

OMICS Group
Conferences
Accelerating Scientific Discovery

Journal of
Molecular
Biomarkers &
Diagnosis Open Access

September 2011 Volume 2 Issue 4

ISSN: 2155-9929

Biomarkers-2011

Proceedings of
2nd World Congress on

BIOMARKERS & CLINICAL RESEARCH

12-14 September 2011 Baltimore, USA

Conference Venue

BWI Airport Marriott,
1743 West Nursery Road,
Linthicum Heights, Baltimore
Maryland 21090-2906 USA
Phone No: (410)859-8300



Conference Secretariat

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

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

About OMICS

OMICS Publishing Group is an Open Access publication model with a mission to influence, encourage and assist scientists that enables the dissemination of research articles to the global community. It provides an open forum to share on science and technology and research policies around the globe and contributes to the creation of an integrated space for science and technology.

OMICS Publishing Group also organizes meetings at the international level and this focus has successfully led to the expansion of the group into rising business areas and an ability to innovate, especially in the digital layout.

- | | | |
|---|--|---|
| H | » Neonatal Biology | R |
| » Hair : Therapy & Transplantation | » Nephrology & Therapeutics | » Radiology: Open Access |
| » Health & Medical Informatics | » Neurology & Neurophysiology | » rDNA Technology |
| » Hereditary Genetics | » Novel Physiotherapies | » Reproductive System & Sexual Disorders |
| » Homeopathy & Ayurvedic Medicine | » Nuclear Energy & Power Generation Technologies | » Rheumatology |
| » Hotel & Business Management | » Nuclear Medicine & Radiation Therapy | S |
| » Human Genetics & Embryology: Current Research | » Nutrition & Food Sciences | » Sleep Disorders & Therapy |
| » Hydrology: Current Research | » Nutritional Disorders & Therapy | » Social & Economical Issues of Biotechnology |
| » Hypertension- Open Access | » Nursing & Care | » Socialomics |
| I | O | » Sports Medicine & Doping Studies |
| » Industrial Engineering & Management | » Obesity & Weight loss Therapy | » Spine |
| » Irrigation and Drainage Systems Engineering | » Organ Biology | » Stem Cell Research & Therapy |
| » Information Technology & Software Engineering | » Organic Chemistry: Current Research | » Steroids & Hormonal Science |
| » Internal Medicine | » Orthopedic & Muscular System: Current Research | » Stock & Forex Trading |
| L | » Otolaryngology | » Surgery |
| » Liver | P | T |
| M | » Pain & Relief | » Telecommunications System & Management |
| » Marine Science: Research & Development | » Palliative Care & Medicine | » Textile Science & Engineering |
| » Mass Communication & Journalism | » Pancreatic disorders & Therapy | » Thermodynamics & Catalysis |
| