD) and Vascular endothelial growth factor (VEGF) mRNA expression in gastric mucosa were significantly higher in *H. pylori* infected mice than that in untreated mice after 72 weeks. Further analysis revealed that *H. pylori* infection induced VEGF through COX-2 gene by the activation of p38MAPK. Thus, inhibition of either COX-2 or p38MAPK suppressed *H. pylori* infection induced VEGF at mRNA and protein level. In conclusion, our study has provided the first direct evidence that *Helicobacter pylori* induces C57BL/6 mice gastric adenocarcinoma and enhances VEGF expression via p38MAPK /COX-2 pathway.

Biography

Qi Li has completed his Ph.D and MD.at Shanghai University of Traditional Chinese Medicine and postdoctoral studies from Cornell University. He is the director of Laboratorial Center and the chief of Research Branch at Putuo Hospital in Shanghai. He has published more than 50 papers in reputed journals, including 5 papers in SCI, and serving as an editorial board member of Tumor, Shanghai Traditional Chinese Medicine, and so on.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Overexpression of 17beta hydroxysteroid dehydrogenase type 12 (hsd17b12) correlates with poor prognosis in ovarian cancer

Marta Szajnik

Poznan University of Medical Sciences, Poland

Introduction: There is growing evidence for the role of 17β-hydroxysteroid dehydrogenase (HSD17B) in the pathogenesis and development of various hormone-dependent carcinomas. The aim of the study was to correlate HSD17B isoform 12 (HSD17B12) expression with clinicopathologic outcome in patients with ovarian cancer and to determine its role in growth and progression of this tumor.

Methods: Tumor specimens from 100 untreated patients with ovarian cancer were evaluated for HSD17B12 by immunohistochemistry and correlated with clinicopathologic characteristics, patient outcome and 5 year follow-up. Ovarian carcinoma cell lines OvCa, A2780 and AD10 were used in this study. Since A2780 OvCa cell line expressed the highest level of HSD17B12, this cell line was used for further studies. siRNA knockdown of the enzyme was performed and its effects on tumor cell proliferation and Annexin V binding were determined.

Results: HSD17B12 expression was observed in all tumor samples, but the staining intensity was variable. Normal ovarian epithelium was negative. Patients with tumor showing weak/moderate expression of HSD17B12 had a better overall survival than those with strongly positive tumors ($p<0.001$). The time to first recurrence was longer for patients with tumors with heterogenous staining relative to patients with tumors that were uniformly positive ($p<0.001$). Upon silencing of HSD17B12, tumor cell growth was inhibited ($p<0.005$), and apoptosis of tumor cells increased ($p<0.05$). Arachidonic acid but not estradiol reversed the growth inhibition mediated by HSD17B12 knockdown.

Conclusion: The overexpression of HSD17B12 is an independent marker of poor survival in patients with OvCa and might be considered the potential target for immunotherapy. Expression and function of this enzyme are essential for OvCa progression.

Biography

Marta Szajnik, MD PhD MPH graduated from Poznan University of Medical Sciences, Poznan, Poland in 2004 and completed her PhD in 2007. She also carried out postdoctoral studies at the University of Pittsburgh Cancer Institute from 2007-2009. She is currently a 2nd year resident in ObGyn at the Department of Gynecology Oncology in Poznan University of Medical Sciences in Poland and continues her research on ovarian cancer immunology in the collaboration with Dr. Theresa L. Whiteside from the University of Pittsburgh Cancer Institute. Dr. Szajnik has co-authorized 18 papers published in peer-reviewed journal. In 2011 she received Scholar-in-training award of the American Association for Cancer Research during the annual meeting in Orlando, FL. She is the Principal Investigator of the ovarian cancer research grant of the Polish Ministry of Sciences and Higher Education.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The mechanism & causes of carcinogenesis and mutagenesis in eukaryotes

Shaukat Iqbal Malik

Mohammad Ali Jinnah University, Islamabad campus, Pakistan

A process by which normal cells are transformed into cancer cells is term as Carcinogenesis. Carcinogenic: A carcinogen is any material, radionuclide or radiation that is a cause directly involved in the exacerbation of cancer or in the increase of its proliferation. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes all cancers involve the failure of genes that control cell growth and division. The process by which cancers develop is called carcinogenesis. This process usually starts when chemicals or radiation damage DNA, of the cells. Viruses induce carcinogenesis by introducing new DNA sequences. Mostly, when DNA becomes damaged the body is able to repair it. In cancer cells, however, the damaged DNA is not repaired and normal cells with damaged DNA die, while the cancer cells with damaged DNA continue to multiply. There is a long time delay between exposure to a carcinogen and the occurrence of cancer. While cellular mutations cause cancer to develop, it is not exactly clear how this happens. Carcinogenesis is a multistep process, in which as many as ten diverse mutations may have to accumulate in a cell before it becomes cancerous. The fact that so many mutations are needed for a cancer to develop indicates that cell growth is normally controlled through many sets of checks and balances. Mutation is the sudden heritable change in the genetic material of an organism. The term mutation is applicable to both the change in genetic material and to the process by which the change occurs. Thus the term mutation is used to define the process as well as the effect. Mutation is simply an alteration in the nucleotide sequence of a DNA molecule. Physical agents like UV or chemical molecules can cause mutations. Molecules or agents that cause mutations are called as mutagens. Mutations occur non specifically and there is no defined process to carry out mutation in a cell or organism.

Recombination on the other hand occurs at a particular time, with the help of a set of enzymes and in a defined process. Thus mutation and recombination are not the same. But mutation and recombination are central events in genetics and evolution. Mutations created in an individual by the process of mutagenesis are called as induced mutations. Damaging to the DNA-such as heat or a lack of oxygen-these also tend to increase the mutation rate in cancer cells.

Biography

Dr. Shaukat Iqbal Malik has earned his PhD Degree in 2004 from the National and Kapodistrian University of Athens & Cancer Cytogenetic and Environmental Hygiene Laboratory, NCSR Demokritos, Athens and two Postdoc 1st from NHEERL, Cancer Biology branch (Cytogenetics section) US Environmental Protection Agency RTP Complex, NC and 2nd from Lineberger Comprehensive Cancer Center, Biomedical Research Imaging Center University of UNC at Chapel Hill, USA. He is Associate prof. in the department of Computer science & Bioinformatics, Mohammad Ali Jinnah University, Islamabad, Pakistan. He has published more than 20 papers in reputed journals and serving as an editorial board member of reputed international journal. He has been received Best Faculty member in 2005 and excellent professor award years 20090-10. His New Cytogenetics Techniques has been published in English, German, French and Greek language. He has been visited about 20 countries including USA and EU for Acedamid and research activities. In 2007 he wins amounting Pak Rs.4.0 Million Research Project under National Research Program for Universities from HEC Pakistan.

Track 8, 8(i) 8(ii) 8(iii)

8: OMICS in Cancer Research
8(i): Oncogenomics
8(ii): Cancer Research: Clinical & Experimental
8(iii): Cancer: Genomics & Proteomics

Session Chair

Dr. Gary Guishan Xiao

Creighton University Medical Centre, USA

Session Co-Chair

Dr. Rakesh Srivastava

The University of Kansas Medical Center, USA

Session Introduction

Title: MicroRNAs induce tamoxifen sensitivity by down-regulation of estrogen receptor alpha signaling in breast cancer

Dr. Gary Guishan Xiao, Creighton University Medical Centre, USA

Title: Characterisation and impact of circulating tumor cell diversity on therapy response and metastasis formation

Dr. Katharina Pachmann, Universitätsklinikum Jena, Germany

Title: Lovastatin inhibits T cell proliferation while preserving the cytolytic function of EBV-,CMV- and MART-1-specific CTLs

Dr. Qing Ma, University of Texas M.D. Anderson Cancer Center, USA

Title: Anti-tumor effect of sFlt-1 gene therapy system mediated by Bifidobacterium Infantis on Lewis lung cancer in mice

Dr. Hong Zhu, West China Hospital, China

Title: An investigation of PD-L1 expression and its association with tumor infiltrating T cells in human cervical carcinomas

Dr. Xu Man, Chongqing Medical University, China

Title: To compare efficacy and cost effectiveness of different 5ht3 blockers in acute and delayed nausea and vomiting:a randomized study

Dr. Shukla Piyush, All India Institute of Medical Sciences, India

Title: Functional genomics to identify cancer targets

Dr. William C. Hahn, Dana-Farber Cancer Institute, USA

Title: The anti-tumor role of gene UBTD1 and a positively regulatory

Dr. Xiaowei Zhang, Fudan University, Shanghai Cancer Center, China

Title: Inhibition of pancreatic cancer stem cell characteristics in human and KrasG12D transgenic mice by resveratrol

Dr. Rakesh Srivastava, The University of Kansas Medical Center, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

MicroRNAs induce tamoxifen sensitivity by down-regulation of estrogen receptor alpha signaling in breast cancer

Gary Guishan Xiao
Creighton University School of Medicine, USA

MicroRNAs (miRNAs) have important regulatory functions in breast cancer tumorigenesis. We previously found that let-7 miRNAs were significantly downregulated in breast cancer tissues, and further demonstrated that these miRNAs target estrogen receptor alpha, resulting in cancer cell apoptosis in breast cancer cell lines. Tamoxifen resistance is a major clinical event in endocrine therapy of breast cancer. Recent studies suggest that overexpression of estrogen receptor (ER)-α36 may be associated with tamoxifen resistance. We hypothesize that let-7 miRNAs family may induce tamoxifen sensitivity by suppressing estrogen receptor (ER)-α36. In this study, we used qRT-PCR to examine expression of let-7 family miRNAs in resistant breast cancer cell lines to tamoxifen as well as expression of estrogen receptor (ER)-α36, a variant of ER-α66, after let-7 miRNA transfection. Immunoblot analysis was employed to check protein expression in FFPE tissue and breast cancer cell lines. Luciferase reporter assay was used to detect direct regulation of let-7 miRNA on ER-α expression. Cell proliferation assay was carried out after transfection of let-7 miRNAs. We found that there was an inverse correlation between the expression of ER-α36 and let-7 family miRNAs (b and i) in the FFPE tissue set. Let-7 miRNA sequences match sequence in the 3' untranslated region (3' UTR) of ER-α36, indicating ER-α36 may be a target of let-7. Co-transfection of let-7 mimics (b and i) with ER-α36 3' UTR luciferase construct decreased the activity of reporter gene. Conversely, let-7 inhibitors (b and i) enhanced the reporter gene activity. Transfection of let-7 mimics (b and i) inhibited both the mRNA and protein levels of ER-α36. On the contrary, transfection of let-7 inhibitors (b and i) enhanced the ER-α36 expression at both mRNA and protein levels in 184A1 cells. The high expression of ER-α36 in tamoxifen resistant MCF7 cells can be inhibited by transfection of let-7 mimics (b and i) and sensitivity toward tamoxifen is enhanced. We conclude that let-7 miRNAs enhance sensitivity of breast cancer cells to tamoxifen through suppression of the expression of ER-α36, suggesting that let-7 could be therapeutic target for breast cancer treatment.

Biography

Dr. Xiao is an Associate Professor and the Director of the Functional Genomics and Proteomics laboratories at the Creighton University School of Medicine, and an internationally recognized expert in the field of genomics and proteomics of cancer and bone disease. Dr. Xiao earns his Ph.D. in molecular computational biology at Chinese Academy of Sciences. He had his postdoctoral research trained in Baylor College of Medicine and UCLA, focusing on pharmacokinetics and biochemistry of non-steroid inflammatory drugs, and cell cycle regulation. He has been regular reviewer or ad hoc reviewer for several medial journals, different funding agency and several journal Editorial Board members.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Characterisation and impact of circulating tumor cell diversity on therapy response and metastasis formation

Katharina Pachmann
Universitätsklinikum Jena, Germany

Shedding of cells from solid tumors can occur during growth, diagnostic manipulation (mammography, finde needle aspiration, punch biopsy) and surgery as the first step in the metastatic pathway. However, it requires additional steps for such cells to settle, grow and invade the host tissue in order to form overt metastasis. Most cells released from the primary tumor seem not to be capable to perform these additional steps.

We have shown, the cells released from solid tumors can recirculate in the body, they respond to therapy in a comparable way as the primary tumor, but in always all cases cells are left over after therapy which sooner or later can regrow and form metastases even after years. We now are investigating which properties allow the cells to survive therapy and which prerequisites are necessary to allow them to regrow. This will not only contribute to clarify the mestastic pathways but also help to find ways to target these cells as the origin of new metastases.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Bifidobacterium Infantis on Lewis lung cancer in mice

Hong Zhu[1], Zhaojun Li[1], Shuhua Mao[2], Buyun Ma[1], Shengtao Zhou[1], Licong Deng[1], Taiguo Liu[1], Dandan Cui[1], Yaqin Zhao[1], Jianping He[1], Cheng Yi[1] and Ying Huang[1]

[1]West China Hospital, Sichuan University, China
[2]Department of Oncology, Center Hospital, China

Soluble fms-1ike tyrosine kinase receptor (sFlt-1) is soluble form of extramembrane part of VEGFR-1 that has antitumor effects. Bifidobacterium Infantis is a kind of nonpathogenic and anaerobic bacteria which may have specific targeting property of hypoxic environment inside of solid tumors. The aim of the present study was to construct Bifidobacterium Infantis-mediated sFlt-1 gene transferring system and investigate its anti-tumor effect on Lewis lung cancer (LLC) in mice. Our results demonstrated that the Bifidobacterium Infantis-mediated sFlt-1 gene transferring system was constructed successfully and the system could express sFlt-1 at the levels of gene and protein. This system could not only significantly inhibit growth of HUVECs induced by VEGF in vitro, but also inhibit the tumor growth and prolong survival time of LLC C57BL/6 mice safely. These data suggest that Bifidobacterium Infantis-mediated sFlt-1 gene transferring system presents a promising therapeutic approach for the treatment of cancer.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

An investigation of PD-L1 expression and its association with tumor infiltrating T cells in human cervical carcinomas

Xu Man[1], Wang Yuqi[1], Xu Guangxu[1], Geng Weipu[1] and Tang Junying[2]

[1]Department of Pathology, Molecular Medicine and Cancer Research Center
[2]Gynecology of the first affiliate hospital, Chongqing Medical University, China

Purpose: To observe the expression of Programmed death receptor-ligand 1(PD-L1) and the association between PD-L1 expression and T cell infiltration in human cervical carcinomas.

Methods : PD-L1 and PD-1 expression was respectively determined in five cases of normal cervical tissue, 7 cases of high-level cervical intraepithelial neoplasia (CIN II-III) and 67 cases of cervical carcinomas by immunohistochemistry staining; the tumor infiltrating $CD4^+$T and $CD8^+$T cells were determined by immunofluorescent staining, and the apoptosis of tumor infiltrating lymphocytes was examined by TUNEL assay in those cases.

Results: No PD-L1 expressed in normal cervical epithelium; PD-L1 negatively or weakly expressed in epithelia of high grade CIN, the average relative optical density was 0.82 ± 0.75; and PD-L1 expressed in 70% (47/67) cervical carcinomas, the average relative optical density in superficial infiltrating (<0.5 cm) and deep infiltrating cervical squamous cell carcinomas was 2.70 ± 1.68 and 2.90 ± 1.72. PD-1 expressed in partial tumor infiltrating lymphocytes in those cases. PD-L1 expression density of cervical carcinomas was significantly higher than that of CIN (P<0.01); PD-L1 expression density of superficial invasive cervical carcinomas was slightly lower than that of deep invasive cases, but there was no significant statistic difference between them; in addition, PD-L1 expression negatively associated with the number of tumor infiltrating $CD8^+$T cells(r =-0.82, P<0.01), but not with the number of $CD4^+$T cells (r =-0.05, P> 0.05). Apoptosis occurred in partial tumor infiltrating lymphocytes of cervical carcinomas.

Conclusion: Human cervical carcinoma cells express PD-L1, and it negatively associates with the number of tumor infiltrating $CD8^+$T cells, but not with the number of $CD4^+$T cells. PD-L1 expression of tumor cells may play role on apoptosis of tumor infiltrating lymphocytes.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

To compare efficacy and cost effectiveness of different 5ht3 blockers in acute and delayed nausea and vomiting:a randomized study

Shukla Piyush

Department of radiotherapy , All India Institute of Medical Sciences, India

AIM:to compare efficacy and cost effectiveness of three different 5-HT3 blockers in controlling early and delayed nausea and vomiting following chemotherapy. MATERIALS AND METHOD:30 patients in each group of advanced head and neck malignancy were given cisplatin based induction chemotherapy.All received anti emetics before and during chemo(group1:condensation iv 16mg prechemotherapy and 8mg iv tds during infusion,group 2:granisetron3mg iv prechemo and 3mg iv during chemo infusion, group 3:palonosetron0.25mg iv prechemo). Nasea &vomiting were assessed according to common toxicity criteria for a period of 3 days baseline was matched for age group , stage and histology of tumor .RESULT : among the 78 patients who completed the study , group 2 had 2 & 4 cases respectively of acute and delayed emesis that was significantly lower than the other 2 groups (6 and 11 for group 1 and 2 & 10 for group 3), also overall cost in controlling delayed nausea & vomiting was much lower in group 2. CONCLUSION: the study reflects that granisetron group was the best 5HT3 blocker in terms of efficacy and cost effectiveness to control acute and delayed nausea and vomiting taking into account the Indian patient with respect to economic and health status .

Keywords : 5HT-3 blockers,chemotherapy,delayed nausea and vomiting.

Biography

Piyush Shukla has completed his MD in Radiation Oncology at the age of 28 from Barkatullah University Bhopal M.P. He is presently working as a Senior Resident in the department of Radiotherapy at All India Institute Of Medical Sciences N.Delhi. One of his paper has been selected in TRICITY H&N CANCER meet 2011 at Singapore.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Functional genomics to identify cancer targets

William C. Hahn
Dana-Farber Cancer Institute, USA

Recent advances in genomics now make it possible to consider enumerating all of the genetic lesions in specific cancers. While these approaches will yield critical information regarding the identify, number, and types of alterations found in human tumors, a complementary approach to decipher the molecular basis of malignant transformation depends upon the application of genome scale tools to annotate the function of genes involved in cancer initiation and progression. Over the past several years, we have developed genome scale RNAi libraries and open reading frame expression libraries that permit a systematic evaluation of genes involved in cancer initiation and maintenance. Using these libraries, we have now performed screens in a panel of human cancer cell lines to systematically identify cancer vulnerabilities. By combining these functional approaches with information derived from mapping the structural abnormalities present in cancer genomes, we have identified several new oncogenes that contribute to cancer development. In addition, many commonly occurring and well-validated oncogenes and tumor suppressor genes remain refractory to molecularly targeted therapies. An alternative strategy for targeting such cancer drivers is to identify gene products that, when suppressed or inhibited, result in cell death only in the presence of an oncogenic allele. Through the use of systematic RNAi screens, we have identified several genes that act as synthetic lethal partners to known oncogenes. Taken together, these studies suggest that combining forward and reverse genetic approaches with information derived from the cancer genome characterization projects will yield a comprehensive list of cancer vulnerabilities and establish a general approach for the rational identification of oncogenic and co-dependent pathways in cancer.

Biography

Dr. Hahn is an Associate Professor at the Dana-Farber Cancer Institute and Harvard Medical School. He is the director of the Center for Cancer Genome Discovery and a Senior Associate Member of the Broad Institute. His laboratory focuses on using functional genomics to study cancer.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The anti-tumor role of gene UBTD1 and a positively regulatory loop between UBTD1 and p53

Xiaowei Zhang, Jin Li and Weijian Guo

Department of Medical Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, shanghai 200032, China

Cellular senescence is a powerful barrier to oncogenesis and the mechanisms is unclear. P53 is one of the important genes in regulating cellular senescence. It was reported that p53 can bind to the promoter of UBTD1, which suggested that it may play an important role in the down stream of p53. Currently little is known about the role and mechanism of gene UBTD1 (Ubiquitin domain containing 1). Here we provide the evidence that UBTD1 is overexpressed in senescent fibroblast cells and normal gastric mucous tissues, and lowexpressed in gastric cancer cell lines and gastric cancer tissues transcriptionally and translationally, which suggests that it may play an important role in oncogenesis. We originally found the function of UBTD1 in inducing senescence, inhibiting oncogenesis and cell migration in both p53 mutant and p53 wild-type cancer cell lines by gene transfection, which suggested that UBTD1 does not depend on p53 absolutely. We also found that Ubiquitin domain is the active part of UBTD1. P53 can positively regulate the expression of *UBTD1* mRNA by directly binding to the promoter of UBTD1 by ChIP assay, and UBTD1 can inversely increase the level of p53 protein possibly by enhancing the stability of p53 protein, which preliminarily elucidate there might be a new positive regulatory loop between UBTD1 and p53. Further research is still necessary to elucidate the exact mechanism, Which may provide useful prognosis factor and new method of therapy for clinical work.

Biography

Xiaowei Zhang is presently working on his PhD at the age of 28 years at Fudan University Shanghai Cancer Center China. He is also an physician in oncology department. At present, His works involve with the target therapy of cancer and the role of some important cancer related genes.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Inhibition of pancreatic cancer stem cell characteristics in human and Kras^{G12D} transgenic mice by resveratrol

R.K. Srivastava[1], S-N. Tang[1], M. Rodova[1], D. Nall[2] and S. Shankar[2]

[1]Department of Pharmacology, Toxicology and Therapeutics, and Medicine, The University of Kansas Medical Center, USA
[2]Department of Pathology and Laboratory Medicine, The University of Kansas Medical Center, USA

Background: Cancer stem cells (CSCs) can proliferate and self-renew extensively due to their ability to express anti-apoptotic and drug resistant proteins, thus sustaining tumor growth. Therefore, the strategy to eradicate CSCs might have significant clinical implications. The objectives of this study were to examine the molecular mechanisms by which resveratrol inhibits stem cell characteristics of pancreatic CSCs derived from human primary tumors and KrasG12D transgenic mice.

Methodology/principal findings: Human pancreatic CSCs (CD133+CD44+CD24+ESA+) are highly tumorigenic and form subcutaneous tumors in NOD/SCID mice. Human pancreatic CSCs expressing high levels of CD133, CD24, CD44, ESA, and aldehyde dehydrogenase also express significantly more Nanog, Oct-4, Notch1, MDR1 and ABCG2 than normal pancreatic tissues and primary pancreatic cancer cells. Similarly, CSCs from KrasG12D mice express significantly high levels of Nanog and Oct-4 than pancreatic tissues from Pdx-Cre mice. Resveratrol inhibits the growth (size and weight) and development (PanIN lesions) of pancreatic cancer in KrasG12D mice. Resveratrol inhibits the self-renewal capacity of pancreatic CSCs derived from human primary tumors and KrasG12D mice. Resveratrol induces apoptosis by activating capase-3/7 and inhibiting the expression of Bcl-2 and XIAP in human CSCs. Resveratrol inhibits pluripotency maintaining factors (Nanog, Sox-2, c-Myc and Oct-4) and drug resistance gene ABCG2 in CSCs. Inhibition of Nanog by shRNA enhances the inhibitory effects of resveratrol on self-renewal capacity of CSCs. Finally, resveratrol inhibits CSC's migration and invasion and markers of epithelial-mesenchymal transition (Zeb-1, Slug and Snail).

Conclusions/significance: These data suggest that resveratrol inhibits pancreatic cancer stem cell characteristics in human and KrasG12D transgenic mice by inhibiting pluripotency maintaining factors and epithelial-mesenchymal transition. In conclusion, resveratrol can be used for the management of pancreatic cancer.

Track 9(i) 9(ii) 9(iii) 9(iv) 9(v)

9(i): Breast cancer
9(ii): Liver, Prostate & Kidney Cancer
9(iii): Blood, Lung & Leukemia Cancer
9(iv): Bone & Thyroid Cancer
9(v): Gastrointestinal & Colorectal Cancer

Session Chair

Dr. Samir A. Farghaly

The Medical College of Cornell University, USA

Session Co-Chair

Dr. Eldad Zacksenhaus

University Health Network, Canada

Session Introduction

Title: **Identifying and targeting tumor initiating cells (TICs) in mouse models of breast cancer**

Dr. Eldad Zacksenhaus, University Health Network, Canada

Title: **Susceptibility alleles of breast cancer in high, moderate and low penetrance genes in a South American population**

Dr. Lilian Jara, School of Medicine-University of Chile, Chile

Title: **Pharmacogenomics predictions for breast cancer treatments´ efficacy and toxicity**

Dr. Hugo A Barrera Saldaña, University of Nuevo León, México

Title: **A novel feedback loop with therapeutic implications in estrogen receptor-negative breast cancer**

Dr. Ali Naderi, The University of Queensland, Australia

Title: **Molecular classification of breast cancer and role of immunohistochemistry for detection of cell types that predicts response to chemotherapy with Santinib (P53)**

Dr. M. H. Bukhari, King Edward Medical University, Pakistan

Title: **Combining biologics and cytotoxics in the treatment of inoperable cholangiocarcinoma**

Dr. Lars Henrik Jensen, Vejle Hospital and University of Southern Denmark, Denmark

Title: **Stability analysis on liver cancer related miRNA in serum**

Dr. Xian-Feng Ding, Zhejiang Sci-Tech University, China

Track 9(i) 9(ii) 9(iii) 9(iv) 9(v)

Title: **The status of anti-metastatic gene therapy in Patients with advanced epithelial ovarian cancer**

Dr. Samir A. Farghaly, The Medical College of Cornell University, USA

Title: **Detection and quantification of circulating Melanoma cells in patients with cutaneous malignant Melanoma**

Dr. Mel Ziman, Edith Cowan University, Western Australia

Title: **A high prevalence of metabolic syndrome in a group of colorectal patient's pre surgery– A pilot study**

Dr. Sissi C. Stove Lorentzen, Oslo University Hospital, Norway

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Identification of a new prognostic signatures and therapeutic targets for HER2+ and triple negative breast cancer using subtype-specific mouse models

Eldad Zacksenhaus

Toronto General Research Institute – University Health Network, Canada

HER2$^+$ and Triple-Negative Breast Cancers (TNBC) represent highly aggressive subtypes. HER2+ BC is commonly treated with chemotherapy plus anti-HER2 drugs, such as Herceptin. Drug resistance, high cost and side effects limit the use and benefits of anti-HER2-therapy worldwide. There is therefore great interest in an effective prognostic predictor and novel therapeutic targets for HER2$^+$ breast cancer. We identified MMTV-Her2/Neu mammary tumor-initiating cells (TICs) and showed that non-adherent tumorspheres can be used as surrogate for TICs (Can Res. 2007, Clin Can Res. 2009). Using improved conditions, we have further enriched Her2/Neu TICs to a frequency of 1/20-1/40. A 17-gene TIC-specific signature derived from differentially expressed genes in TICs versus non-TICs predicts survival in multiple human HER2$^+$ BC cohorts with hazard ratios of over 8, and can be used to stratify HER2$^+$ patients for anti-HER2 therapy (submitted). Using a lentiviral shRNA screen, we also identified several kinases required for Her2/Neu tumorsphere growth, for which no previous requirement for their function in HER2$^+$ BC has been described (in progress).

TNBCs often contain loss-of-function mutations/alterations in the tumor suppressors RB1, p53 and Pten. We showed that conditional deletion of Rb in mammary stem cells/bipotent progenitors led to tumors that clustered with luminal-B or TNBC. The latter contained mutations in p53. Combined deletions of Rb and p53 led exclusively to TNBC (J. Clin Invest. 2010, Cell Cycle, 2011). Similarly, inactivation of Pten in mammary epithelium induced diverse tumor types, whereas combined deletion of Pten and p53 led to TNBC-like tumors (in progress). Drug and shRNA screens have identified several agents/targets that specifically kill Rb/p53, Pten/p53 mutant TNBC as well as human TNBC lines but not immortalized mammary epithelial cells (in progress).

Biography

Dr. Eldad Zacksenhaus earned his PhD at the University of Toronto in Molecular Genetics on the cloning of UBE1, and postdoctoral training at the Hospital for Sick Children on the tumor suppressor RB. He is senior scientist at University Health Network and Associate Professor of Medicine, University of Toronto. His research is focused on tumor suppressors, in particularly Rb, breast cancer, cancer stem cells and targeted therapy for HER2 and TNBC (JCI, 2010, JCB, 2010, Cancer Res. 2010, Autophagy, 2011, PLoS One, 2011, Cell Cycle 2011). He's a co-organized of the "International RB Symposium" Nov. 17-18, 2011, Toronto, Canada.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Susceptibility alleles of breast cancer in high, moderate and low penetrance genes in a South American population

Lilian Jara

Faculty of Medicine, University of Chile, Chile

Breast cancer (BC) is the most common cancer among women worldwide. There are few studies of BC susceptibility alleles in South American populations. Here we describe the identification of risk variants in genes BRCA1, BRCA2 (high penetrance), CHEK2, RAD51, XRCC3 (moderate penetrance), rs2981582 and rs1219648 (low penetrance) in Chilean families at high-risk for breast/ovarian cancer (n=326). Germline BRCA1/2 point mutations were found in 7.1% of families. Families with at least three BC and/or OC cancer cases showed the highest frequency of mutation (15.9%). We identified 14 point mutations, of which 3 in BRCA1 and 3 in BRCA2 were recurrent, possibly reflecting region-specific founder effects. In CHEK2, the 1100delC mutation was not detected in the 1320 samples analyzed. The Thr241Met (XRCC3) polymorphism was associated with increased BC risk (OR=2.44, 95%CI=1.34–4.43). The RAD51 135G>C polymorphism increased BC risk among BRCA1/2-negative women with a) a family history of BC and b) age at onset <50 years (OR=2.17, 95%CI=1.11-4.29). The combined Thr/Met–E/G (RAD51D) genotype was associated with increased BC risk among the same group of women (OR=10.5 [95%CI 1.16–94.5]). Our results suggest that variability in XRCC3 and RAD51D plays a role in BC risk via a mutual interaction between the genes. The combined SNPs rs2981582 – rs1219648 (A/A–G/G) of FGFR2 genotypes were associated with increased risk for estrogen-receptor positive BC (OR=2.6, 95%CI=1.2–5.6]). Our results are consistent with a polygenic model for familial BC susceptibility.

Biography

Lilian Jara completed her PhD at 30 at a Chilean University, and postdoctoral studies at Sheffield University (UK). She is a full professor in the Human Genetics Program, University of Chile School of Medicine. She has published over 60 papers in reputed journals and serves as a WJMG editorial board member. She conducts longitudinal studies of women from Chilean families with genetic mutations related to breast cancer. She is also interested in gene-gene interactions underlining hereditary breast cancer. She collaborates with research groups studying the genetics of breast cancer from Argentina, Colombia, Spain, Canada, and the USA.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Pharmacogenomics predictions for breast cancer treatments´ efficacy and toxicity

Hugo A. Barrera-Saldaña

Vitaxentrum and School of Medicine of Autonomous University of Nuevo León. México

Breast cancer is the major cause of death among Mexican women between 35 and 50 years of age. Among the most prescribed chemotherapeutic agents are Capecitabine, a precursor of 5-flourouracil, which inhibits the synthesis of thymidine and DNA replication, and tamoxifen, a chemotherapeutic adjuvant that prevents recurrence in estrogen receptor positive patients that have undergone surgery. Capecitebine needs to be efficiently eliminated by dihydropyrimidine dehydrogenase (DPD) to avoid its accumulation and adverse effects. Tamoxifen is a prodrug that needs the P450 liver enzyme isoform CYP2D6 for conversion to its active form, endoxifen. Therefore, prediction of efficacy and toxicity in breast cancer chemotherapy depends on pharmacogenomics.

PHARMAchip™ is a DNAchip developed by Progenika Biopharma, SA (Bilbao, Spain) that consists of a microscopic slide carrying hundreds of oligonucleotides to screen for mutations and single nucleotide polymorphisms in genes of phase I, phase II, transporters, receptors and other enzymes and proteins with which drugs interact after entering the patient´s body and metabolism. Among the genes present on this DNAchip genotype are those for the P450 and pyrimidine metabolism enzymes described above.

We are using the PHARMAchip to investigate its usefulness as a predictor of chemotherapy efficacy and toxicity in Mexican breast cancer patients. The first fifty genomic DNAs from these patients analyzed reveal that most (almost 85%) patients carry a genotype corresponding to a phenotype of normal to extensive metabolism of tamoxifen with no mutations in the DPD gene that would otherwise cause 5-Fluorouracil derivative accumulation.

Biography

The author completed his PhD at the age of 25 and is a distinguished alumnus from the University of Texas at Houston. His postdoctorate was at Louis Pasteur University in Strasbourg, France. He has created prestigious Molecular Biology Research and Graduate Programs and Centers in Mexico. He is the founder of Vitaxentrum, a premier Biotechnology and Genomics Consulting and Servicing Organization. He has published over 100 papers in prestigious journals and has served as reviewer of international journals and national academic committees. His team is recognized in Latin America as a pioneer and leader in molecular biology, DNA diagnostics, biotechnology, and gene therapy.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

A novel feedback loop with therapeutic implications in estrogen receptor-negative breast cancer

Ali Naderi

The University of Queensland Diamantina Institute, Australia

Estrogen receptor-negative (ER-) breast cancer is a heterogeneous disease with limited therapeutic options. Molecular apocrine subtype constitutes 50% of ER- breast tumors and is characterized by a steroid-response signature including androgen receptor (AR) and a high rate of ErbB2 amplification. We have identified a positive feedback loop between the AR and ERK signaling pathways in molecular apocrine breast cancer. In this process, AR regulates ERK phosphorylation and kinase activity. In addition, AR inhibition results in the down-regulation of ERK target proteins including phospho-RSK1. Furthermore, AR-mediated induction of ERK requires ErbB2 and AR activity, in turn, regulates ErbB2 expression as an AR-target gene. These findings suggest that ErbB2 is an upstream connector between the AR and ERK signaling pathways. Another feature of this feedback loop is an ERK-mediated regulation of AR. In this respect, the inhibition of ERK phosphorylation reduces AR expression and CREB1-mediated transcriptional regulation of AR acts as a down-stream connector between the AR and ERK signaling pathways.

Importantly, this feedback loop has therapeutic implications in molecular apocrine breast cancer. There is an *in vitro* synergy between AR and MEK inhibitors in reducing cell viability and inducing apoptosis in molecular apocrine cells. In addition, we have demonstrated an *in vivo* synergy between AR and MEK inhibitors using a xenograft molecular apocrine model. Moreover, the combination therapy with these inhibitors can overcome trastuzumab resistance in molecular apocrine cells. Therefore, a combination therapy strategy with AR and MEK inhibitors may provide an attractive therapeutic option for ER-/AR+ subtype of breast cancer.

Biography

Ali Naderi is a clinician-scientist in oncology with a special interest in breast cancer research. He carried out his medical oncology fellowship at Mayo clinic, Minnesota and a post-doctoral research fellowship at Hutchison/MRC Research Center, University of Cambridge UK. He currently has a faculty position as a clinician-scientist at the University of Queensland, Australia. He has an American board certification in Medical Oncology and more than 25 publications in cancer research field.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Molecular classification of breast cancer and role of immunohistochemistry for detection of cell types that predicts response to chemotherapy with Santinib (P53)

M. H. Bukhari

King Edward Medical University, Lahore, Pakistan

Breast cancer is a heterogeneous group of malignant lesion resulted by abnormal gene expression within neoplastic cells. Recent advances in molecular techniques have enabled researchers to identify the gene expression, fingerprint, of individual tumors that would help predict the clinical course and select specific treatment. Molecular techniques have also been used to refine the classification of special type cancers. Four major molecular subgroups of breast cancer normal-like, luminal (ER-positive), basal-like (mostly ER-negative), or erbb2+ (mostly HER-2 amplified) have been previously defined, based on expression of 424 genes involved in cancer development. Scientists have already shown that each subgroup has a different prognosis as luminal A, luminal B, HER2 and basal-like types. Luminal A cancers are ER+ and/or PR+, HER2- and have a Ki67 labeling index <14%. Luminal B tumors are either ER+ and/or PR+ and HER2+ (the luminal-HER2 subtype) or ER+ and/or PR+ with a Ki67 labeling index >14%. HER2 tumors are ER-, PR and HER2+. As discussed below, basal-like cancers are most commonly ER-, PR-, HER2- and show expression of CK5/6 and/or EGFR.

The classification of breast cancer into molecular subgroups may be needed in order to develop the most accurate predictors of treatment response. In our experience, different sets of genes present in different molecular subgroups may determine the response to a particular regimen of chemotherapy. Luminal A type breast carcinoma shows better prognosis and best response to endocrine therapy and less response to chemotherapy. Patients with basal like are heterogeneous group of young age victims and triple negative with poor prognosis but shows good response to chemotherapy (Taxol/FAC). The cancers having extra copies of the HER2 gene and several other genes are called HER2 group. They usually have a high-grade appearance under the microscope. These cancers tend to grow more quickly and have a worse prognosis, Women with a relatively uncommon type of breast cancer are significantly more likely to face its recurrence and spread, Although they often can be treated successfully with targeted therapies such as trastuzumab (Herceptin), Santinib (P53) and lapatinib.

Biography

Dr Bukhari completed his doctorate in Surgical Pathology with the theoretical and practical combination of Histopathology, Immunohistochemistry and PCR at the King Edward Medical University in 2007. After his doctorate he attended the special course of Breast Pathology in Harvard School of Public Health in 2009. He has started work with Prof Abbas Iqbal and Eyyad H A Kamel on Chemothearpeutic effect of Sanatinib.e in triple negative patients and HER 2 Positive cases.

Combining biologics and cytotoxics in the treatment of inoperable cholangiocarcinoma

Lars Henrik Jensen

Department of Oncology, Vejle Hospital and University of Southern Denmark, Denmark

Cholangiocarcinomas are adenocarcinomas arising in the biliary tract epithelium either intrahepatic or extrahepatic. The disease is rare and a standard chemotherapy regime for inoperable disease has only been internationally accepted in the last few years. Based on phase III data from the ABC02 trial, gemcitabine combined with a platinum is now the treatment of choice. In other tumors from the gastrointestinal tract, the addition of newer biological compounds such as monoclonal antibodies and tyrosine kinase inhibitors has increased the efficacy of cytotoxics. Data on this approach is sparse in cholangiocarcinoma.

A comprehensive literature search identified a few studies on monotherapy with biologics. Only sorafenib, erlotinib, and lapatinib have been tested in reasonably large studies to estimate whether the drugs may be efficacious as monotherapy. The most promising drug was erlotinib with a response rate of 8%. Sorafenib has low activity with a 2% response rate while no responses were observed with lapatinib. Cetuximab and midostaurin have shown specific effect, but in a very limited number of patients.

More data is available for biologics combined with cytotoxics. Bevacizumab, cetuximab, and selumetinib have been shown to be tolerable and to have effect when combined with chemotherapy. It may not be superior to chemotherapy alone, but e.g. cetuximab have been shown to revert chemoresistance.

More phase II data preferably from randomized trials is needed in order to select the most promising combination of biologics and cytotoxics for phase III trials. International collaboration is mandatory for conducting larger trials.

Biography

Lars Henrik Jensen is a medical doctor currently working in a hospital setting serving half of the Danish population with inoperable cholangiocarcinoma. He completed his Ph.D in 2007 and has been an exchange visitor at University of Southern California. His primary areas of research are gastrointestinal cancers, clinical trials, and molecular markers.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Stability analysis on liver cancer related miRNA in Serum

DING Xian-Feng, LI Yan and GUO Jiang-Feng
Zhejiang Sci-Tech University, P.R. China

MicroRNAs (miRNA) are non-coding, single-stranded RNAs of ~22 nucleotides and constitute a novel class of gene regulators that are found in both plants and animals. Recent evidence has shown that miRNA mutations or aberrantly expression correlate with various human cancers and indicated that miRNAs can function as tumour suppressors and oncogenes. While many studies have focused on miRNA expression in physiological and pathological processes, variables related to miRNA for new serum biomarkers have simultaneously emerged. Now miRNA has been applied to early detection of cancer and monitoring of cancer recovery by using detection of peripheral blood.

Up to present, there are no reports regarding of liver cancer specific miRNA biomarkers in serum for the great threat of liver cancer to human life. Therefore a systemic research on the characteristic of miRNA is quite necessary.

Liver cancer Huh-7 cell-line, liver tumor tissues and clinical serum samples were performed in the role of experiment material. A systemic treatment, such as different temperature(-80□, -20□, 4□, room temperature and 37□) treated for 3h, in room temperature treated for 0, 1, 3, 6, 12, 24 hours, RNase A treated for 0, 3, 6, 12 hours incubation in 37□, DNase I treated for 0, 3, 6, 12 hours incubation in 37□, different free-thaw cycles (0, 2, 5, 7, 10 cycles) treated, different pH value (control, pH=1, 6, 9, 13) of solution treated for 3h incubation in 37□ were performed before Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) analysis with 40 cycles. Furthermore, liver cancer related miRNAs were detected in each reaction. We used 18S rRNA as control gene. All the results indicated that 18S rRNA was fragile for decreased relative expression sharply. MiRNAs could be resistant to harsh conditions simultaneously. The p-value indicated the repeatability of the data by using the Student's t-test. $P < 0.05$ was considered to be significant.

Meanwhile, we evaluated the Pearson's correlation coefficient of liver cancer related miRNAs expression of 22 healthy human subjects by qRT-PCR. Expression levels of serum miRNAs were reproducible and consistent among 22 healthy human subjects for the R value was access to 1, p-value □0.05. The result was considered to be significant. Pearson correlation scatter plot of the relative serum miRNAs expression between male and female of R^2 was 0.0953. Results suggested that miRNA expression is not correlated between genders.

Taken together, these results implied that liver cancer related miRNA (miRNA-21, -25, -29c, -93, -198, -221, -222) expression levels in serum were quite stable, also present and detectable, reproducibly consistent among individuals of the same species in serum. They will be potential for serum liver cancer biomarkers in future.

On the other side, it is difficult to obtain abounding and high-quality of RNA in serum. Our tests have shown that pre-heating procedure is a robust serum RNA extraction method and efficient for RNA isolation. This method is also essential for further serum source microRNA study. In fact, after qRT-PCR, the C_T (threshold cycle) value decreased at least 5. In conclusion, based on our study, pre-heating provided an optimized protocol for serum RNA isolation.

Biography

Xianfeng Ding is an associate professor of Biology, and is Director of the Biological Science Experiment center at the Zhejiang Sci-Tech University,Xianfeng Ding holds a BS degree in chemistry from Shanxi Normal University and a MD degree in Chemistry from Jiangnan University ; Pursuing research in the interdisciplinary areas of chemistry and biology, she did some research biochip technology for novel methods in emerging life and medical science fields by biochip technology at Dr. Gao' lab at University of Houston, seeking for a potential molecular biomarker for liver injury, correlation and quantitation of microRNA aberrant expression in tissues and sera from different tumors, research has been continuously funded by the National High-Tech Research & Development Program of China (Grant No. 2007AA02Z165) and Zhejiang Nature Science Foundation of China((Grant No.Y2100681), She has published more than 20 papers in reputed journals, has more than six issued and pending patents and is general manager of biotechnology companies with success in product commercialization.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The status of anti-metastatic gene therapy in patients with advanced epithelial ovarian cancer

Samir A. Farghaly
Medical College of Cornell University, USA

Ovarian cancer is the foremost cause of death from gynecological cancer in the developed world. In the USA 27,000 new cases of ovarian cancer, and 14,000 deaths are reported each year. About 80% of patients with ovarian cancer present with metastatic disease. The overall 5-year survival rate for women with cancer is 30%. The epithelial cells of the ovary constitute 1% of the total ovarian mass but constitute 90% of the ovarian neoplasms. Epithelial ovarian cancer (EOC) spreads initially by direct extensions into adjacent organs, especially the fallopian tubes, uterus, and contralteral adenexa and occasionally the rectum, bladder, and pelvic side wall . After direct extension, epithelial ovarian cancer frequently disseminates via transcoelmic route, with 70% of patients having peritoneal metastases at staging laparotomy. The correlation between molecular profiles and metastatic spread varies depending on tumor type and metastatic site and is combination of 2 models. First, tumors are genetically heterogeneous and that metastases arise from colones with a genetically acquired metastatic phenotype, and that the clonoal genotype determines the final site of metastases. The second model is that metastatic cells are not a genetically primary tumor, instead they arise as stochastic event, with a low but finite probability from tumor cell clones distinct from the primary tumor. Several cofactors , such as MMP-2/-9 inhibitor, TNF, lypmphotoxin a, Fas Ligand Fas L, APO3L, TRAIL, interleukin -8, and P38 MAPK regulating ovarian cancer cells attachment to omentum and /or peritoneum have been identified, and would have noticeable clinical inhibition of the metastatic process, by enabling the identification of cellular or molecular targets that therapeutically viable. That would be able to block the steps necessary for ovarian cancer metastasis within the peritoneal cavity.

Biography

Samir A. Farghaly is a physician / Scientist- faculty member at the Medical College of Cornell University, and the New York Presbyterian Hospital/ Cornell University Medical Center, New York, NY – USA. He received his M.D degree from University College, London University and his PhD degree in molecular biology from London University. He was affiliated with Columbia University College of Physicians and surgeons/ Columbia University medical center, New York, NY. He received several clinical and research awards. He has been an invited speaker in several national and international conferences on Women's health, Molecular genetic of female cancers, Gynecological cancer and Oncology. He is a member of several national and international societies, organizations, foundations of Women health and Cancer. He is an editor, member of editorial boards, editorial advisory boards and reviewers of several medical journals of Cancer Science & Therapy, Gynecology, Gynecological Cancer, Ovary Research, Genomics, Clinical & Experimental Obstetrics and Gynecology, and Oncology. He has published 78 articles in reputed peer review journals. He is an editor of a book on ovarian cancer (To be published in 2011).

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Detection and quantification of circulating melanoma cells in patients with cutaneous malignant melanoma

M Ziman, M. Millward, R. Pearce, M. Lee, P. Kumarasinghe and A. Ireland
Edith Cowan University, Western Australia

Our research is aimed at detection, characterisation and quantification of circulating melanoma cells in patients with Cutaneous Malignant Melanoma. This research will assist with development of a prognostic blood test for the detection of melanoma micrometastases in patients before and after surgery and during therapy to assess efficacy. To date we have used qRT-PCR to assess circulating melanoma cells in 300 melanoma patients and 100 healthy volunteers. The frequency and level of expression of markers was correlated to Breslow tumour thickness and tumour progression and results were statistically analysed. Control blood samples spiked with cells from metastatic melanoma cell lines were used as positive controls. Antibodies to melanoma cell markers have also been used in flow cytometry and immunomagnetic bead capture experiments to isolate circulating cells from patient blood samples. Our results clearly demonstrate the presence of circulating melanoma cells in 79% of patients with stage III and IV disease whilst these markers were observed in only 20-30% of early stage patients. Assay sensitivity tests showed that markers can be detected from as few as 5 cells per blood sample. Surprisingly, melanoma cells are found in peripheral blood of patients with early stage tumours and in patients from whom tumours were removed several years previously. Using immunomagnetic bead capture we have quantified the circulating cells in patient blood and found that cell number correlates with disease stage particularly when specific cell surface markers are used to isolate cells. Further research will clarify the molecular signature of metastatic circulating melanoma cells.

Biography

Mel Ziman completed her Ph.D at the University of Cape Town and postdoctoral studies from the University of Western Australia School of Medicine. She is the director of ECU Melanoma Research Foundation, a leading melanoma research group in Western Australia. She has published more 70 papers in reputed journals and serves as a reviewer for several journals and grant review panels worldwide.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

A high prevalence of metabolic syndrome in a group of colorectal patients pre surgery– A pilot study

Sissi C. Stove Lorentzen, Ingunn Bergstad, S.Gharagozlian
Oslo University Hospital, Norway

Introduction: Colorectal cancer (CRC) is considered a cancer of high income countries and several environmental factors including body fatness and abdominal fat are associated with CRC. Nutritional status of the patients will have an impact on the postoperative recovery period and long term survival. A pilot study was designed to evaluate the appropriateness of commonly used physical and nutritional screening tools on the colorectal patient population at the time of the pre-surgery assessments.

Methods: Over a 6 month recruitment period, 29 patients (median age 65 (62;72) were included into the study. Baseline nutritional status was determined for all patients before intervention by using Subjective Global Assessment (SGA), Body mass index and waist circumference. Metabolic syndrome was determined using the International Diabetes Foundation criteria. Selected biochemical markers and physical tests were also included.

Results: Twenty-two patients (76 %) were classified as well nourished and seven patients (24 %) as moderately malnourished. Sixteen patients (55 %) had metabolic syndrome. Among the physical tests, the handgrip test was significantly associated with SGA ($p = 0.02$).

Conclusion: The results from the pilot confirm results from other studies which show that CRC patients may suffer from overnutrition as well as undernutrition. SGA should not be the only screening in assessing CRC patients prior to surgery. The high number of patients with metabolic syndrome must be confirmed, however, this knowledge suggests a necessity for nutritional counselling in this patient group post surgery, which is in accordance with the World Cancer Research Fund recommendations of 2007.

Biography

Sissi Stove Lorentzen has completed her MS /RD at the age of 48 from the University of Oslo in 2009. She is currently working at Oslo University Hospital as a clinical nutritionist/dietitian in the field of surgery and cancer. Her master thesis was a pilot study which investigated the effect of perioperative nutrition given to a group of colorectal cancer patients.

Sedegheh Gharagozlian has completed her Ph.D at the age of 50 years from Oslo University. She has published 3 papers in reputed journals and has been served as a journal referee for 2 journals. She has worked at Oslo University Hospital as a clinical nutritionist/dietitian in the field of gastrointestinal surgery and intensive nutrition, since 1998.She is a member of the Norwegian scientific committee for food safety. She is also a member of Advisory group in Oslo university hospital to develop a common guideline for ICU.

10: Cancer Genetics

Session Chair

Dr. John E. Thompson

University of Waterloo, Canada.

Senesco Technologies Inc., USA

Session Co-Chair

Dr. P. Ryan Potts

UT Southwestern Medical Center, USA

Session Introduction

Title: SNS01- An eIF5A-based biologic with significant anti-tumoral activity following systemic administration in a murine model of multiple myeloma

Dr. John E. Thompson, University of Waterloo, Canada & Senesco Technologies Inc., USA

Title: The MAGE protein family: Protein degradation, genome stability, and cancer

Dr. P. Ryan Potts, UT Southwestern Medical Center, USA

Title: GATA4 represses ERBB2 expression in cancer cells : A new tumor suppressor?

Dr. Jean Imbert, Inserm - Université de la Méditerranée, France

Title: GUC as potential DNA topoisomerase inhibitors to reduce the growth of cervical cancer cells

Dr. Hassan Hadi Abdallah, Universiti Sains Malaysia, Malaysia

Title: Influence of hypoxia on signaling pathways upon treatment with CK2 inhibitors in selected human tumor cell lines

Dr. Olaf Georg Issinger, University of Southern Denmark, Denmark

Title: The small GTPase hRAB37 acts as a metastatic suppressor via inhibition of MMP/FAK/RhoA signal in lung cancer

Dr. Yi-Ching Wang, National Cheng Kung University, Taiwan

Title: Gene Silencing in HIV-1 Latency by Polycomb Repressive Group

Dr. Kyung-Chang Kim, Korea National Institute of Health, Korea

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

SNS01- An eIF5A-based biologic with significant anti-tumoral activity following systemic administration in a murine model of multiple myeloma

John E. Thompson[1,2], Catherine Taylor[1] and Richard Dondero[2]

[1]Department of Biology, University of Waterloo, Canada
[2]Senesco Technologies Inc., USA

Eukaryotic translation initiation factor 5A (eIF5A) is post-translationally modified to hypusine-eIF5A and is the only known protein to contain hypusine. Recent studies have indicated that unhypusinated eIF5A is strongly pro-apoptotic, initiating both mitochondrial and death receptor mediated apoptosis, whereas hypusine-modified eIF5A has a pro-survival function

SNS01 has two therapeutic components: (1) an RNAi-resistant plasmid with a B-cell-specific (B29) promoter encoding $eIF5A^{K50R}$, a mutant of eIF5A that cannot be hypusinated; and (2) an siRNA that selectively suppresses endogenous hypusinated eIF5A which promotes growth of cancer cells. SNS01 nanoparticles are formed by complexing these therapeutic nucleic acids with polyethylenimine (PEI), a synthetic cationic polymer that serves as a delivery vehicle. SNS01 induces apoptosis in both IL-6-responsive (KAS-6/1) and IL-6-independent (U266) myeloma cell lines and exhibits anti-tumoral activity when administered systemically to SCID mice bearing subcutaneous human multiple myeloma (KAS-6/1) tumors. Control mice treated with PEI nanoparticles containing a non-expressing plasmid and a non-targeting siRNA had an average tumour volume of 284 mm^3 at the time of sacrifice, whereas mice treated with 1.5 mg/kg or 0.75 mg/kg SNS01 exhibited significant tumor regression and had average tumor volumes of 13 mm^3 (95 % inhibition; *p = 0.026) and 24.5 mm^3 (91 % inhibition; *p = 0.03), respectively. TUNEL-labeling of tumor tissue indicated that tumor regression induced by SNS01 is attributable to apoptosis. Bio-distribution studies have indicated that that SNS01 nanoparticles are also taken up by B cells in the bone marrow. Thus SNS01 may be an effective treatment option for multiple myeloma patients.

Biography

John Thompson is Professor of Biology and Associate Vice-president, Research at the University of Waterloo, Chief Scientific Officer for Senesco Technologies Inc and a Fellow of the Royal Society of Canada.

Catherine Taylor is a Senior Research Associate in John Thompson's laboratory.

Richard Dondero is Vice-president, Research and Development at Senesco Technologies Inc.

The MAGE protein family: Protein degradation, genome stability, and cancer

P. Ryan Potts
UT Southwestern Medical Center, USA

Cancer-testis antigens (CTAs), including the MAGE protein family, are genes whose expression is typically restricted to the germline, but are aberrantly expressed and presented as antigens in human tumors. Surprising recent evidence suggests that the aberrant expression of MAGE CTAs in tumors is not simply an inert consequence of widespread genomic deregulation, but rather an important functional event promoting tumorigenesis. Furthermore, the expression of MAGE CTAs correlates with poor prognosis in a variety of cancer types. However, the mechanism through which MAGE CTAs promote tumorigenesis has been enigmatic. In this study, we investigated the biochemical and cellular function of the large MAGE protein family comprising more than 60 members, many of which are CTAs. Using a variety of *in vitro* and cellular assays, we identified common binding partners of more than ten MAGE proteins, solved the crystal structure of one MAGE protein, investigated the biochemical activity of MAGEs, and discovered a cellular function of several MAGE CTAs relevant to their oncogenic activity. We found that a common feature of MAGE proteins is their ability to bind to and enhance the activity of E3 RING ubiquitin ligases, such TRIM28/KAP1, through a conserved tandem winged-helix domain. Importantly, we show that several MAGE-TRIM28 ubiquitin ligase complexes directly ubiquitylate and degrade the critical p53 tumor suppressor. Thus, we have identified a novel, cancer-specific regulator of p53 degradation and discovered the function of the enigmatic MAGE protein family. These results underscore the importance of MAGE proteins as therapeutic targets for cancer.

Biography

Ryan Potts obtained his B.S. from the University of North Carolina in 2000. In 2003 he entered into the Cell Regulation Ph.D. program at UT Southwestern Medical Center under the mentorship of Hongtao Yu in the department of Pharmacology. He completed his dissertation in 2007 studying the molecular and biochemical processes that safeguard the genome. Afterward, he stayed on at UT Southwestern Medical Center as an independent investigator in the department of Biochemistry as a Sara and Frank McKnight fellow. Currently, his research is focused on understanding the basic molecular, genetic, and cellular events that give rise to cancer.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

GATA4 represses ERBB2 expression in cancer cells : a new tumor suppressor?

Jean IMBERT

Inserm and Université de la Méditerranée, France

Overexpression of the receptor tyrosine kinase ERBB2 observed in 20-30% of breast cancers is a poor prognosis indicator associated with resistance to chemotherapy. We have shown that a negative feedback regulatory loop associates the tyrosine kinase receptor ERBB2 and the transcription factor GATA4 in breast cancer cells[1]. At least six transcription factors (CSDA/ZONAB, FOXP3, GATA4, MYB, PAX2, PEA3) acting as transcriptional repressors of the *ERBB2* gene have been described so far. We have recently proposed that *ERBB2* gene amplification is used to overcome repression of its expression by sequence-specific transcription factors[2]. In parallel, nuclear translocation of some RTKs has been previously described. Hence, ERBB2 and 2 other members of the EGFR family were reported to translocate in the nucleus, to bind to gene promoters and to activate or repress the transcription of specific genes. Although the mechanism how intact receptors extricate themselves from the plasma membrane remains unclear. For ERBB2, a nuclear translocation process involving endocytosis, endosomal sorting, importin β and nuclear pore complex protein has been proposed. This gene encodes 2 major isoforms (ERBB2a and b). ERBB2b lacks a signal peptide and can located in the nucleus. Humanized monoclonal antibodies targeting the membrane-anchored form of ERBB2 are a major anti-cancer therapy in ERBB2+ patients. Nevertheless, resistance to treatment is often observed. Whether the nuclear form of ERBB2b is a cause of this resistance remains to be demonstrated.

Biography

Jean Imbert completed a Ph.D. at Université de la Méditerranée (Marseille) and postdoctoral studies at NHI/NCI (Bethesda, MD). He co-headed the laboratory of Molecular and Functional Immunology before establishing his own research group in 1996 at Inserm U119. In 2007, he moved to the campus of Marseille-Luminy where he leads the research group of Transcriptional Regulations and the platform Transcriptomics and Genomics Marseille-Luminy (TGML). He is currently studying the transcriptional regulatory networks involved in various cancers. He has contributed more than 70 peer reviewed international journals in the field and provided more than 100 lectures in France and abroad.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

GUC as potential DNA topoisomerase inhibitors to reduce the growth of cervical cancer cells

Hassan Hadi Abdallah[1], Mohammad T.M Al-dajani[2], Jamal Talaat[3], Akeem Akiboro[1], Khoo Boon Yin[4] and Nornisah Mohamed[2]

[1]School of Chemical Sciences, Universiti Sains Malaysia, Malaysia.
[2]School of Pharmaceutical Sciences, Universiti Sains Malaysia, Malaysia.
[3]Virginia Commonwealth University, USA.
[4]Institute for Research in Molecular Medicine (INFORMM), University Sains Malaysia, , Malaysia

Many topoisomerase inhibitors are recently being identified as anticancer agents, capable of interrupt the normal functions of type I and type II topoisomerases needed for the progression of cell division; hence, uncontrolled proliferation of cancerous cells can be hindered. In view of this, we investigated the inhibitory effects of five new synthesized compounds on the activities of topoisomrases I and II , and on the growth of HeLa and Hs27 cells. The growth of HeLa cells was significantly inhibited when the cells were treated with 500 ng/ml and 1000 ng/ml of the compound (PYMBV) for 48 h, resulting to 62.5% ($p<0.05$) and 58.2% cell viability, respectively. This was similar to the growth inhibition of the HeLa cells when treated with different concentrations of the compound (26PANM) for 48 h. The inhibitory effect of the compound (26PANM) on the growth of HeLa cells incubated for 24 h. was significant ($p \leq 0.05$) at all the tested concentrations. For the compound (GUC), inhibition of the growth of HeLa cells treated with 500 and 1000 ng/ml concentrations of this compound for 48 h. was significantly different from control. The compound (MP5NO) significantly inhibited HeLa cells' growth when treated with 500 ng/ml concentration. However, inhibition of the growth of HeLa cells by the compound (26PAN) was not significant for 24 h and 48 h treatments. None of the synthesized compounds was able to inhibit the growth of Hs27 cells incubated for 24 h and 48 h. The observed antiproliferative activity of these compounds against HeLa cells could not be unconnected with their chemical structures. These results suggest that the compound (26PANM), among the synthesized compounds, stands promising as an anticancer drug.

Biography

Hassan Hadi Abdallah has completed his Ph.D at the age of 29 years from Baghdad University and postdoctoral studies from Universiti Sains Malaysia (USM). He is senior lecturer at the school of chemical sciences, USM, Malaysia. He has published more than 20 papers in reputed journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Influence of hypoxia on signaling pathways upon treatment with CK2 inhibitors in selected human tumor cell lines

Tine D. Rasmussen, Louise Linnebjerg Bohn Christoffersen, Olaf-Georg Issinger

Institute for Biochemistry and Molecular Biology University of Southern Denmark, 5230 Odense, Denmark

CK2 is an antiapoptotic protein kinase which has been shown to be elevated in all so far investigated tumors. CK2 is a druggable kinase, mainly owing to its multiple involvement in various diseases. Several selective inhibitors have been described and characterized *in vitro* and partly in mammalian cell lines. Here, we report the efficiency of some of the known CK2 inhibitors under normoxia and hypoxia in selected human tumor cell lines.

We have focused on signaling molecules such as: HIF1α, acetyl--cocarboxylase, CK2 subunits, Pim1, Pim3, PI3K, AKT, AMPK, ERK, p38, JNK and characterized their expression and activation (phosphorylation status) under normoxia and hypoxia and in the presence and absence of various CK2--specific inhibitors. We also investigated the influence of the various parameters on cell death induction. Beside these experiments using immunoblot analyses from cellular lysates, kinase activity measurements were performed using synthetic peptides harboring the corresponding kinase--specific consensus sequences. Moreover, immunohistochemical investigations were performed in order to study possible subcellular changes in signaling molecule locations upon the various challenges applied.

In summary the results showed some of the CK2--specific inhibitors were anti-- hypoxic, i.e. they prevented the expression of HIF1α during hypoxia thus establishing a link between protein kinase CK2 and hypoxia.

Biography

Olaf-Georg Issinger has completed his Ph.D at the age of 26 at the University of Freiburg in Germany followed by postdoctoral studies at the University of California, Davis. Currently he is professor at the Department for Biochemistry & Molecular Biology at the University of Southern Denmark. He has published more than 150 papers mostly on cancer research.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The small GTPase hRAB37 acts as a metastatic suppressor via inhibition of MMP/FAK/RhoA signal in lung cancer

Yi-Ching Wang

College of Medicine, National Cheng Kung University, Taiwan

Our previous data demonstrates that a small GTPase hRAB37, which is a member of Rab superfamily, plays a role in lung cancer progression. This study aims to investigate the functions of hRAB37 to regulate vesicle trafficking and its cell signals involved in cell migration. We demonstrated that hRAB37 is a tumor metastatic suppressor protein in lung cancer. Clinical data showed that low hRAB37 protein expression and promoter/exon1 hypermethylation of *hRAB37* gene correlated markedly with poor progression-free survival and overall survival in lung cancer patients. Overexpression of hRAB37 resulted in loss of migration/invasion ability in CL1-5 lung cancer cells-based assays and remarkably reduced lung tumor metastasis in animal models. Migration/invasion ability of CL1-5 cells was inhibited under the treatment of conditional medium taken from hRAB37 overexpressed CL1-5 cells resulting from an increased protein level of secreted TIMP-1 protein, which is an inhibitor of matrix metalloproteinases (MMPs). In addition, the decreased expression of MMP2 and MMP9, and FAK-mediated metastasis pathway, including p-FAK, p-AKT and RhoA activity, provided a potential mechanism for the metastasis suppression effects of hRAB37. Furthermore, confocal analysis demonstrated a co-localization of hRAB37 with the secretory marker VAMP2 and the RAB3a exocytosis protein. Confocal images demonstrated a colocalization between RAB37 and TIMP-1, an MMP inhibitor. Our data provided first compelling evidence from cell, animal, and clinical studies that hRAB37 small GTPase is a metastasis suppressor through exocyticly trafficking the anti-metastatic proteins such as TIMP-1. Low expression of hRAB37 due to promoter hypermethylation leads to poor survival of lung cancer.

Biography

Yi-Ching Wang is currently a Distinguished Professor at National Cheng Kung University, Taiwan. Prof. Wang received her Ph.D. from Genetic Program of Michigan State University in 1993. She studies the molecular mechanisms involved in lung tumorigenesis. Candidate gene study and research on cancer genomics and epigenomics are her main focus. Several potential anti-cancer drugs are also developing in her laboratory. Prof. Wang has published more than 50 SCI papers in prestigious journals such as J. Clin. Oncol., J. Clin. Invest., Cancer Res. and Oncogenes. Prof. Wang was one of the recipients for Excellent Research Award of Taiwan National Science Council.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Gene Silencing in HIV-1 Latency by Polycomb Repressive Group

Kyung-Chang Kim[1,4], Hyeon Guk Kim[1], Tae-Young Roh[2,3], Jihwan Park[2], Kyung-Min Jung[1], Joo-Shil Lee[1], Sang-Yun Choi[4], Sung Soon Kim[1] and Byeong-Sun Choi[1]

[1]Division of AIDS, Center for Immunology and Pathology, Korea National Institute of Health, Chung-buk, Republic of Korea
[2]Division of Molecular and Life Sciences, Pohang University of Science and Technology (POSTECH), Gyeongbuk, Republic of Korea
[3]Division of Integrative Biosciences and Biotechnology, Pohang University of Science and Technology (POSTECH), Gyeongbuk, Republic of Korea
[4]School of Life Science and Biotechnology, Korea University, Seoul, Republic of Korea

Latently infected memory T cells, which are a major obstacle to HIV-1 eradication, are very are (1million) in a patient and have a long half-life of over 44 months on average. The molecular linkage between HIV-1 latency and epigenetic control is not fully understood. We investigated HIV-1 latency related with Polycomb group (PcG)-proteins mediated gene silencing in novel HIV-1 latently infected cell lines, NCHA cells. The expression profiles for histone deacetylases (HDACs) and PcG proteins (EED, BMI1, RNIG2) in NCHA cells were characterized by RT-PCR, ELISA, IP, and western blot. The levels of histone acetylation and methylation at histone H3 Lys^{9} (H3K9) and Lys^{27} (H3K27) in HIV-1 latently infected cells were analyzed by western blot and chromatin immunoprecipitation-sequencing (ChIP-seq).

Histone H3K9 and H3K27 acetylations in NCHA cells showed no difference in parental and NCHA cells, whereas the levels of di- and tri-methylation at histone H3K9 and H3K27 were dramatically increased in NCHA cells except ACH2 cells. The expression of EED which is a component of polycomb repressive complex 2 (PRC2), and BMI-1 and RING2 which are constituents of PRC1 were upregulated in NCHA cells. In addition, more ubiquitylation at histone H2A was detected in NCHA cells. Also, high enrichment of H3K9me3 in the chromatin states of HIV-1 proviral genome was observed in HIV-latent cells, whereas there was no enrichment of H3K27me3.

Our result demonstrates that tri-methylation of H3K27 and H2A ubiquitylation via polycomb repressive complexes should be involved in HIV-1 latency and contribute to epigenetic gene silencing.

Biography

Dr. Kyung-Chang Kim has completed his Ph.D from Korea University, Korea, in this year. He is the staff scientist of Korea National Institute of Health. He works in a diagnosis of HIV and researches on HIV Latency.

Posters

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on Cancer Science & Therapy

15-17 August 2011 Las Vegas, USA

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Inhibition of breast cancer growth and angiogenesis by a medicinal herb: Spatholobus suberectus

Wang Zhiyu, Wang Neng and Chen Jianping

School of Chinese Medicine, University of Hong Kong, Hong Kong

Spatholobus suberectus (*SS*) is a traditionally used medicinal herb, which shows anti-inflammation, hematopoiesis and immunity enhancing properties. So far no detailed studies have been reported on its effects on human cancers. Thus we analyzed its effects on human breast cancer utilizing *in vitro* and *in vivo* methodologies. Aqueous extracts were prepared from dried roots of *SS*. Human breast cancer cell line MCF-7 and MDA-MB-231 were utilized for evaluating *SS* influences on tumor progression and angiogenesis process like proliferation, cell cycle, apoptosis, tube fromation and migration abilities. Both cancer xenografts were also built to determine the herb efficay in vivo. *SS* extracts inhibits proliferation and induces G2/M phase arrest in both cancer cells. Annexin V-PI staining and Western blotting analysis indicates that the mitochondrial pathway apoptosis is activated by *SS*. Angiogenesis experiments revealed that *SS* could inhibt VEGF expression in both cancer cells. Meanwhiel, the proliferation, tube formation and migration abilities of endothelial cells were also inhibited. The VEGFR-2 kinase activity of endothelial cells was also suppressed after *SS* administration. *In vivo* experiments demonstrated that *SS* extracts reduced tumor size and neoangiogenesis in both cancer xenografts. The preclinical study implied that *SS* might be of value as a breast cancer preventive and therapeutic agent by inducing apoptosis and inhibiting angiogenesis.

Biography

Mr. Wang Zhiyu is a PhD student focusing on cancer prevention by natural plants in school of Chinese Medicine, the University of Hong Kong. The research interests of our team can be divided into following directions: (1) Identification of cancer prevetion molecular targets; (2) Isolation and determination of active components from natural plants.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Isolation and immunomodulatory potential of oryzanol from crude rice bran oil in experimental animal models

Somsuvra B. Ghatak

Institute of Pharmacy, Nirma University,Gujarat, India

Tumor mediated immunosuppression is the greatest challenge in cancer treatment. Harnessing the immune system to stimulate and increase the immunocompetence and immune defense systems in cancer patients is the major goal of immunotherapy. Many of the presently available immunomodulators are not free from side effects including fever, neutropenia, leucopenia and allergic reactions. Hence, there is an urgent need to evaluate the potential of natural products as adjuvants to counteract the side effects of modern therapy. Recently, there has been a surge of global interest pertaining to the beneficial effects of commercially important bioactive phytochemicals like oryzanols and tocopherols, obtained from crude rice bran oil. Therefore, the present study was undertaken to investigate the effect of oryzanol on cell mediated and humoral immunity in various experimental animal models. The effects on immune response were assessed using haemagglutinating antibody titre, delayed-type hypersensitivity response, carbon clearance test and cyclophosphamide-induced myelosuppression models in experimental animals, divided in groups such as control, control induced, oryzanol treated (25, 50 and 100 mg/kg p.o.) and vitamin-E (100mg/kg p.o., as a naturally occurring conventional dietary antioxidant) treated. The treatment with oryzanol and vitamin-E was given for 28 days except in the cyclophosphamide induced myelosuppression model (for 10 days). Oryzanol and vitamin-E evoked a significant increase in antibody titre values in the haemagglunation test and potentiated the delayed type hypersensitivity reaction induced by sheep red blood cells. Both the drugs significantly ameliorated the serological parameters in cyclophosphamide induced myelosuppression and showed an increase in phagocytic index in the carbon clearance assay.

Biography

Somsuvra B. Ghatak is currently pursuing his Ph.D. in Pharmacology at Nirma University, India. He has been awarded with the INSPIRE Fellowship by the Department of Science & Technology, Govt. of India, in 2010. He has received the Gold Medal for being the 'BEST STUDENT' of the Masters of Pharmacy program in 2008.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Ellagic acid, a phenolic compound, exerts anti-angiogenesis effect through VEGF production and VEGFR-2 signaling pathway

Wang Neng, Wang Zhiyu and Chen Jianping

School of Chinese Medicine, University of Hong Kong, Hong Kong

Ellagic acid (EA) is natural phenolic constituent widely found in various berries, nuts and woody plants. It was reported that EA interfered with some angiogenesis-dependent pathologies. Yet the mechanisms involved were not fully understood. Thus we analyzed its anti-angiogenic effects and mechanisms on human breast cancer utilizing in vitro and in vivo methodologies. Effects of EA on VEGF secretion were detected by Elisa and RT-PCR assay using human breast cancer cell lines MCF-7 and MDA-MB-231. The influences of EA on endothelial cells were studied by proliferation, tube formation and migration experiments. Western blotting and gelatin zymography were utilized to explore the effects of EA on VEGFR-2 induced signaling pathway. Chorioallantoic membrane model and breast cancer xenografts were built to determine the anti-angiogenic effects of EA *in vivo*. We found that EA significantly inhibited cell viability of VEGF secretion of breast cancer cell lines. The VEGF-induced angiogenic processes including proliferation, migration and tube formation of human umbilical vein endothelial cells were also suppressed. We also found that EA could directly inhibit VEGFR-2 tyrosine kinase activity and VEGFR-2/MAPK pathways in endothelial cells. EA significantly inhibited neovessel formation in chick chorioallantoic membrane and tumor growth in mouse xenografts. The microvessel density and the VEGF and P-VEGFR-2 expression in tumors treated with EA were also significantly decreased. Taken together, EA can exert anti-angiogenesis effect through both VEGF production and VEGFR-2 signaling pathway.

Biography

Wang Neng is pursuing her MPhil degree in the direction of cancer prevention in school of Chinese Medicine at University of Hong Kong. The research interests of our team can be divided into following directions: (1) Identification of cancer prevetion molecular targets; (2) Isolation and determination of active components from natural plants.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

NONO and RALY are required for YB-1 oxaliplatin induced resistance in colon adenocarcinoma cell lines

Serges P. Tsofack
Université Laval, Canada

YB-1 is a multifunctional protein that affects transcription, splicing, and translation. Overexpression of YB-1 in breast cancers causes cisplatin resistance. In this study, we determined that YB-1 confers oxaliplatin resistance in colorectal adenocarcinomas. We also identify by mass spectrometry analyses important YB-1 interactors required for such oxaliplatin resistance in two colorectal cancer cell lines. A tagged YB-1 construct was used to identify proteins interacting directly to YB-1 in such cells. We then focused on proteins that are potentially involved in colorectal cancer progression based on the Oncomine public microarray database. Genes encoding for these YB-1 interactors were also examined in the public NCBI comparative genomic hybridization database to determine whether these genes are localized to regions of chromosomes rearranged in colorectal cancer tissues. From these analyses, we obtained a list of proteins interacting with YB-1 and potentially involved in oxaliplatin resistance. Oxaliplatin dose response curves of SW480 and HT29 colorectal cancer cell lines transfected with several siRNAs corresponding to each of these YB-1 interactors were obtained to identify proteins significantly affecting oxaliplatin sensitivity upon gene silencing. Only the depletion of either NONO or RALY sensitized both colorectal cancer cell lines to oxaliplatin. Furthermore, depletion of NONO or RALY sensitized otherwise oxaliplatin resistant overexpressing YB-1 SW480 or HT29 cells. These results suggest that NONO and RALY are significant potential target to counteract oxaliplatin resistance in colorectal cancers including tumors overexpressing the YB-1 protein.

Biography

Mr Serges P. Tsofack is a Ph.D. student at age of 27 at Cancer research center of Université Laval, Qc, Canada, working on deciphering the molecular mechanism(s) of chemoresistance in colon cancer, used Oxaliplatin drug. He carries out his Master's work at J. Craig Venter Institute, MD, USA. During the 2008-2009 on Oseltamivir (Tamiflu) drug resistance of H1N1 influenza virus and defended it at University of Dschang, Cameroon.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

A synergitic effect of therapeutic stem cells expressing a suicide enzyme, sytosine deaminase, with a prodrug and interferon-beta in the inhibition of endometrial cancer cell growth *In vitro*

Nam-Hee KANG, Hye-Rim LEE and Kyung-Chul CHOI

Laboratory of Veterinary Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University, Republic of Korea

In recent, gene-directed enzyme/prodrug theraphies (GEPT) have been highly regarded as an alternative means of gene therapy in anti-cancer treatments. As one of GEPT, *cytosine deaminse (CD)*/ 5-fluorocytosine (5-FC) system induces metabolic suicide of cancer cells following administration of prodrug 5-FC which is converted to a toxic agent, 5-fluorouracil(5-FU) by *CD*. In addition, human *interferon-beta* (*IFN-b*) gene presents antitumor effect by expressing *IFN-b*, a immunotherapeutic cytokine. In this study, we explored the therapeutic efficacy of *CD*/5-FC system and human *IFN-b* gene that were engineered into the human neural stem cell lines having the inherent tumor-tropic properties. Parental stem cell, HB1.F3, was modified by *E.coli CD* gene and human *interferon-beta* (IFN-b) gene to produce engineered stem cells, HB1.F3.CD and HB1.F3.CD. IFN-b, respectively. Endometrial Ishikawa cancer cell lines and engineered stem cells were cultured in 10% FBS containing DMEM. Using RT-PCR, we confirmed *CD* and *IFN-b* gene expressions in the engineered stem cells and of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2, in cancer cell lines. In a migration assay using modified transwells, HB1.F3.CD and HB1.F3.CD.IFN-b were effectively migrated to endometrial Ishikawa cancer cell lines, which can be attributed to chemoattractants secreted by cancer cells. In the cytotoxicity test using co-culture system and MTT assay, the viability of endometrial Ishikawa cancer cells was decreased in the presence of engineered stem cells. Especially, the viable cancer cells was more effectively reduced when co-cultured with HB1.F3.CD.IFN-b rather than HB1.F3.CD., which means that the fusion of *CD* and *IFN-b* genes may have a synergic antitumor effect. These results suggest that engineered stem cells expressing *CD* and/or *IFN-b* may have a therapeutic potential against endometrial cancer cells *in vitro* via a strong tumor tropism of stem cells and a cytotoxic effect of engineered gene products. Furthermore, our data provide proof for the use of genetically modified stem cell-based gene therapy through a targeted delivery of therapeutic gene products to endometrial cancer sites.

[This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No. 2010-0003093).]

Biography

Nam-Hee Kang is doing her master course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Identification of altered proteins by siRNA-mediated knockdown of nucleophosmin in glioblastoma cell line

Gimenez M

University of Sao Paulo, Brazil

In previous study, we reported that the protein nucleophosmin (NPM) was increased in glioblastoma multiforme (GBM) by 2D-electrophoresis analysis of tumor patient samples, when compared with normal brain tissue. NPM is a nucleolar phosphoprotein related to apoptosis, ribosome biogenesis, mitosis and DNA repair, but details about its function remain unclear. We have been investigating possible targets that can be altered when NPM gene is silenced by siRNA. The NPM knockdown was performed transfecting cells derived from GBM (U87MG) with siRNA (2, 4 and 7 days) followed by confirmation of silencing with real-time PCR and western blot. Non-transfected cells and cells transfected with siRNA scramble were used as control. We obtained a reduction of 80% in the NPM expression by siRNA after the fourth day of transfection, which was maintained until the seventh day in U87MG cell line. Peptides tagged with iTRAQ were separated by 2D-HPLC and identified by ESI-Q-TOF-MS. CID-MS/MS spectra were processed by MassLynx 4.0 and submitted to MASCOT (score >35 and $p<0.05$). We were able to identify 74 proteins. Four proteins were increased in cells transfected with siRNA-NPM and 14 presented reduction of expression (2-fold alteration in siRNA-NPM in comparison with controls). Among them, GRP78 presented a reduction of expression in siRNA-NPM1 cells. GRP78 is highly expressed in GBM patient samples and its expression level was confirmed by western blot. GRP78 is involved in ER stress response, anti-apoptotic process and chemo-resistance in cancer. The results reported here indicate that NPM may be a candidate for therapeutic target.

Biography

Marcela Gimenez is a Ph.D student from Brazil. She completed her Master Degree in Molecular and Cellular Biology at University of Sao Paulo, where develops her doctoral studies that will be concluded next year. She has experience with Biochemistry and Molecular Biology especially in proteomics and gliomas.

The role of ras signaling in tropomyosin-1 suppression in esophagus cancer

Maryam Zare

National Institute of Genetic Engineering & Biotechnology (NIGEB), Tehran, Iran

Esophagus cancer is the sixth most common cause of cancer-related death worldwide that its major subtype is squamous cell carcinoma (SCCE). Despite improvement in multimodality therapy, the survival rate of patients remains low. Therefore, a major research effort has been directed at better understanding of the underlying molecular alterations to provide new treatment. The progression of this tumor is associated with multiple genetic and epigenetic alterations. However, the contribution of Ras signaling pathway in esophageal cancer has not been extensively documented.

Tropmyosins (TM) are a family of cytoskeleton proteins that binds to actin microfilaments. Multiple isoforms of TM are expressed in non-muscle cells, including TM1, TM2, and TM3, which are downregulated in several human cancers. However, little is known about its underlying mechanism.

In this study expression of TM1 was analyzed in SCCE, relative to primary cell culture of normal esophagus, by immunoblot and real-time RT-PCR, also the involvement of Ras dependent signaling in TM1 downregulation further investigated. Our results showed that TM1 expression, both at protein and mRNA level, was significantly decreased in SCCE, relative to normal esophagus cells; indicating the importance of TM1 suppression in tumorigenesis of esophagus cancer. Moreover, inhibition of MEK/ERK and PI3K/Akt effectory pathways of Ras signaling could restore TM1expression in esophagus cancer cells. These data indicate that TM1 suppression occurs basically in SCCE; also activation of MEK/ERK and PI3K/Akt pathways involved in TM1 suppression, provide a new finding of the implication of Ras effectorry signaling in carcinogenesis of esophageal cancer.

Biography

Maryam Zare is the last year Ph.D student of Molecular Genetics in National Institute of Genetic Engineering & Biotechnology (NIGEB), Tehran, Iran. Her researches focused on genetic and epigenetic alterations, such as promoter hypermethylation and signaling pathways in squamous cell carcinoma of esophagus.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Salivary level of NF-*k*B cytokines in patients with oral squamous cell carcinoma and oral lichen planus patients compared to healthy subjects

Mahnaz Sahebjamee

Tehran University of Medical Sciences, Department of Oral Medicine and Dental Research Center, Iran

There are number of studies available in the literature that have studied and showed significant increase of NF-*k*B dependent cytokines, TNF-α, IL-1α, IL-6, and IL-8 in patients with oral squamous cell carcinoma (OSCC) and oral lichen planus (OLP). The aim of this study is to compare concentration level of such cytokines in whole unstimulated saliva (WUS) of patients with OSCC, OLP, and healthy subjects to find a potential simple and non-invasive method for monitoring malignant transformation of OLP. To this end, 25 cases from each OSCC, OLP, and age-sex-dental status matched control were enrolled in the study. The WUS samples were collected, and concentration levels of TNF-α, IL-1, IL-6, IL-8 were determined by ELISA. The results showed that the levels of the mentioned cytokines were significantly higher respectively in OSCC and OLP patients compared with the control group ($P<0.05$).According to the results, the average concentration level of TNF-α in OSCC was significantly higher than that in OLP, and in OLP higher than healthy subjects, respectively. In terms of IL-1α and IL-8, the average concentrations in OSCC were found to be significantly higher than that in control group. With respect to IL-6, average concentration in OSCC was determined to be significantly higher than that in OLP and control. The results indicate that change of NF-*k*B dependent cytokines in WUS may in part reflect the malignant transformation of OLP and the analysis of saliva may provide a useful and non-invasive method surrogates for monitoring OLP.

Biography

Mahnaz Sahebjamee has completed her Doctoral of Dental Surgery and specialty in Oral Medicine and Diagnosis both from Tehran University of Medical Sciences where she currently is a professor of dentistry. She has published numerous refereed scientific articles and has authored/co-authored 5 books. She has conducted several distinguished scholarly research projects leading to outstanding national and international awards.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Antitumor activity of the vh complementarity-determining region 3 (cdr3) synthetic peptide derived from monoclonal antibody a4 in melanoma cells

Santos L C P

Experimental Oncology Unit, São Paulo, SP, Brazil

Malignant melanoma is a skin cancer with increased worldwide incidence. Tumor-specific monoclonal antibodies (mAb) have been used as an alternative to conventional chemotherapy for treatment of metastases. Recently, we showed that a murine melanoma B16F10-directed mAb, named A4, recognizes the cell adhesion molecule protocadherin β13 and is cytotoxic in vitro and in vivo against melanoma cells. MAb A4 is internalized, induces activation of caspase-9, 3 and 6, degradation of total- and phospho-β-catenin, TCF-4 down-regulation and apoptosis in melanoma B16F10-Nex2.1 cells. Similarly, the antibody V_H CDR3 (A4 H3) is cytotoxic in vitro against B16F10-Nex2 cells and have the properties of a microantibody. Presently, we aimed at determining the cytotoxic mechanism triggered by A4 H3 in melanoma cells. A4 H3 competes with mAb A4, suggesting that it also recognizes protocadherin β13. As with mAb A4, peptide A4 H3 induced tumor cell apoptosis, as shown by induction of superoxide anion production, chromatin condensation and DNA degradation. MAb A4 and peptide A4 H3 were also cytotoxic in vitro to several human tumor cells, and A4 H3 showed a significant antimetastatic effect in the syngeneic murine melanoma model. We conclude that peptide A4 H3 is functionally similar to mAb A4 in vitro and in vivo, and both are promising new therapeutic agents against melanoma.

Biography

Luana Cheven Perbore dos Santos graduated in Biological Sciences at the Campinas State University, completed her M.Sc. in Microbiology and Immunology and is engaged in the PhD program at the Experimental Oncology Unit, Federal University of São Paulo, Brazil. She presented oral communication at the International Congress of Immunology, and was awarded in poster sections in two other meetings (Biochemistry and Cell Biology) both held in Brazil.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Telomerase activity and Fas expression in acute leukemic

Liliane L.Henna

October 6 University, Faculty of Pharmacy, Egypt

Telomerase is a ribonucleoprotein enzyme that maintains protective structure at the ends of eukaryotic chromosomes. Telomeric repeat amplification protocol (TRAP) was used to determine telomerase activity (TA) in WBC_s of 45 pediatric patient with acute lymphoblastic leukemia (ALL) before treatment and after complete remission and in WBC of 6 healthy donors that were selected as a control group.CD95 (Fas/APO-1) is a cell surface receptor able to trigger apoptosis in a variety of cell types. The expression of CD95 antigen on leukemia blasts from the 45 patients before treatment; on leukocytes after complete remission and on leukocytes of the control group were determined by flow cytometry. The results obtained in the present study indicate that, telomerase activity and Fas expression increased significantly in the studied cases before treatment compared to the control group. After treatment, there was significantly decrease in TA while there was significant increase in Fas expression compared to before treatment. These results suggest that telomerase activity and Fas expression might be useful in diagnosis and follow-up of ALL in pediatric patients.a

Biography

Liliane L.Henna is presently working on her master degree at the age of 27 years,she is a teaching assistant in the biochemistry Department at the Faculty of Pharmacy ,October 6 University,She is also an outstanding Pharmacist . At present, she is studing lymphoblastic leukemia before and after treatment in pediatric patient.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Coexpression of cytosine deaminase and carboxyl esterase in genetically engineered stem cells migrated ovarian cancer cells and reduced their cell growth through tumor tropic effect

Kyung-a hwang, Min-a park and Kyung-chul choi
College of Veterinary Medicine, Chungbuk National University, Republic of Korea

Genetically engineered stem cells (GESTECs) producing suicide enzymes have recently emerged as an novel therapeutic gene therapy for anticancer treatments. *Cytosine deaminase (CD)* and *carboxyl esterase (CE)* are suicide enzymes that convert non-toxic prodrugs, 5-fluorocytosine (5-FC) and camptothecin-11 (CPT-11) to toxic metabolites, 5-fluorouracil (5-FU) and SN-38, respectively. In this study, we manufactured *CD* or *CE*-expressing neural stem cells (HB1.F3.CD or HB1.F3.CE cells) as GESTECs and evaluated whether they were able to migrate to human ovarian cancer cells and to exhibit a potential therapeutic efficacy against these cancer cells *in vitro* following prodrug (5-FC or CPT-11) administration. Ovarian cancer cells, SKOV-3 (an ovarian adenocarcinoma derived from the ascites of an ovarian cancer patient), and these engineered stem cells were cultured in the DMEM with 10% FBS. Using RT-PCR, we confirmed *CD* and *CE* gene expressions in the neural stem cells and the expressions of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2, in ovarian cancer cells. To determine migration ability of these GESTECs compared to primary cells, we performed a modified trasnwell assay. In this test, HB1.F3.CD and HB1.F3.CE cells appeared to migrate selectively toward ovarian cancer cells due to the inherent tumor-tropic properties of neural stem cells and the chemoattractant molecules secreted by cancer cells. A [^{3}H] thymidine incorporation assay was conducted to measure the proliferative index in which these HB1.F3.CD and HB1.F3.CE cells resulted in an anti-proliferative effect on ovarian cancer cells. In the co-culture system and MTT assay, these GESTECs expressing suicide genes effectively suppressed the growth of SKOV-3 cancer cells *in vitro* with application of prodrug (5-FC or CPT-11). Our results in this study indicate that these GESTECs have an exceptional advantage in anticancer therapy via a strong tropism toward ovarian cancer cells and an effective suppression on tumor growth *in situ*.

Biography

Kyung-A Hwang is doing her Ph.D. course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Potential use of therapeutic engineered stem cells expressing chemo- and immuno-therapeutic genes for selective target of human non-small cell lung carcinoma cells

Bo-Rim YI and Kyung-Chul CHOI

College of Veterinary Medicine, Chungbuk National University, Republic of Korea

Genetically engineered stem cells (GESTECs) producing suicide enzymes and immunotherapeutic agents along with their strong tumor tropism have a definite therapeutic potential in anticancer treatment. Suicide enzymes can convert non-toxic pro-drugs to toxic metabolites that can reduce tumor growth. *Cytosine deaminase (CD)* is a suicide enzyme that changes a pro-drug, 5-fluorocytosine (5-FC) into a toxic agent, 5-fluorouracil (5-FU). As an immunotherapeutic agent, human *interferon-beta (IFN-b)* is a typical cytokine having an antitumor effect. In this study, we used human neural stem cells (HB1.F3) transduced with *E.coli CD* gene and human *IFN-b* gene as GESTECs (HB1.F3.CD or HB1.F3.CD.IFN-b) and evaluated whether these GESTECs were capable of migrating to human non-small cell lung carcinoma cells (A549) and of exerting the cytotoxicity against cancer cells *in vitro*. Using RT-PCR, we confirmed the expression of *CD* and *IFN-b* gene in these GESTECs and of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2 in A549 cell line. In a modified trasnwell migration assay, GESTECs (HB1.F3.CD or HB1.F3.CD.IFN-b) appeared to migrate selectively toward lung cancer cells. It can be attributed to the prominent migrating capacity of GESTECs toward various chemoattractants secreted by cancer cells. In addition, using co-culture system and MTT assay, we tested a therapeutic efficacy of GESTECs. When A549 and GESTECs were co-cultured in the presence of 5-FC, HB1.F3.CD or HB1.F3.CD.IFN-b cells showed the inhibition of cancer cell growth. Moreover, a stronger inhibitory effect on A549 cell growth was induced by HB1.F3.CD.IFN-b rather than by HB1.F3.CD alone, which means the synergic effect of *IFN-b* and 5-FU converted from 5-FC by *CD*. The results of this study have shown that GESTECs expressing CD or CD.IFN-b genes may migrate toward lung cancer cells selectively and exert anticancer capacity *in situ*. Consequentially, it is suggested that GESTECs can be a promising alternative anticancer therapy over radiotherapy and/or chemotherapy.

Biography

Bo-Rim Yi is doing her master course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Glycotargeting to hepatocytes using novel cationic liposomal formulations

Kovashnee Naicker, Moganavelli Singh and Mario Ariatti
University of KwaZulu-Natal, Department of Biochemistry, South Africa

The efficiency of liver gene therapy largely depends on the ability to specifically target hepatocytes for corrective gene transfer. Receptor-mediated gene transfer has shown potential for the treatment of liver diseases. The asialoglycoprotein receptor is a cell-surface receptor that is highly expressed on hepatocytes (liver cells). Genes targeted to this receptor can be delivered in a highly selective manner to the liver via glycotargeting. Glycotargeting relies on carrier molecules possessing carbohydrates that are recognized and internalized by these receptors. Glycosylation of liposomes have shown immense potential in the targeting of specific liver cells and can be achieved by incorporation of synthetic glycolipids into the liposomal bilayer. This study is aimed at producing synthetic targeted cationic liposome gene carrier systems for study in a human hepatoma cell line (HepG2). Targeted transfection was facilitated by the formulation of liposomes comprising of glycosylated cholesterol (MSβGal), novel cationic cholesteryl derivative *N,N*-dimethylaminopropylamidosuccinylcholesterylformylhydrazide (MS09), dioleoylphosphatidylethanolamine (DOPE) and polyethylene glycol (PEG_{2000}). The sugar moiety present in the liposomal bilayer is intended to bear specificity towards the membrane lectins, and the cationic component to bind electrostatically to the negatively charged DNA. Gel retardation, nuclease digestion and ethidium intercalation assays confirmed that DNA was fully liposome-associated, stable and protected from serum nucleases. Transfection activity of the cationic lipoplexes was determined using the luciferase reporter gene assay and cytotoxicity *in vitro* was evaluated using the MTT test. These findings support the notion that these lipoplexes could prove to be useful targeted gene carriers to liver hepatocytes and may be extended to an *in vivo* system.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Alteration of cxcr7 expression mediated by tlr4 promotes tumor cell proliferation and migration in human colorectal carcinoma

Huanbai Xu and Yanyun Zhang

Shanghai Institute of Immunology Shanghai, China

The link between inflammation and colorectal carcinoma has been acknowledged. However, the impact of bacterial lipopolysaccharide (LPS) binding to Toll-like receptor 4 (TLR4) on chemokine receptors in human colorectal carcinoma cells still remains to be elucidated. The present study shows that exposure to LPS elevated CXC chemokine receptor 7 (CXCR7) expression in colorectal carcinoma cell line SW480 expressing TLR4/ myeloid differential protein (MD-2). CXCR7/CXCL12 is associated with SW480 cell proliferation and migration. However, exposure of SW480 cells to LPS had no effect on CXCR4 expression. To further support the above results, the expression of TLR4, MD-2, and CXCR7 was analyzed in human colorectal carcinoma tissues. Higher rates of TLR4 (53%), MD-2 (70%), and CXCR7 (29%) expression were found in colorectal carcinoma tissues than in normal tissues. We demonstrated that the recombination of TLR4, MD-2 and CXCR7 strongly correlated with tumor size, lymph node metastasis and distant metastasis in colorectal carcinoma tissue samples ($p = 0.037$, $p = 0.002$, $p = 0.042$, resp.). Accordingly, simultaneously examination of the expression of TLR4, MD-2 and CXCR7 in cancer tissues of colorectal carcinoma may provide valuable prognostic diagnosis of carcinoma growth and metastasis. Interplay of TLR4, MD-2 and CXCR7 may be of interest in the context of novel immunomodulatory therapies for colorectal carcinoma.

Biography

Huanbai Xu is presently working on her PhD at the age of 34 years at Shanghai Jiao Tong University School of Medicine China. She is also an outstanding physician. At present, she is studing tumor immunology. Her works involve with the interdisciplinary research for oncology, immunology, endocrinology, celluar and molecular biology.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Discovery of Artemisinin derivatives as anticancer drug candidates

Dongguk Min and Mankil Jung

Department of Chemistry, Yonsei University, Korea

Artemisinin, a sesquiterpene isolated from *Artemisia annua* L., and its derivatives have been used clinically to treat drug-resistant malaria. Recently, a variety of researchers have reported on the potential antitumor properties of artemisinin and its derivatives. We have special interest of its antitumor activity against human cancer cells. We synthesized novel derivatives of non-acetal deoxoartemisinin and tested in vitro anticancer activity against major human cancer cell lines(A549, SK-V3, SK-MEL-2, XF498, HCT15). Some of synthesized deoxoartemisinin derivatives showed potent anticancer activity and desreve for further investigation as potential and clinically useful anticancer drug candidates.

Biography

Dongguk Min has completed his M.S. in 2009 from Yonsei University under the guidance of Professor Mankil Jung. His thesis focused on synthesis and biological evaluation of novel aromatic compounds for the treatment of neurodisease. Currently he is reading for his Ph. D. with working on synthesis and anticancer activity of artemisinin, a natural sesquiterpene endoperoxide.

Mankil Jung has completed his Ph.D in 1981 from Oxford University and postdoctoral studies from Harvard University. He is the director of the Bioorganic & medicinal Chemistry Laboratory. He has published more than 108 papers in reputed journals and serving as an editorial board member of Current Medicinal Chemistry.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Does mammographic breast cancer screening impact disease stage presentation and survival in Asian women?

V Wang, CM Seah, WL Chow, SH Lim, CK Cheong and SM Tan

Breast centre, Department of Surgery, Changi General Hospital, Singapore

Introduction: Breast cancer is the leading cause of cancer death amongst Singaporean women for the past 30 years. Mammographic screening has been shown to be effective in early detection of breast cancer in Western populations; however there are few studies evaluating its impact among Asian women.

Objectives: This study aims to examine the differences in disease stage at presentation and outcome between breast cancer patients who were detected by screening (screen-detected) and those who presented symptomatically (symptomatic) from the experience of a regional hospital in Singapore.

Methods: Data of female patients diagnosed with primary breast cancer and treated from January 2002 - December 2008 were extracted from the prospectively collected breast cancer registry and analyzed with SPSS v15.0. Univariate and multivariate analyses were performed to examine the profile of symptomatic patients and factors that influence presentation at an early disease stage. Survival and recurrence rates were computed by Kaplan-Meier method and compared by log rank test.

Results: The study population consisted of 761 patients (82 screen-detected and 679 symptomatic). The screen-detected patients were more likely to present at an earlier stage (OR=25.3, 95% CI: 3.7-184, p=0.001) and have better overall cancer-specific survival as compared to symptomatic patients (p=0.008).

Malay women (OR=0.31, 95% CI: 0.11-0.89, p=0.029 for Malays vs Chinese) and those without a family history of breast cancer (OR=0.36, 95% CI: 0.19-0.64, p=0.001) were found to be less likely to be detected by screening.

Conclusions: Mammographic screening appeared to enable the detection of oncologically more favorable lesions and conferred better overall cancer-specific survival in Asian women. There is possibly room for more targeted education efforts to reach out to Malays women and those without family history of breast cancer to attend breast cancer screening.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The expressions of fusion genes, cytosine deaminase and interferon-beta, in genetically engineered stem cells migrated to breast cancer cells and induced their cell growth inhibition

Bo-Rim YI and Kyung-Chul CHOI

College of Veterinary Medicine, Chungbuk National University, Republic of Korea

Recent studies of genetically engineered stem cells (GESTECs) have received a great deal of attention as an alternative potent anti-tumor treatment to various human cancers. In this study, human neural stem cells (HB1.F3) having a powerful tumor tropism were engineered as GESTECs to harbor fusion genes, a bacterial *cytosine deaminase (CD)* gene and a human *interferon-beta (IFN-b)* gene which are related with the cytotoxic effect on cancer cells. *CD* gene is a suicide gene expressing *cytosine deaminase* that can convert a non-toxic prodrug, 5-fluorocytosine (5-FC), to an active form, 5-fluorouracil (5-FU. Also, human *interferon-beta (IFN-b)* was well known as a cytokine to have an antitumor effect. In the present work, we evaluated the coupling effect of CD and IFN-b genes in the cytotoxicity on breast cancer cells (MDA-MB-231 and MCF-7) with tumor targeting capacity of these GESTECs. Cancer cells (MDA-MB-231 and MCF-7) and GESTECs (HB1.F3.CD, and HB1.F3.CD. IFN-b) were cultured in RPMI and DMEM containing 10% FBS. Expressions of *CD* and *IFN-b* genes and chemoattractant ligands such as SCF/c-kit, VEGF/VEGFR2, and SDF-1/CXCR4, were identified in these GESTECs and breast cancer cells, respectively by RT-PCR method. To evaluate migratory ability of these GESTECs, we performed a modified transwell assay where both HB1.F3.CD and HB1.F3.CD.IFN-b cells migrated selectively toward breast cancer cells, MCF-7 and MDA-MB-231. Migration capacity of these GESTECs can be attributed to a strong tumor tropism of stem cells toward chemoattractants secreted by cancer cells. In addition, using MTT assay, we tested cytotoxic effect of engineered stem cells against breast cancer cells *in vitro*. The viability of breast cancer cells was significantly reduced by co-culture with HB1.F3.CD and HB1.F3.CD.IFN-b in the presence of a prodrug, 5-FC. More potent inhibition was observed by HB1.F3.CD.IFN-b compared to HB1.F3.CD, which means that 5-FU (converted from 5-FC by *CD*) and *IFN-b* affected cancer cells synergically. These data provide a promise that these GESTECs expressing fusion genes, *CD* and/or *IFN-b,* may have a therapeutic potential against breast cancer cells *in vitro* via their strong anticancer effect and tumor tropism. A further study is needed to prove *in vivo* efficacy for human breast cancer therapy by applying these GESTECs in a xenograft animal model. Also, immuno-deficient, transgenic or knockout mouse models can be employed to elucidate a mystery of therapeutic usefulness of these GESTECs.

Biography

Bo-Rim Yi is doing her master course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The VH complementarity-determining region 2 (CDR2) of mAb C7 promotes beta-actin polymerization and induces apoptosis in cancer cells

Arruda Denise Costa

Experimental Oncology Unit, Federal University of São Paulo, Brazil

Malignant melanoma is the main cause of death in patients with skin cancer. Conventional chemotherapy is rather ineffective so that other strategies, including immunotherapy, have been tried to treat the metastatic form of melanoma. Recently, we described the antitumor effect of V_H CDR2 from mAb C7 tested as a synthetic 16-mer peptide (C7H2) against murine melanoma B16F10-Nex2 cells *in vitro* and *in vivo* (PLoS One 2008;3:e2371). We report now on the cytotoxicity of C7H2 to human tumor cells including melanoma (A2058), breast cancer (SKBR3, MCF7, MDA), glioblastoma (U87MG), cervical carcinoma (HeLa, SiHa) and colon carcinoma cells (LS180, HCT-8). The peptide was not toxic in 3 non-tumorigenic cell lines. C7H2 caused apoptosis in all cancer cells identified by annexin V binding, activation of caspase-3 and -8, chromatin condensation and DNA degradation. It induced abundant anion superoxide production, nuclear lamin disintegration and DNA leakage in the cytoplasm. Alanine-scanning showed that tyrosine and cysteine at the N-terminal sequence are essential for the protective activity of C7H2 *in vivo.* Biotinylated-C7H2 is internalized and colocalizes with phalloidin-rhodamine to actin-network. *In vitro*, C7H2 binds to beta-actin and induces actin polymerization. The C-terminal heptapeptide binds to actin but does not promote F-actin formation. An effect on actin dynamics could be linked to apoptosis in human tumors making C7H2 a potential therapeutic agent to be developed as an anticancer drug.

Biography

Denise Costa Arruda has graduated in Pharmacy at Federal University of Santa Catarina, and completed her Ph.D at the University of São Paulo, and postdoctoral studies at Federal University of São Paulo, Brazil. She has published 5 papers in reputed journals and got awards for poster presentation at two international meetings.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Characterization of pancreatic cancer cell lines based on sensitivity to the MEK inhibitor CI-1040

Adrian Bivol
University of San Francisco,USA

Pancreatic cancer is one of the most severe forms of cancer, with a poor prognosis despite treatment. We analyze microarray data on 22 pancreatic ductal adenocarcinoma cell lines to explore the effects of CI-1040, a highly specific inhibitor of MEK1 and MEK2. Using BRDU assay to distinguish sensitive and resistant cell lines, we investigate two different methods, Benjamini & Hochberg FDR controlled t-statistics (the multtest package in Bioconductor), and support vector machine (R-SVM, Zhang et al.), to classify samples, perform feature selection, and predict sensitivity to treatment. We refine our SVM-based predictor by integrating gene-selection information from other models and test its accuracy on new cell lines. We analyze these gene sets for pathway enrichment using EGAN and explore possible drug targets and mechanisms. We examine the relevance of several gene signatures from the literature to further characterize the biology of these cell lines and implications for patient treatment.

Biography

Adrian Bivol holds an M.D. degree from the University of Medicine and Pharmacy "Caro Davila" of Bucharest, Romania (2001). He also holds a Bachelor's Degree in Computer Science, and is currently a graduate student (Computer Science) at the University of San Francisco, California.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The Regulation of Gene Expression in a Breast Cancer Cell Model using Novel Gene Delivery Agents

Adhika Balgobind, Moganavelli Singh and Mario Ariatti

University of KwaZulu-Natal, South Africa

Breast cancer is one of the most common female cancers worldwide and a major cause of cancer death in women. Advances in the understanding of the molecular mechanisms underlying the malignant transformations of breast cancer cells has enabled the possible regulation of the expression of specific genes that are linked to breast cancer. Gene therapy based on small interfering RNA (siRNA) has emerged as an exciting and diverse new therapeutic approach. This molecular tool holds great potential for the treatment of diseases that have until now been considered incurable. However, poor stability and insufficient cellular uptake have limited its usefulness. Therefore, this study focused on the delivery of siRNA to an upregulated breast cancer gene via the use of novel cationic liposomes (non-steric and steric stabilized) which have been synthesized and chemically analyzed. The cholesteryl cytofectin, *N,N*-dimethylaminopropylamidosuccinylcholesterylformylhydrazide (MS09) was synthesized from cholesterol chloroformate. Cationic liposomes were constructed from near equimolar quantities of MS09, dioleoylphosphatidylethanolamine (DOPE) and polyethylene glycol (PEG_{2000}) forming submicron stable unilamellar liposomes. Gel retardation, ethidium displacement and nuclease digestion assays confirmed that siRNA was fully liposome-associated, stable and protected from serum nucleases. Transfection activity of the cationic lipoplexes was determined using the luciferase reporter gene assay and cytotoxicity *in vitro* was evaluated using the cell viability (MTT) assay. Preliminary results suggest that these new cationic liposomal systems have an immense potential to be used for efficient delivery of siRNA therapeutics to bring about silencing of oncogenes associated with breast cancer.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

cxcr4 promotes oral squamous cell carcinoma migration and invasion through inducing expression of mmp-9, 13 via the erk signaling pathway

Yingying Wu

West China College of Stomatology, Sichuan University, China

The increased migration and invasion of oral squamous cell carcinoma cells are key events in the development of metastasis to the lymph nodes and distant organs. Although the chemokine receptor CXCR4 and its ligand, stromal-cell-derived factor-1α, have been found to play an important role in tumor invasion, its precise role and potential underlying mechanisms remain largely unknown. In this study, we showed that knockdown of CXCR4 significantly decreased Tca8113 cells migration and invasion, accompanied with the reduction of MMP9 and MMP13 expression. Inhibition of ligand binding to CXCR4 by a specific antagonist TN14003, also led to reduced cancer cell migration and invasion. Because the degradation of the ECM and the basement membrane by proteases, such as matrix metalloproteinases (MMPs) is critical for migration and invasion of cancer cells, we investigated the expression of several MMPs and found that the expression of functional MMP9 and MMP13 was selectively decreased in CXCR4 knockdown cells. More importantly, decreased cell migration and invasion of CXCR4 knockdown cells were completely rescued by exogenous expression of MMP9 or MMP13, indicating that the two MMPs are downstream targets of CXCR4-mediated signaling. Furthermore, we found the level of phosphorylated extracellular signal-regulated kinase (ERK) was significantly decreased in CXCR4-silenced cells, suggesting that ERK may be a potential mediator of CXCR4-regulated MMP9 and MMP13 expression in Tca8113 cells. Taken together, our results strongly suggest the underlying mechanism of CXCR4 promoting Tca8113 migration and invasion by regulating MMP9 and MMP13 expression perhaps via activation of the ERK signaling pathway.

Biography

Yingying Wu is a Ph.D student at the age of 27 years from Sichuan University, China. She has published more than 5 papers in reputed journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Primary melanoma of the central nervous system: A case report and review of the literature

Rogers E and Hamm C

Department of Oncology, Schulich School of Medicine and Dentistry, University of Western Ontario, Windsor Regional Cancer Centre, Canada

Primary melanoma of the CNS is a very rare phenomenon. It can often be difficult to distinguish between a primary CNS melanoma and a metastasis, especially when the lesion lies within the delicate architecture of the spinal meninges. Here we present the case of a 59-year-old woman suffering progressively worsening headaches, eyesight deterioration, and intra-cranial hypertension. Shortly following the onset of saddle paresthesia and loss of complete urinary control, an MRI of the lower thoracic spine indicated a solitary spinal mass. Dermatological and radiological investigations ruled out any metastatic lesion and the diagnosis of a primary melanoma of the CNS was established. A surgical resection was performed, confirming the presence of a pigmented mass within the leptomeninges subsequently confirmed to be malignant melanoma via pathological analysis. The patient was treated with radio- and chemotherapy. Included also is a discussion of the literature relating to primary and secondary CNS malignant melanoma as well as the tools and techniques involved in differentiating between them.

Biography

Eamonn Rogers is currently completing the 3rd year of his medical studies at the Schulich School of Medicine and Dentistry at the University of Western Ontario. He currently chairs the distributed medical education (DME) Taskforce of the Canadian Federation of Medical Students (CFMS). This is his first foray in the field of academic medical research.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Vascular endothelial growth factor antibody conjugated dextran-coated iron oxide nanoparticles for *in vivo* tumor targeting and imaging

Yuh-Lien Chen

Institute of anatomy and cell Biology, College of Medicine, National Taiwan University, Taiwan

Vascular endothelial growth factor (VEGF) is a critical component in many cancer types, which provides an opportunity for designing antibody-targeted approaches for cancer imaging and detection. VEGF targeted nanoparticles (VEGF-NP) are developed by conjugating a VEGF antibody to surface functionalized supermagnetic iron oxide nanoparticles in our previous study. To determine if the systemic delivery of VEGF-NP leads to target specific accumulation, we injected these particles through the jugular vein into the Balb/c mice bearing colon cancer from the VEGF-positive mouse colon cancer cell line, CT 26. Magnetic resonance imaging (MRI) scan showed the significant decrease of significant T*2 signal and T2 relaxation in the VEGF-NP injected-mice but not in nanoparticles (NP) alone-injected mice. Examination of paraffin sections of tumor tissues revealed strong blue reaction obtained from the mice that received VEGF-NP, but low reaction was found in mice with NP alone injection by Prussian blue staining. A lot of VEGF-NP was present in cells and extracellular matrix in tumor tissues than NPinjected mice by transmission electron microscopy. These results demonstrated *in vivo* tumor targeting and efficient accumulation of the VEGF-NP in tumor tissues after systemic delivery of colon cancer model. Therefore, VEGF-NP has the potential to be used as a molecular-targeted tumor imaging agent *in vivo*.

Biography

Yuh-Lien Chen has completed her Ph.D at the age of 29 years from National Taiwan University. She has published numerous refereed scientific articles and is a professor in Institute of Anatomy and Cell Biology, College of Medicine, National Taiwan University, Taiwan

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Elevated serum levels of peroxiredoxin I in patients with breast carcinoma

Mee-Kyung Cha, Byung-Joon Park and Il-Han Kim

Paichai University, Depatment of Biochemistry. Daejeon 302-735, Republic of Korea

Peroxiredoxin (Prx) is a novel group of peroxidases containing high antioxidant efficiency. The mammalianPrx family has six distinct members (Prx I-VI) in various subcellularlocations, including peroxisomes and mitochondria, places whereoxidative stress is most evident. The function of Prx I in particular has been implicated in regulating cell proliferation, differentiation, and apoptosis. In previous study, we demonstrated that the mRNA and protein levels of Prx I in breast carcinoma are much higher than those of the normal controls. The aim of this study was to assess the clinical significance of serum Prx I levels in patients with breast carcinoma. To clarify whether both plasma levels of Prx I could be a breast cancer marker, we measured the serum levels in patients with breast carcinoma using an ELISA, and investigated its associations with the tumor grading from I to III. We have found that the plasma Prx I level of the cancer patients were significantly higher than those of normal subjects. The serum levels were correlated with progress of the carcinoma.At the cut-off value1.171mg/ml on the receiver operating characteristic (ROC) curve, Prx I could discriminate breast carcinoma patients from normalsubjects with a sensitivity of 89.8%, specificity 82%, and area under curve (AUC) 0.909+/-0.015. For other members of Prx family (Prx II-VI)at their cut-off points, they could not well discriminate the two groups with a lower sensitivity and specificity compared to Prx I. We also investigated the serum level of Prx I in various patients with lung, colon, and kidney carcinomas. Analysis of the corresponding ROC curve indicated that Prx I could be most potential biomarker for breast carcinoma. Taken together, we concluded that serum Prx I level is a new biomarker for breast carcinoma. **This work was financially supported by Regional Research and Development Cluster Project (B0009735) funded by the Ministry of Knowledge Economy (MKE) of Korea.*

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Interleukin (IL)-23 promotes growth and proliferating activity of oral squamous cell carcinomas

Masakatsu Fukuda[1], Kaoru Kusama[2] and Hideaki Sakashita[1]

[1]Second Division of Oral and Maxillofacial Surgery, Meikai University School of Dentistry, Japan
[2]Division of Pathology, Department of Diagnostic and Therapeutic Sciences, Meikai University School of Dentistry, Japan

Interleukin (IL)-23 is a heterodimeric cytokine, comprising IL-12 p40 and the recently cloned IL-23-specific p19 subunit. Like IL-12, IL-23 is expressed predominantly by activated dendritic cells and phagocytic cells, and both cytokines induce IFN-γ secretion by T cells. Whereas IL-12 promotes infiltration of cytotoxic T cells, IL-23 promotes inflammatory responses, and increases angiogenesis but reduces CD8 T-cell infiltration. Although it has been currently reported that IL-23 expression is observed in various organs, it is unclear whether IL-23 is expressed in human oral squamous cell carcinomas (HOSCC). This study examined the expression of IL-23 in HOSCC and attempted to clarify the role of IL-23 in those cells. As the results, it was demonstrated that IL-23 is spontaneously expressed and increased by TNF-α in HOSCC cells. Luciferase reporter assay indicated that anti-IL-23 antibody induced a 2-fold decrease of NF-κB-dependent transcription at 4 h, which was further reduced by knockdown of IL-23 using RNA interference. Immunohistochemistry revealed a weak IL-23 immunoreactivity in the cytoplasm of inflammatory infiltrating cells and in the cancer cells derived from 14 of 40 cases (35%) of oral SCC. In contrast, strong RelA immunoreactivity was observed in 30 of 40 cases of SCC (75%), especially consistent with IL-23 positive cells in SCC tissues. These data suggest that IL-23 up-regulates the growth and cell proliferation of oral cancer by promoting the nuclear transactivation of NF-κB.

Biography

Masakatsu Fukuda has completed his Ph.D at the age of 31 years from Nihon University and postdoctoral studies from International Agency for Research on Cancer (IARC; Lyon, France). He is an assistant professor of Second Division of Oral and Maxillofacial Surgery, Department of Diagnostic and Therapeutic Sciences, Meikai University School of Dentistry. He has published more than 30 papers in reputed journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Thioredoxin1, a novel serum marker for human breast carcinoma

Byung-Joon Park, Mee-Kyung Cha, and Il-Han Kim

Paichai University, Depatment of Biochemistry. Daejeon 302-735, Republic of Korea

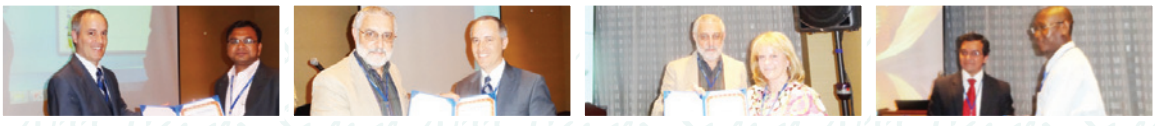
Thioredoxin1 (Trx1) is known to contain an active site with a redox-active disulfideand to be secreted extracellularly. Function of Trx1 has been implicated in regulating cell proliferation, differentiation, and apoptosis.We investigated whether serum Trx1 levels are elevated in patients with various carcinomas (breast, lung, colon, kidney, ovarian, prostatic, and gastric cancers).In previous study, we demonstrated that the mRNA and protein levels of Trx1 in breast carcinoma are much higher than those of the normal controls. The aim of this study was to assess the clinical significance of serum Trx1 level in patients with breast carcinoma. To clarify whether serum levels of Trx1 could be a serum marker for breast carcinoma, we measured the serum levels in patients with breast carcinoma using an ELISA, and investigated its associations with the tumor grading from I to III. We have found that the plasma Trx1 level of the cancer patients was significantly higher than those of normal subjects. The serum level was correlated with the progress of carcinoma. At the cut-off point 73.68ng/ml on the receiver operating characteristic curve, Trx1 could well discriminate breast carcinoma from normal controls with a sensitivity of 94.9%, specificity 88.0%, and area under curve (AUC) 0.970+/-0.013. We also investigated the serum level of Trx1 in various patients with lung, colon, kidney, ovarian, prostatic, and gastric carcinomas. Analysis of the corresponding ROC curve indicated that Trx1 could be most potential biomarker for breast carcinoma. Taken together, we concluded that serum Trx1 level is a new biomarker for breast carcinoma. **This work was financially supported by Regional Research and Development Cluster Project (B0009735) funded by the Ministry of Knowledge Economy (MKE) of Korea.*

Accepted Abstracts

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on Cancer Science & Therapy

15-17 August 2011 Las Vegas, USA



OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The mechanism & causes of carcinogenesis and mutagenesis in eukaryotes

Shaukat Iqbal Malik

Mohammad Ali Jinnah University, Islamabad campus, Pakistan

A process by which normal cells are transformed into cancer cells is term as Carcinogenesis. Carcinogenic: A carcinogen is any material, radionuclide or radiation that is a cause directly involved in the exacerbation of cancer or in the increase of its proliferation. This may be due to the ability to damage the genome or to the disruption of cellular metabolic processes all cancers involve the failure of genes that control cell growth and division. The process by which cancers develop is called carcinogenesis. This process usually starts when chemicals or radiation damage DNA, of the cells. Viruses induce carcinogenesis by introducing new DNA sequences. Mostly, when DNA becomes damaged the body is able to repair it. In cancer cells, however, the damaged DNA is not repaired and normal cells with damaged DNA die, while the cancer cells with damaged DNA continue to multiply. There is a long time delay between exposure to a carcinogen and the occurrence of cancer. While cellular mutations cause cancer to develop, it is not exactly clear how this happens. Carcinogenesis is a multistep process, in which as many as ten diverse mutations may have to accumulate in a cell before it becomes cancerous. The fact that so many mutations are needed for a cancer to develop indicates that cell growth is normally controlled through many sets of checks and balances. Mutation is the sudden heritable change in the genetic material of an organism. The term mutation is applicable to both the change in genetic material and to the process by which the change occurs. Thus the term mutation is used to define the process as well as the effect. Mutation is simply an alteration in the nucleotide sequence of a DNA molecule. Physical agents like UV or chemical molecules can cause mutations. Molecules or agents that cause mutations are called as mutagens. Mutations occur non specifically and there is no defined process to carry out mutation in a cell or organism.

Recombination on the other hand occurs at a particular time, with the help of a set of enzymes and in a defined process. Thus mutation and recombination are not the same. But mutation and recombination are central events in genetics and evolution. Mutations created in an individual by the process of mutagenesis are called as induced mutations. Damaging to the DNA-such as heat or a lack of oxygen-these also tend to increase the mutation rate in cancer cells.

Biography

Dr. Shaukat Iqbal Malik has earned his PhD Degree in 2004 from the National and Kapodistrian University of Athens & Cancer Cytogenetic and Environmental Hygiene Laboratory, NCSR Demokritos, Athens and two Postdoc 1st from NHEERL, Cancer Biology branch (Cytogenetics section) US Environmental Protection Agency RTP Complex, NC and 2nd from Lineberger Comprehensive Cancer Center, Biomedical Research Imaging Center University of UNC at Chapel Hill, USA. He is Associate prof. in the department of Computer science & Bioinformatics, Mohammad Ali Jinnah University, Islamabad, Pakistan. He has published more than 20 papers in reputed journals and serving as an editorial board member of reputed international journal. He has been received Best Faculty member in 2005 and excellent professor award years 20090-10. His New Cytogenetics Techniques has been published in English, German, French and Greek language. He has been visited about 20 countries including USA and EU for Acedamid and research activities. In 2007 he wins amounting Pak Rs.4.0 Million Research Project under National Research Program for Universities from HEC Pakistan.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The anti-tumor role of gene UBTD1 and a positively regulatory loop between UBTD1 and p53

Xiaowei Zhang, Jin Li and Weijian Guo

Fudan University Shanghai Cancer Center; China

Cellular senescence is a powerful barrier to oncogenesis and the mechanisms is unclear. P53 is one of the important genes in regulating cellular senescence. It was reported that p53 can bind to the promoter of UBTD1, which suggested that it may play an important role in the down stream of p53. Currently little is known about the role and mechanism of gene UBTD1 (Ubiquitin domain containing 1). Here we provide the evidence that UBTD1 is overexpressed in senescent fibroblast cells and normal gastric mucous tissues, and lowexpressed in gastric cancer cell lines and gastric cancer tissues transcriptionally and translationally, which suggests that it may play an important role in oncogenesis. We originally found the function of UBTD1 in inducing senescence, inhibiting oncogenesis and cell migration in both p53 mutant and p53 wild-type cancer cell lines by gene transfection, which suggested that UBTD1 does not depend on p53 absolutely. We also found that Ubiquitin domain is the active part of UBTD1. P53 can positively regulate the expression of *UBTD1* mRNA by directly binding to the promoter of UBTD1 by ChIP assay, and UBTD1 can inversely increase the level of p53 protein possibly by enhancing the stability of p53 protein, which preliminarily elucidate there might be a new positive regulatory loop between UBTD1 and p53. Further research is still necessary to elucidate the exact mechanism, Which may provide useful prognosis factor and new method of therapy for clinical work.

Biography

Xiaowei Zhang is presently working on his PhD at the age of 28 years at Fudan University Shanghai Cancer Center China. He is also an physician in oncology department. At present, His works involve with the target therapy of cancer and the role of some important cancer related genes.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Analysis of socio-demographic factors influence on Health Care Utilizations at the Last Year of Life for Cancer Decedents

Sung Won Jung
Suwon Women's College of Nursing Department, South Korea

Objectives: This study investigated 1-year medical cost before die and the expenditure behavioral patterns and examined related socio-demographic factors of the most frequently incident cancer-stomach cancer, colorectal cancer, liver cancer, lung cancer, thyroid cancer- and gender specific cancer-prostate cancer and cervical cancer.

Method: Logistic regression model was utilized to investigate the effect socio-demographic factors between never-visited decedents(n=3,753) and once or more-visited decedents(n=40,733) and Multiple regression analysis was utilized to estimate medical cost per socio-demographic characteristics of the once or more-visited decedents(n=40,733).

Results: All the decedents due to cancer expended 7,911,000 won during 1-year before die. They expended 2,378,000 won as an injection cost including antibiotics, chemotherapy, blood transfusion, 924,000 won as a lab test, 634,000 won as a radiation therapy. During 1 year, they were hospitalized about 48.3 days and visited clinics 28.3 times. They expended plenty of cost during the last 1 month (30 days) of total cost, total treatment cost, IPD cost and OPD cost. But in terms of treatment ICU cost, Anesthesia cost and Radiation cost were spent mostly in last 2 month of life (31-60 days). They were used to hospitalize about 25.26 days during last 1 month but the frequency of visiting clinic was decreased during last 3 month(respectively, 4.36-4.20-3.21). Socio-demographic factor of the decedents due to cancers concerning using of medical service was age, education level, occupations and marriage status.

Conclusion: Cancer decedents spent almost all their money for medical treatment during LYOL, in particular, one month before death. It means, they dissipated excessive medical services, health care resource during last one month. There must be some following researches about optimal use of medical services at the end-of-life.

Biography

She has finished her Ph.D(Major: Health Policy and Hospital Management) at last semester from Korea University in Seoul, South Korea. She has been teaching at Suwon Women's College from last September. She is a full time lecturer of Nursing Department at SWC. She has steadily presented papers in various international and domestic conferences. She is a member of Korean Nurses Association and Korean Academy Society of Nursing Education.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

microRNA93 modulates breast cancer stem cells by regulating their EMT/MET states, proliferation and differentiation

Suling Liu
University of Michigan Cancer Center, USA

MicroRNAs (miRNAs) play important roles in normal cellular differentiation and oncogenesis. mircroRNA93 (mir93), a member of the mir106b-25 cluster, located in intron 13 of the MCM7 gene, although frequently overexpressed in human malignancies may also function as a tumor suppressor gene. Using a series of breast cancer cell lines representing different stages of differentiation and mouse xenograft models, we demonstrate that mir93 modulates the fate of breast cancer stem cells (BCSCs) by regulating the EMT/MET conversion as well as their proliferation and differentiation states. In "claudin^{low}" SUM159 cells, expression of mir93 induces MET associated with downregulation of TGFβ signaling and downregulates multiple stem cell regulatory genes including JAK1, STAT3, Akt, SOX4, EZH1 and HMGA2 resulting in cancer stem cell (CSC) depletion. Enforced expression of mir93 completely blocks tumor development in mammary fat pads and development of metastases following intracardiac injection in mouse xenografts. The effects of mir93 on the CSC population is dependent on the cellular differentiation state with mir93 expression increasing the CSC population in MCF7 cells which display a more differentiated "luminal" phenotype. These studies demonstrate that miRNAs can regulate CSC states, the existences of which have important biological and clinical implications.

Biography

Suling Liu, PhD is an Assistant Professor at the University of Michigan. Her research interests have been focusing on Cancer Stem cell Biology. Evidence from this research is of obvious significance for the development of new diagnosis tools and innovative treatments for cancer. After getting PhD from Ohio State University in Dec 2003, her research interest on breast carcinogenesis took her to focus on cancer therapy to find novel treatments to cancer by targeting the cancer stem cells. She has published over 30 peer-reviewed papers together with three manuscripts in preparation and filed four patent applications as a co-inventor; she has been serving as reviewers and in editor board of many journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Isolation and immunomodulatory potential of oryzanol from crude rice bran oil in experimental animal models

Somsuvra B. Ghatak
Institute of Pharmacy, Nirma University, India

Tumor mediated immunosuppression is the greatest challenge in cancer treatment. Harnessing the immune system to stimulate and increase the immunocompetence and immune defense systems in cancer patients is the major goal of immunotherapy. Many of the presently available immunomodulators are not free from side effects including fever, neutropenia, leucopenia and allergic reactions. Hence, there is an urgent need to evaluate the potential of natural products as adjuvants to counteract the side effects of modern therapy. Recently, there has been a surge of global interest pertaining to the beneficial effects of commercially important bioactive phytochemicals like oryzanols and tocopherols, obtained from crude rice bran oil. Therefore, the present study was undertaken to investigate the effect of oryzanol on cell mediated and humoral immunity in various experimental animal models. The effects on immune response were assessed using haemagglutinating antibody titre, delayed-type hypersensitivity response, carbon clearance test and cyclophosphamide-induced myelosuppression models in experimental animals, divided in groups such as control, control induced, oryzanol treated (25, 50 and 100 mg/kg p.o.) and vitamin-E (100mg/kg p.o., as a naturally occurring conventional dietary antioxidant) treated. The treatment with oryzanol and vitamin-E was given for 28 days except in the cyclophosphamide induced myelosuppression model (for 10 days). Oryzanol and vitamin-E evoked a significant increase in antibody titre values in the haemagglunation test and potentiated the delayed type hypersensitivity reaction induced by sheep red blood cells. Both the drugs significantly ameliorated the serological parameters in cyclophosphamide induced myelosuppression and showed an increase in phagocytic index in the carbon clearance assay.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Cancer and quality of life

Sibel Eyigor

Ege University Faculty of Medicine, Turkey

There has been an increase in the life span of cancer patients, thanks to the advances in diagnostic tools and treatment modalities. Most of these patients gain functional capacity and return to their normal life. Recently, however, it has been emphasized that an improvement in the quality of life is a prerequisite to conclude that a treatment is successful. Consequently, there has been an increase in studies on quality of life and factors influencing it.

Many adverse events can be observed in cancer patients, either due to the disease itself or the treatment. Cancer related symptoms may affect the biological behavior of the tumor and therefore may be important for prognosis. Pain is one of the major problems faced by cancer patients. It has been argued that pain is present in 30% of the patients at the time of diagnosis, increasing to 65-85% as the disease progress. Meanwhile, fatigue, observed in some 61% of cancer patients, is the most common complaint. Pain and fatigue are important because they stand at the forefront of factors adversely affecting these patients with regard to general health, function and quality of life. It has been reported that pain and fatigue are particularly important for survival. It should be kept in mind that if the clinicians do not have the knowledge on quality of life and symptoms such as pain and fatigue, they may be mistaken in their choice of appropriate and realistic treatment and estimation of survival.

Biography

Sibel Eyigor has been graduated from Ege University, Faculty of Medicine in 1996. She received her residency training in Physical Therapy and Rehabilitation (June 1997-December 2001) in the Ege University School of Medicine. She has been appointed as an Associate Professor in 2008 in the Department of Physical Therapy and Rehabilitation at Ege University Faculty of Medicine. She is also working in Oncology Department and Geriatric Division. She interests palliative care in cancer patients. She is also member of executive committe of " Ege University Palliative Care Unit".

Her main research interests are oncologic rehabilitation, dysphagia and rehabilitation, and geriatric patients and rehabilitation. She attended the graduate course in Normal and Disordered Swallowing at the University of Illinois at Urbana, Champaign during the spring semester of 2004. She spent extended hours observing instrumental evaluations and treatment of dysphagia at Northwestern University Medical Center in Chicago, Illinosis. She was an observer on the Geriatric Rehabilitation program at the Toronto Rehabilitation Institute in 2007. She is member of executive committe of Agean Geriatric Society and local division of Turkish Society of Physical Therapy and Rehabilitation. She is member of Turkish Society of Rheumatism, Turkish Society of Physical Therapy and Rehabilitation, Turkish Society of Osteoporosis.

She was the author or co-author of numerous articles and book chapters in Turkish and English.

She is still working in Ege University Faculty of Medicine in Izmir, TURKEY.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Endothelial Cell Involvement in JAK2V617F Positive Myeloproliferative Neoplasms

Selcuk Sozer Tokdemir

The Institute of Experimental Medicine, Istanbul University, Turkey

Myeloproliferative neoplasms (MPN) are clonal hematological malignancies which are frequently associated with an acquired somatic mutation in JAK2 (JAK2V617F). Patients with MPN are at a high risk of developing thrombotic events. Endothelial cell (EC) abnormalities are thought to contribute to this prothrombotic state and involvement of hematopoietic cells (HC) and EC by JAK2V617F provides important information about the cellular origins of the MPN. In order to characterize the involvement of EC in this malignant process in vitro and in vivo methods were performed. EC were assayed in vitro from the peripheral blood of MPN patients and each EC colonies were analaysed for its immunephonotypical and genotypical characteristics. Furthermore, $CD34^+$ cells from MPN patients were assayed for EC following their transplantation into immunodeficient mice. Selected cells from nonhematopoietic organs of these mice were shown to express transcripts characteristic of EC but not hematopoietic cells and to be JAK2V617F positive. Reduced numbers of colonies from EC culture that were composed of angiogenic monocytes (AM) were present in the blood of MPN patients with a high JAK2V617F burden. These AM were able to contribute to the EC lining and the subendothelium of livers of NOD/SCID mice. These studies indicate that the thrombotic tendency in MPN patients might be due to involvement of EC by JAK2V617F which would lead to apoptosis and reduced numbers of circulating AM progenitors which might impair repair of injured vessels.

Biography

Selcuk Sozer Tokdemir has received her M.D. degree from Istanbul University, School of Medicine in 1997 in Istanbul Turkey and PhD from University of Kentucky in 2004 in Kentucky, USA. She performed her postdoctoral studies at University of Illinois at Chicago (UIC) and Mount Sinai School of Medicine. She is now working as an assistant professor at the Institute of Experimental Medicine at Istanbul University and visiting assistant professor at Mount Sinai School of Medicine. She has published many papers in reputed journals and book chapters.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

In-Vitro Cytotoxic Activity of Methanolic Extract of Hemidesmus Indicus R. Br.

Papiya Mitra Mazumder[1], Saumya Das[2], Sanjita Das[2] and Manas Kumar Das[3]

[1]Department of Pharmaceutical Sciences, Birla Institute of Technology, India
[2]Department of Pharmaceutical Technology, Noida Institute of Engineering and Technology, India
[3]Department of Pharmacy, IEC-CET, India

Natural products represent a reservoir of diverse templates and are being tapped to outsource novel anticancer agents. *Hemidesmus indicus* R.Br.(Fam: Asclepidaceae) has been reported to be useful for the treatment of inflammation, cuts, wounds, burns, snake bite, skin and blood diseases, ulcers, immunological disorders . In the present study, the methanolic extract of the roots of *Hemidesmus indicus*, was investigated against human colon cancer cell line (HT29) to explore its anticancer potential. The effect of *Hemidesmus indicus* methanolic extract (HIME) on proliferation of HT29 cancer cell line was determined by microculture tetrazolium assay (MTT). The cells were exposed to different concentrations (100, 50 , 25, 12.5 , 6.25, 3.125 and1.5 µg/ml) of HIME or vehicle for 48 h. Cisplatin (5, 2.5 and 1.25 µg/ml) acted as positive control and vehicle (DMSO) as negative control. Following treatment, the cells were exposed to Tetrazolium dye (5mg/ml) for 4 h. The formation of the purple coloured formazan complex was dissolved by adding DMSO (100 µl) and read at 490 nm using ELISA microtiter plate reader to determine the inhibitory concentration, IC50. About 40% increment in cell killing was seen when the dose of HIME was increased from 1.5-25 µg/ml. At concentration of 100 µg/ml, 49.81%, cytotoxicity was recorded. The IC50 value of HIME was 1.8964 µg/ml after 48 h of incubation. In this study, it was observed that HIME induces a concentration dependent inhibition of HT29 cells, with an IC50 value of 1.8964 µg/ml after 48 h of incubation.

Biography

Mrs. Saumya Das is Persuing her Ph.D from Birla Institute of Technology, Ranchi, Mesra, India. She is a faculty of Pharmacology in Noida Institute of Engineering and Technology, Greater Noida, India. She has published more than 12 papers in reputed International and National journals and serving as an editorial board member and reviewer of repute. She is life member of Indian Pharmacological Society and Indian Pharmacy Graduate Association. Her area of interest is Phytopharmacology, Toxicology and Anticancerous agents.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

The usefulness of preoperative determination of CEA and TPS concentrations in patients with colorectal cancer

Robert Partyka, Artur Sandelewski, Przemysław Jałowiecki and Danuta Kokocińska

Department of Anesthesiology, Intensive Treatment and Emergency Medicine SUM in Zabrze, Poland

Purpose: According to an account published by The European Group on Tumour Markers (EGTM) of 2003, CEA is the main marker used in detecting colorectal cancer. It is important to point out, however, that approximately 10-15 % of patients do not produce CEA at all or secreted only minimal amounts of it. In such cases the normal level of CEA concentration does not exclude the existence of a neoplasm even at an advanced stage. The test for TPS concentration should be added to the list of markers for this group of patients. TPS increases the sensitivity in detecting early stages of colorectal carcinoma. At the advanced stage of colon and rectal carcinomas the CEA concentration can increase eightfold and CA 19-9 concentration can increase fourfold. Recently an increased interest in the soluble fragments of cytokeratins, especially the 18^{th} (TPS), has been noted.

Methods: In this research the preoperative CEA and TPS concentrations in a group of 178 patients with colorectal cancer were estimated. The patients were divided into 4 groups according to the Dukes's stage level of carcinoma advancement.

Results: In determining TPS the observed profile of TPS concentration was different from the profile of CEA concentration because the TPS concentration was increased even at the earliest stage of tumour development.

Conclusions: The determination of TPS concentration in patients with colorectal cancer provides essential information in detecting the carcinoma, especially at the earliest stages of its development

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Pro-inflammatory mediators in cancer development and progression

Rajendra K Singh and Bal L. Lokeshwar
Miller School of Medicine, University of Miami, USA

Chronic or acute inflammatory conditions together with genetic and epigenetic changes in various organs are believed to trigger cancer genesis and progression. These conditions promote an increase in cytokines that activate a variety of pro-tumorigenic activities, such as stimulation of alternate proliferative pathway, chemotactic motility, increased survival and increased invasive potential. In prostate cancer, for example, chronic infection and/or altered fatty acid metabolism are known to trigger carcinogenesis and progression. Interleukins and members of TGF-β family are linked to such conditions.

We and others reported recently that constitutive activation of a pro-inflammatory chemokine, IL-8 promotes androgen-independent prostate tumor growth, motility, invasion, and angiogenesis. This was further demonstrated by the depletion of IL-8 expression in tumor cells significantly reduced their proliferation (>60%), growth arrest at G0/G1 phase, invasion and increased sensitivity (>50%) to docetaxel. Further, we showed increased IL-8 transregulates other, unrelated CXC-chemokine receptors, CXCR4 and CXCR7 in prostate cells, which are over-expressed and implicated in metastasis. Moreover, we reported that CXCR1, the co-receptor for IL-8 and CXCR7 also control proliferation by activating ERK1/2 MAP kinase and epidermal growth factor receptor though direct or indirect (G-protein coupled receptor activation) pathways. In addition, our work suggests, the early carcinogenesis is also regulated by IL-8 that triggers classic and non-canonical signaling via Nuclear Factor-kB, resulting in rapid cancer progression. The presentation will be focused on an overview of the cellular determinants of inflammatory process and mechanism of regulation of pro-inflammatory factors in prostate and other related malignancy for advancement of novel therapeutic strategies.

Biography

Dr. Rajendra K Singh received his Ph.D from Avadh University, India in Biochemistry and Molecular Toxicology. He did his postdoctoral training in Environmental Carcinogenesis and Molecular Cancer Biology from reputed laboratories in USA. Currently, he is working at University of Miami, Miller School of Medicine, Miami-Florida. His major research interest is to understand mechanism by which environmental factors cause malignant transformation in mammalian cells and examine the patho-physiology of pro-inflammatory mediators in oncogenic transformation and progression. He has published several papers in high impact journals. He is Editorial board of Journal of Cancer Science and Therapy and Journal of Carcinogenesis and Mutagenesis. He is also an ad hoc reviewer for several reputed journals in Molecular Carcinogenesis and Toxicology research areas.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

To Compare Efficacy and Cost Effectiveness of Different 5th 3 Blockers in Acute and Delayed Nausea and Vomiting:A Randomized Study

Shukla Piyush
All India institute of Medical sciences, India

AIM: To compare efficacy and cost effectiveness of three different 5-HT3 blockers in controlling early and delayed nausea and vomiting following chemotherapy.

Materials and method: 30 patients in each group of advanced head and neck malignancy were given cisplatin based induction chemotherapy. All received anti emetics before and during chemo(group1:condensation iv 16mg prechemotherapy and 8mg iv tds during infusion, group 2:granisetron3mg iv prechemo and 3mg iv during chemo infusion, group 3:palonosetron0.25mg iv prechemo). Nasea &vomiting were assessed according to common toxicity criteria for a period of 3 days baseline was matched for age group , stage and histology of tumor.

Result: Among the 78 patients who completed the study , group 2 had 2 & 4 cases respectively of acute and delayed emesis that was significantly lower than the other 2 groups (6 and 11 for group 1 and 2 & 10 for group 3), also overall cost in controlling delayed nausea & vomiting was much lower in group 2.

Conclusion: the study reflects that granisetron group was the best 5HT3 blocker in terms of efficacy and cost effectiveness to control acute and delayed nausea and vomiting taking into account the Indian patient with respect to economic and health status .

Keywords: 5HT-3 blockers,chemotherapy,delayed nausea and vomiting.

Biography

Piyush Shukla has completed his MD in Radiation Oncology at the age of 28 from Barkatullah University Bhopal M.P. He is presently working as a Senior Resident in the department of Radiotherapy at All India Institute Of Medical Sciences N.Delhi. One of his paper has been selected in TRICITY H&N CANCER meet 2011 at Singapore .

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

*KEAP*1 aberrant methylation is a novel marker of patients outcome in malignant gliomas

Paola Parrella

IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy

The Keap1 (Kelch-like ECH-associated protein 1) protein tightly regulates the functions of Nrf2 (nuclear factor-erythroid 2-related factor 2) which plays a pivotal role in the cellular response to oxidative stress. We determined whether *KEAP1* gene is epigenetically regulated in malignant gliomas and if promoter aberrant methylation may impact patient's outcome. We developed a QMSP assay to analyze 86 malignant gliomas and 20 normal brain tissues. The discriminatory power of the assay was assessed by ROC curve analysis. The AUC value of the curve was 0.823 (95%CI: 0.764-0.883) with an optimal cut off value of 0.133 yielding a 74% sensitivity (95%CI: 63%-82%) and an 85% specificity (95%CI: 64%-95%). Bisulfite sequencing analysis confirmed QMSP results and demonstrated a direct correlation between percentage of methylated CpGs and methylation levels (Spearman's Rho 0.929, P=0.003). Remarkably, a strong inverse correlation was observed between methylation levels and *KEAP1* mRNA transcript in tumour tissue (Spearman's Rho -0.656 P=0.0001) and in a cell line before and after treatment with 2-deoxy-5 Azacytidine (P=0.003). RECPAM multivariate statistical analysis studying the interaction between *MGMT* and *KEAP1* methylation in subjects treated with radiotherapy and temozolomide (n=70), identified three prognostic classes of glioma patients at different risk to progress. While simultaneous methylation of *MGMT* and *KEAP1* promoters was associated with the lowest risk to progress, patients showing only *MGMT* methylation were the subgroup at the higher risk (HR 5.54, 95% CI 1.35-22.74). Our results strongly indicate that aberrant KEAP1 methylation may represent a novel predictor of outcome in glioma patients.

Biography

Paola Parrella received the Medical Doctor degree (summa cum laude) in 1993. From 1998 to 2002 she was a Post Doctoral Fellow at the Division of Head and Neck Cancer Research at The Johns Hopkins University, Baltimore USA. Since 2002 she is Staff Scientist at the Laboratory of Oncology, IRCCS Casa Sollievo della Sofferenza (FG), Italy. Dr. Parrella is the author of more then 40 peer reviewed publication and Principal Investigator and co-investigator of several grants related to cancer biomarkers development.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Effect of counseling intervention post mastectomy for women undergoing adjuvant chemotherapy on their quality of life

Nessrien O. El-Sayed[1] and Zeinab Hussein Ali[2]

[1]Faculty of Nursing, Ain Shams University
[2]Helwan University

Post mastectomy treatment for women diagnosed with breast cancer is complex, dynamic, and controversial. More choices are available for the control and indications for adjuvant therapy. However, this treatment can lower long-term quality of life. Thus the aim of this study was to evaluate the effect of counseling intervention post mastectomy for women undergoing adjuvant therapy on their quality of life. This quasi-experimental study was conducted for women who received chemotherapy post mastectomy. The study group subjects were exposed to counseling sessions. The study included a consecutive sample of 42 women, following mastectomy, who received adjuvant chemotherapy eligible from the Oncology Department in Nasser Institute Hospital, the Outpatient Breast Clinic of the Clinical and Nuclear Medicine Center in Ain Shams University, EL-Naser Insurance hospital at Helwan city and the National Cancer Institute, affiliated to Cairo University. Two tools were utilized to collect data;(1) patient's questionnaire sheet, (2) Self administered questionnaires that include The European Organization for Research and Treatment Cancer Quality of Life questionnaire C30known as the Quality of Life Question (EORTC QLQ-C30), and it's breast cancer supplementary measure The European Organization for Research and Treatment Cancer Quality of Life questionnaire BR23 (EORTC QLQ-BR23).The results of this study showed highly statistically significant differences among group in relation to decreasing systemic therapy side effect of adjuvant chemotherapy on patients ($p<0.000$).There was also statistically significant improvement among women as regards physical, and psychosocial status as well as global quality of life. The pre-post and follow-up changes in knowledge scores revealed also statistically significant improvement in the study group $p<0.000$.These results imply that the counseling intervention has succeeded with highly significant positive effect in improving patient's knowledge, and quality of life. Therefore, it is recommended to generalize these counseling intervention among women post mastectomy undergoing other type of adjuvant therapy.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

An inhibition of cell growth was induced by therapeutic stem cells expressing a suicide enzyme and interferon-beta via their migratory capability in human hepatocarcinoma cells *In vitro*

Kyung-A HWANG and Kyung-Chul CHOI

College of Veterinary Medicine, Chungbuk National University, Republic of Korea

Recently, studies of stem cells in anticancer therapy have been regarded as an ingenious alternative having advantages over radiotherapy and/or chemotherapy. When genetically engineered with suicide genes and/or immunotherapeutic genes, stem cells can exhibit a potent therapeutic efficacy combined with their strong tumor tropism toward cancer cells. In the present study, we introduced genetically engineered stem cells (GESTECs) and evaluated their therapeutic efficacy against liver heaptocarcinoma cells, Hep3B. These GESTECs are neuronal stem cells engineered with a bacterial *cytosine deaminase (CD)* gene and a human *interferon-beta (IFN-b)* gene (HB1.F3.CD and HB1.F3.CD.IFN-b). *CD* gene is a suicide gene expressing *cytosine deaminase* that can convert a non-toxic prodrug, 5-fluorocytosine (5-FC), to an active form, 5-fluorouracil (5-FU), which has a powerful cytotoxic effect on cancer cells. Human *interferon-beta (IFN-b)* is a typical cytokine having an antitumor effect. Using RT-PCR, we confirmed *CD* and *IFN-b* gene expressions in GESTECs and the expressions of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2, in cancer cell lines. To determine the migratory ability of engineered stem cells, we performed a modified trasnwell assay in which HB1.F3.CD or HB1.F3.CD.IFN-b cells selectively migrated toward liver cancer cells due to the migrating capacity of neural stem cells toward various chemoattractants expressed by cancer cells. In the cytotoxicity test using co-culture system and MTT assay, HB1.F3.CD or HB1.F3.CD.IFN-b cells showed the significant inhibition of Hep3B cell growth following administration of 5-FC. More potent inhibitory effect on Hep3B cell growth was induced by HB1.F3.CD.IFN-b rather than by HB1.F3.CD alone, which means the synergic effect of *IFN-b* and 5-FU converted from 5-FC by *CD*. From the data presented in this study, we suggest that GESTECs expressing both CD and *IFN-b* may have a prominent advantage for treating human hepatocarcinoma with their coupling effect of fusion genes and selective tumor targeting of stem cells.

Biography

Kyung-A Hwang is doing her Ph.D. course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

A synergitic effect of therapeutic stem cells expressing a suicide enzyme, sytosine deaminase, with a prodrug and interferon-beta in the inhibition of endometrial cancer cell growth *In vitro*

Nam-hee Kkang, Hye-rim Lee and Kyung-chul Choi

College of Veterinary Medicine, Chungbuk National University, Republic of Korea

In recent, gene-directed enzyme/prodrug theraphies (GEPT) have been highly regarded as an alternative means of gene therapy in anti-cancer treatments. As one of GEPT, *cytosine deaminse (CD)*/ 5-fluorocytosine (5-FC) system induces metabolic suicide of cancer cells following administration of prodrug 5-FC which is converted to a toxic agent, 5-fluorouracil(5-FU) by *CD*. In addition, human *interferon-beta* (*IFN-b*) gene presents antitumor effect by expressing *IFN-b*, a immunotherapeutic cytokine. In this study, we explored the therapeutic efficacy of *CD*/5-FC system and human *IFN-b* gene that were engineered into the human neural stem cell lines having the inherent tumor-tropic properties. Parental stem cell, HB1.F3, was modified by *E.coli CD* gene and human *interferon-beta* (IFN-b) gene to produce engineered stem cells, HB1.F3.CD and HB1.F3.CD. IFN-b, respectively. Endometrial Ishikawa cancer cell lines and engineered stem cells were cultured in 10% FBS containing DMEM. Using RT-PCR, we confirmed *CD* and *IFN-b* gene expressions in the engineered stem cells and of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2, in cancer cell lines. In a migration assay using modified transwells, HB1.F3.CD and HB1.F3.CD.IFN-b were effectively migrated to endometrial Ishikawa cancer cell lines, which can be attributed to chemoattractants secreted by cancer cells. In the cytotoxicity test using co-culture system and MTT assay, the viability of endometrial Ishikawa cancer cells was decreased in the presence of engineered stem cells. Especially, the viable cancer cells was more effectively reduced when co-cultured with HB1.F3.CD.IFN-b rather than HB1.F3.CD., which means that the fusion of *CD* and *IFN-b* genes may have a synergic antitumor effect. These results suggest that engineered stem cells expressing *CD* and/or *IFN-b* may have a therapeutic potential against endometrial cancer cells *in vitro* via a strong tumor tropism of stem cells and a cytotoxic effect of engineered gene products. Furthermore, our data provide proof for the use of genetically modified stem cell-based gene therapy through a targeted delivery of therapeutic gene products to endometrial cancer sites.

Biography

Nam-Hee Kang is doing her master course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Gene Silencing in HIV-1 Latency by Polycomb Repressive Group

Kyung-Chang Kim[1,3], Hyeon Guk Kim[1], Tae-Young Roh[2], Jihwan Park[2], Kyung-Min Jung[1], Joo-Shil Lee[1], Sang-Yun Choi[3], Sung Soon Kim[1] and Byeong-Sun Choi[1]

[1]Center for Immunology and Pathology, Korea National Institute of Health, Chung-buk, Republic of Korea
[2]Pohang University of Science and Technology (POSTECH), Republic of Korea
[3]School of Life Science and Biotechnology, Korea University, Republic of Korea

Latently infected memory T cells, which are a major obstacle to HIV-1 eradication, are very rare (~1 million) in a patient and have a long half-life of over 44 months on average. The molecular linkage between HIV-1 latency and epigenetic control is not fully understood. We investigated HIV-1 latency related with Polycomb group (PcG)-proteins mediated gene silencing in novel HIV-1 latently infected cell lines, NCHA cells. The expression profiles for histone deacetylases (HDACs) and PcG proteins (EED, BMI1, RNIG2) in NCHA cells were characterized by RT-PCR, ELISA, IP, and western blot. The levels of histone acetylation and methylation at histone H3 Lys^{9} (H3K9) and Lys^{27} (H3K27) in HIV-1 latently infected cells were analyzed by western blot and chromatin immunoprecipitation-sequencing (ChIP-seq).

Histone H3K9 and H3K27 acetylations in NCHA cells showed no difference in parental and NCHA cells, whereas the levels of di- and tri-methylation at histone H3K9 and H3K27 were dramatically increased in NCHA cells except ACH2 cells. The expression of EED which is a component of polycomb repressive complex 2 (PRC2), and BMI-1 and RING2 which are constituents of PRC1 were upregulated in NCHA cells. In addition, more ubiquitylation at histone H2A was detected in NCHA cells. Also, high enrichment of H3K9me3 in the chromatin states of HIV-1 proviral genome was observed in HIV-latent cells, whereas there was no enrichment of H3K27me3.

Our result demonstrates that tri-methylation of H3K27 and H2A ubiquitylation via polycomb repressive complexes should be involved in HIV-1 latency and contribute to epigenetic gene silencing.

Biography

Dr. Kyung-Chang Kim has completed his Ph.D from Korea University, Korea, in this year. He is the staff scientist of Korea National Institute of Health. He works in a diagnosis of HIV and researches on HIV Latency.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Cucurbitacin B enhances the cytotoxicity of doxorubicin by increasing intracellular drug accumulation

Jiao Yang[1,2], Xueying Zhou[1], Yanli Wang[1], Wen Li[1] and Meixia Zhang[1]

[1]Department of Clinical Pharmacology, China Medical University, China
[2]Department of Pharmacy, The General Hospital of Daqing Oilfield, Chin

We investigated the combined antitumor activity of cucurbitacin B (CuB) and doxorubicin (Dox) in hepatocellular carcinoma cells and explored the potential mechanisms. The cytotoxicity of combined CuB and Dox in HepG2 was investigated with a 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay. The effect of CuB on Dox concentration in HepG2 cells was determined by evaluating the influx of Dox and the efflux of Dox from such cells. In vivo effect of combined CuB and Dox on the growth of murine H22 cells was also determined. Our data demonstrated that the cytotoxicity induced by CuB and Dox was additive in HepG2 cells. CuB has significantly increased intracellular Dox concentration by promoting Dox influx and suppressing Dox efflux as well. In vivo anti-tumor activity assay also showed that the combination of two drugs can result in more significant tumor regression compared with single drug usage. In conclusion, our results suggested that combined CuB and Dox may be an promising regime for the chemotherapy of HCC.

Biography

Jiao Yang got her bachelor's degree from Heilongjiang University of Chinese Medicine in 2004. She is now a master student in China Medical University.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Using GlycoExpress for production of highly active antibodies directed against novel and existing targets

Steffen Goletz
Glycotope GmbH, Ermany

Glycosylation is the major post-translational modifications of biotherapeutics that depends on the cell line used for production. By establishment of the GlycoExpress Toolbox we have generated a set of glycoengineered human cell lines to optimize the human glycosylation of biotherapeutics.

PankoMab-GEX™ is a novel glycooptimized humanized monoclonal antibody produced in GlycoExpress. It recognizes a unique carbohydrate-induced conformational epitope (TA-MUC1). This epitope is tumor-distinctive and is present in the majority of cases of a variety of carcinomas. PankoMab-GEX™ is currently in late Phase I trial.

Tumors carrying target molecules like Her2/neu, EGFR, CD20 and others are currently challenged by antibody therapeutics like Herceptin, Erbitux and Rituxan. However, clinical data shows that the success of the therapy depends on the FcγRIIIa allotype present within the treated patient. By Using GlycoExpress existing antibodies can be optimized in respect to manifold improvement of anti-cancer activity enabling clinicians to treat patients carrying the low affinity FcγRIIIa allotype and thus broadening the patient spectra. The activity of the antibodies was improved several hundred fold when measured by means of an ADCC assay. Furthermore the antibodies are improved with respect to half-life elongation and removal of immunogenic components. Two biobetter antibodies are currently in Phase I clinical trials.

Biography

Dr. Steffen Goletz, CEO, CSO and founder of the biotech company GLYCOTOPE, studied biology, biochemistry and molecular biology at the universities in Heidelberg, Kaiserslautern, Manchester (UK) and Berlin and holds a Ph.D. in biochemistry. During his research, Dr. Goletz has focused on glycobiology, tumor immunology, antibody engineering and cellular engineering. As CSO, Steffen is responsible for the development of GLYCOTOPEs product pipeline of glycooptimized biotherapeutics with four products currently in clinical trials.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Modification of mitochondrial DNA in breast cancer

Chin-San Liu[1,2,3], Shou-Dong Chen[4], Shou-Jen Kuo[4], Jui-Chih Chang[1] and Ta-Tsung Lin[1]

[1]Vascular and Genomic Research Center, Changhua Christian Hospital, China
[2]Department of Neurology, Changhua Christian Hospital, Changhua, China
[3]Graduate Institute of Integrated Medicine, China Medical University, China
[4]Department of Surgery, Changhua Christian Hospital, China

Alterations in mitochondrial DNA have been identified in breast cancer, however, the definite biomarkers of mitochondrial DNA (mtDNA) for cancer detection and prediction of the biological behavior and outcome of breast tumors still need to be confirmed forwardly. The object of this study is to investigate the influences of mitochondrial metabolism and mtDNA polymorphism correlated to histologic subtypes of breast cancer on a biological marker TP53 gene (p53) and clinicopathological parameters such as distal metastasis and disease-free survival (DFS) which measured at 5 years. The copy number, oxidative stress (formation of 8-OHdG in mtDNA), mtDNA 4,977-bp common deletion ($mtDNA^{4977}$) and somatic mutations in the D-loop region of mtDNA in breast cancer and paired nontumorous breast tissues from Taiwanese—patients were examined. We found that tumor group relative to normal group with a higher **relative copy number** and lower mtDNA oxidation individually displayed high level distal metastasis increase and poorer DFS. High percentage of *TP53* mutation only observed in tumor group with a higher **relative copy number**. For alterations in mtDNA variation in the breast cancer, the mtDNA from tumor tissues with negative $mtDNA^{4977}$ and high-level of D-loop mutation had high-level increase of *TP53* mutation percentage and distal metastasis following the poorer DFS. These results reveled that patients with higher copy number, lower oxidative damage, D-loop mutation of mtDNA and without $mtDNA^{4977}$, the malignant progression of breast cancer could be raised. The related regulation factor could be related with P53-**mediated** cell death for cancer cells.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Methylation array analysis of tissue DNA in oral squamous cell cancer patients in Taiwan

Yu-Fen Li[1], Yi-Hsiu Hsiao[1] and Chien-Kuo Tai[2]

[1]Graduate Institute of Biostatistics, China Medical University, Taiwan
[2]Department of Life Science, National Chung Cheng University, Taiwan

Purpose: The aim of this study is to perform a genome-wide methylation profile of 1,505 CpG sites of 807 cancer-associated genes and search for diagnosis and screening biomarkers for oral squamous cell cancer (OSCC).

Methods: Buccal tissue samples of 40 OSCC patients obtained from the tissue bank of China Medical University Hospital were served as the case group. A total of 15 normal samples composed the control group. Specificity, sensitivity, and the area under the Receiver Operating Characteristic curve (AUC) were calculated along with 5-fold cross validation to evaluate the accuracy of a predictive model.

Results: Thirty-four single CpG sites with both the sensitivity and specificity higher than 70% were selected as the classifier. A total of 8 panels consisted of two or three CpG sites showed a perfect specificity and a high sensitivity (85%~90%). The panel of genes ASCL1 and FLT4 represented the best combination with a perfect specificity, 90% of sensitivity, AUC=95%, and 92.6% (standard error 0.1%) of the mean correct classification rate in 5,000 times of the 5-fold cross validation.

Conclusions: In the present study we found the methylation status of the selected CpG sites might have a great potential to serve as the diagnostic biomarkers for OSCC. These promising candidate CpG sites deserve for further study in the early diagnosis and screening of OSCC.

Biography

Yu-Fen Li has completed her Ph.D in 2004 at University of Southern California. She has published more than 25 papers in reputed journals.

Chien-Kuo Tai has completed his Ph.D from University of Southern California and postdoctoral studies from UCLA. He is an associate professor at National Chung Cheng University.

Derivatives of 1,2 Diketo Propane and its role in anti cancer activity

Susmita Santra and Arindam Pramanik
Indian Institute of Technology-Kharagpur, India

Cancer which has become the most devastating disease of this era is an uncontrolled growth of cells through division beyond normal limits. Till now in research there are a number of therapies which have come up to fight against this disease. But unfortunately most of them are so toxic and injurious that the medicines become cause of the death of the patient. Among the safer therapeutics, Methylglyoxal is a one suggested by Albert Szent-Gyorgyi in 1963 which he termed as Retine.

This dicarbonyl compound which has both an aldehyde and ketone groups has been found to have anti-cancer property and produced by metabolic pathways like "glycolysis" to fight cancer in biological system through the destruction of mitochondria inside our body and it has been found that heat shock protein 27 (Hsp27) as a specific target of posttranslational modification by methylglyoxal in human metastatic melanoma cells. Biological origin and its role in anti-cancer activity are well established by Ray et al.

We have synthesized many derivatives which are modification of methylglyoxal and tested on cancer cell lines like B-16, HeLa, YAC-1 etc and found the results very promising. The compounds like 1,2-diketobutane , 3-methoxy and 3-ethoxy 1,2 diketopropane , 3(4methoxy) 1,2 diketopropane and many other derivatives have been synthesized and derivatives effectively inhibit the growth of cancerous cells and not causing any harm to the healthy cells. Preliminary treatment of these derivatives show, the tumoral growth is completely subsided by the healthy cells. Early results on animal models are highly encouraging.

Biography

Arindam Pramanik has completed his post graduation (MSc in Microbiology) at the age of 23 from University of Kalyani and currently doing research activities in the Nanometerials laboratory of Indian Institute of Technology (IIT), Kharagpur, India. His area of focus is on nanomedicines and its application on cancer and microbial system. He has 2 recent publications in international journals in 2010 and few more under communication. Susmita Pramanik has completed her post graduation (MSc in Biochemistry) from Bangalore University, India and currently residing in Windsor Ontario, Canada. She has 3 publications in reputed international journals.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Proteasome inhibitors target FOXM1 and induce p53-independent apoptosis in human cancer cells

Andrei L. Gartel
University of Illinois at Chicago, USA

Proteasome inhibitors are currently in the clinic or in clinical trials, but the mechanism of their anticancer activity is not completely understood. The oncogenic transcription factor FoxM1 is one of the most overexpressed genes in human tumors, while its expression is usually halted in normal non-proliferating cells. Previously, we established that thiazole antibiotics Siomycin A and thiostrepton inhibit FoxM1 and induce apoptosis in human cancer cells. We found that they also act as proteasome inhibitors in vitro. More importantly, we also found that well-known proteasome inhibitors such as MG115, MG132 and Velcade inhibit FoxM1 transcriptional activity and FoxM1 expression. Furthermore, we found that well-known proteasome inhibitors such as MG132 and bortezomib as well as the recently discovered proteasome inhibitor thiostrepton induced p53-independent apoptosis in human cancer cell lines that correlated with p53-independent induction of proapoptotic Noxa, but not Puma proteinOur data confirm that proteasome inhibitors generally induce p53-independent apoptosis in human cancer cells. We investigated the therapeutic potential of the combination of thiostrepton and proteasome inhibitor bortezomib (Velcade) on various human tumor cell lines. Combination of sublethal concentrations of thiostrepton and bortezomib induced potent apoptosis and inhibition of long-term colony formation in a wide variety of human cancer cell lines. The synergistic relationships between thiostrepton and bortezomib combination was also quantitatively demonstrated by low combination index between 0.1 and 0.8. The synergy between these drugs was based on their proteasome inhibitory activities of both drugs, because structurally similar thiostrepton modification, thiostrepton methyl ester that did not have inhibitory activity failed to increase apoptosis in combination with bortezomib. Thiazole antibiotic, thiostrepton was identified as an inhibitor of oncogenic transcription factor FoxM1, later demonstrated to exhibit proteasome inhibitory activity. We found that polymeric micelle-encapsulated thiostrepton reduced tumor growth rate in xenografts induced by human breast and liver cancer cell lines Encapsulation of thiostrepton into polymeric micelles can aid its solubilization and increase its accumulation into tumor sites. Furthermore, its anti-cancer effects on breast cancer xenografts were found to be through reducing cell proliferation and inducing cell death. Thiostrepton is sulfur containing highly modified macrocyclic antibiotic with a central pyridine/tetrapyridine/ dehydropiperidine ring with up to three thiazole substituents' on positions 2, 3 and 6, which has macrocyclic loop connecting thiazole rings at position 2 and 3 described as ring A. In addition, it has a quinaldic acid macrocycle also connected to thiazole on position 2 described as ring B. Structural modification of thiostrepton to thiostrepton methyl ester (with open B ring) did not demonstrate proteasome inhibitory activity. These data suggest that B ring of thiostrepton and similar thiazole antibiotic Siomycin A that is absent in other thiazole antibiotics determines the proteasome inhibitory activity of these drugs.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Saffron: A possible target for a novel anti-cancer drug against hepatocellular carcinoma

Amr Amin, Alaaeldin A. Hamza, Sayel Daoud
U.A.E University, UAE

Background & Aims: Saffron has been proposed as promising candidate for cancer chemoprevention. The purpose of this investigation was to investigate the chemopreventive action and the possible mechanisms of ethanolic extract of saffron's stigmas against induced-liver cancer in rats. The hepatocarcinogenesis was initiated by diethylnitrosamine (DEN) and promoted by 2-acetyl aminofluorene. Administration of saffron at doses 75 mg/kg, 150 mg/kg and 300 mg/kg per day started two weeks prior to the DEN injection and continued for 22 weeks.

Results: Saffron attenuated the carcinogenic changes induced by DEN. It reduced the DEN-induced elevation of the number and the incidence of hepatic dyschromatic nodules. Saffron also decreased the number and the area of glutathione-S-transferase, placental form -positive foci in livers of DEN-treated rats. Furthermore, saffron counteracted DEN-induced oxidative stress in rats as assessed by restoration of superoxide dismutase, catalase, glutathione-S-transferase and glutathione levels and diminishing myeloperoxidase, malondialdehyde and protein carbonyl in liver. The results of immunohistochemical staining of rat liver showed that saffron inhibited the DEN-mediated elevations in numbers of cells positive for Ki-67, cyclooxygenase 2, inducible nitric oxide synthase and nuclear factor-kappa B-p 65. Saffron also blocked the depletion in the number of cells positive for TUNEL and caspase-3 in liver tissues of DEN-treated rats. **Conclusions:** The present study provides evidence that saffron exerts a significant chemopreventive effect against liver cancer through inhibition of cell proliferation and induction of apoptosis. This report also show some evidence that saffron protects rat liver from cancer via modulating oxidative damage and suppressing inflammatory response.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Syzygiumcumini (pomposia) active principles exhibit potent anticancer and antioxidant activities

Hany A. El-Shemy, Abd El-Moneim M. R. Afify, Sayed A. Fayed, Emad A. Shalaby

Faculty of Agriculture, Cairo University, Egypt

The antioxidant and anticancer activities of fruit extracts *(Syzygiumcumini)* were investigated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical-scavenging assay and viability of leukemia cancer cells (AML cell line) respectively. The successive extracts; hexane, chloroform, ether, ethyl acetate, ethanol and water were prepared and subjected to antioxidant activities and anticancer activities evaluation. The results showed that the ethanol extract had stronger antioxidant and antileukemia activities than the other ones. Spectroscopic analytical data of active ingredients separated from ethanol extract indicated that *S. cumini*fruit extracts contained phenolic compounds, such Kaempferol 7-O-methylether and sterols such as γ-Sitosterol responsible for their antioxidant and anticancer activities. A significant linear relationship between anticancer potency, free radical-scavenging ability and the content of active compounds of fruit extracts supported this observation.

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Extended lymphadenectomy and Multiorgan Resection for Adenocarcinoma of Gastroesophageal Junction

Xijiang Zhao, Jie Yue, Xiangming Liu, Peng Tang, Peng Ren and Mingquan Ma

Tianjin Medical University Cancer Institute and Hospital, China

Background: To Study the extent of the lymphadenectomy and the value of resection of combined visceral organs in surgical treatment of the carcinoma of gastroesophageal junction (GEJ).

Methods: 323 patients with GEJ who underwent surgical resection had been treated as follows: 256 with proximal gastrectomy, 67 with total gastrectomy 185 with a combined-visceral resection, of which 154 underwent a splenectomy plus partial pancreatectomy, 21 with splenectomy alone and 10 with partial hepatectomy and diaphragmatectomy.The extent of lymphadenectomy was divided into five types(D0 to D4) and the curability of operation was graded as A, B and C.

Results: The total patients were divided into 3 groups: 138 with a gastrectomy alone, 21 with gastrectomy and splenectomy, and 164 with gastrectomy and splenectomy plus pancreatectomy and other organ. There were 185 patients who underwent a gastrectomy combined with a splenectomy and (or) the pancreatectomy, in which 222 No.10 lymph nodes were eliminated. Among the 138 patients not received a splenectomy but with elimination of lymph nodes, 154 underwent a gastrectomy combined partial a pancreatectomy, of which 231 lymph nodes were eliminated for the No. 11 group.

The overall survival rates were similar in the 3 groups showing no statistical differences, but was higher in the Stage III patients with a combined resection of multi-organs.For patients in the Stage IV without resection of multi-organs, the survival rate was higher. The lymph node metastasis occurred in 242 cases (75.0%). The metastasis rate in the group 1, 2, 3, 4, 7, 9, 12 , 110 and the pulmonary ligament group were higher than other groups. 4268 lymph nodes were removed, in which 912 (21.4%) demonstrated the existence of metastasis. The total ratio of metastatic lymph node in these groups was higher compared to the other groups.

Conclusions: The survival rate in the D1 lymphadenectomy and D2 was similar for all patients, and there may be some differences in the 2nd and 3rd years for the stage-IIIb patients. The survival rate of D2 lymphadenectomy in stage IIIb was better than D1 and that was superior to D1 in stage-IV patients. The survival rate of grade A and B operation was much better than grade C, and the survival rate of grade A was also higher than B.

The combination of a splenectomy and partial pancreatectomy result in a higher survival rate and had an important significance for eliminating the lymph nodes of group 10 and 11. The application of a resection combining multi-organs should be based on on the condition that the cancerous tissue is totally resected .

AUTHOR INDEX

OMICS Group Conferences
Accelerating Scientific Discovery

Conferences

Previous Conferences

2011


International Conference & Exhibition on Proteomics & Bioinformatics 6-8 June 2011 HICC, Hyderabad, India


International Conference & Exhibition on Pharmaceutical Biotechnology 6-8 June 2011 HICC, Hyderabad, India


2nd World Congress on Bioavailability & Bioequivalence: Pharmaceutical R & D Summit 6-8 June 2011 Las Vegas, USA


International Conference on Pharmaceutics & Novel Drug Delivery Systems 7-8 June Las Vegas,USA


World Congress on Biotechnology 21-23 March 2011 Hyderabad, India


International Conference & Exhibition on Clinical Research: Dermatology, Ophthalmology and Cardiology 5-6 July 2011 San Francisco, USA


International Conference & Exhibition on Cancer Science & Therapy 15-17 August 2011 Las Vegas, USA

2008-2010


International Conference on Diabetes and Metabolism 13-14 December 2010 Santa Clara, USA


International Conference on Biomarkers & Clinical Research 22-23 November 2010 Santa Clara, USA

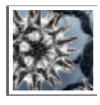

International Conference and Exhibition on Analytical and Bioanalytical Techniques: Pharmaceutical R & D Summit, 01-03 November 2010 Hyderabad, India


International Conference & Exhibition on Bioequivalence & Bioavailability, Pharmaceutical R & D Summit, March 01-03, 2010

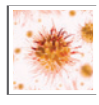

Integrating Glycomics with other Omics in Cancer Detection and Diagnosis January 19-20, 2010, Stanford University School of Medicine, USA


3rd World Congress of Gene-2009 December 1-7, 2009


7th Annual World Congress of International Drug Discovery Science & Technology October 22-25


2nd Annual World Summit Antivirals

July 18-20, 2009


1st CCSB-2009

February 16-17, 2009

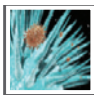

2nd PRICPS-4th AOHUPO

June 22-26, 2008


95th ISCA

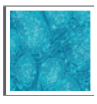
January 5-8, 2008

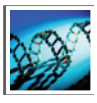
Upcoming Conferences

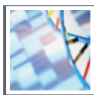

International Conference and Exhibition on Virology 5-7 September 2011 Baltimore, USA


International Conference on Pharmaceutical Regulatory Affairs 6-7 September 2011 Baltimore, USA


2nd World Congress on Biomarkers & Clinical Research 12-14 September 2011 Baltimore, USA


International Conference and Exhibition on Vaccines & Vaccination 22-24 November 2011 Philadelphia, USA

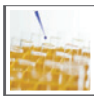

International Conference and Exhibition on Cell Science & Stem Cell Research 29 Nov-1 Dec 2011 Philadelphia, USA


OMICS Group 2nd World Congress on Biotechnology 29 Nov-1 Dec 2011 Philadelphia, USA


2nd World Congress on Diabetes & Metabolism 6-8 December 2011 Philadelphia, USA

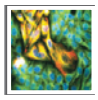

OMICS Group World Congress on Paediatrics & Gynaecology 6-8 December 2011 Philadelphia, USA

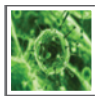

International Conference on Metabolomics & Systems Biology 19-22 February 2012 San Francisco, USA


OMICS Group 2nd World Congress on Clinical Research 4-6 March 2012 Omaha, USA

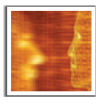

International Conference and Exhibition on Biometrics & Biostatistics 5-7 March 2012 Omaha, USA


OMICS Group World Congress on Gastroenterology & Urology 11-14 March 2012 Omaha, USA

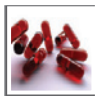

International Conference and Exhibition on Nanotechnology & Nanomedicine 11-14 March 2012, Omaha, USA


OMICS Group 2nd World Congress on Cancer Science & Therapy 9-11 July 2012 Pheladelphia, USA

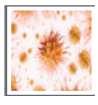

International conference and Exhibition on Biosensors & Bioelectronics April 2012 Baltimore, USA


OMICS Group 2nd World Congress on Proteomics & Bioinformatics 14-16 May 2012 Las Vegas, USA


International Conference and Exhibition on Neurology & Neurophysiology 14-16 May 2012 Las Vegas, USA


OMICS Group 3rd World Congress on Bioavailability & Bioequivalence June 2012 Hyderabad, India


OMICS Group 2nd World Congress on Pharmaceutics & Novel Drug Delivery Systems June 2012 San Francisco, USA


OMICS Group 2nd World Congress on Virology July 2-4 2012 Las Vegas, USA


International Conference and Exhibition on Addiction Research & Therapy July 2-4 2012 Las Vegas, USA


OMICS Grooup 3rd World Congress on Biomarkers & Clinical Research August 20-22 2012 Las Vegas, USA


International Conference and Exhibition on Clinical & Cellular Immunology August 20-22 2012 Las Vegas, USA


OMICS Group 2nd World Congress on Vaccines & Vaccination August 2012 San Francisco, USA

OMICS Group Conferences

2360 Corporate Circle.Suite 400, Henderson, NV 89074-7722, USA
Ph: +1-650-353-4497, Fax: +1-650-618-1417, Toll free: 1-800-216-6499(USA & Canada)
0805-080048 (Europe), +81-345780247 (Japan), 1-800-651-097 (Australia)

Encyclopedia of Bioequivalence and Bioavailability (E-BABE)

Analytical and Bio-Analytical Methodology Database

- World's only database powered by an updated bioanalytical methods of pharmaceuticals for suitable method selection with over thousands of combinations and automatic checks against thousands of methods: all at your finger tips.
- Intelligent processing which understands your analytical terminology and lets you generate, select of your priority and much more in seconds.
- Use the comprehensive analytical and bio-analytical methodology tool to select important method for an insight into regular quality control.
- Now selection of Analytical and Bio-analytical methods of pharmaceuticals for analysis/routine quality control is on your finger tips for a click!
- All-in-one database with multi-user access.
- As of now it has 5000 methods and is updated regularly.

http://ebabe.gsblifesciences.org

Bookmark your dates

2nd World Congress on

Cancer Science & Therapy

9-11 July 2012 Philadelphia, USA

OMICS Publishing Group
5716 Corsa Ave, Suite 110
Westlake, Los Angeles
CA 91362-7354, USA
Ph: +1-650-268-9744
Fax: +1-650-618-1414

OMICS Group Conferences
2360 Corporate Circle · Suite 400
Henderson, NV 89074-7722, USA
Ph: +1-650-353-4497
Fax: +1-650-618-1417

OMICS Publishing Group
26Joseph Drive, Hillside
Victoria 3037, Australia
Ph: +61 3 9449 0958

OMICS Group
1-90/1, Plot No.20, Kavuri Hills,
Madhapur - HITEC City
Hyderabad, A P, INDIA - 500 081
Ph: 040-40138580/81

Toll free
USA & Canada: 1-800-216-6499
Europe: 0805-080048
Japan: +81-345780247
Australia: 1-800-651-097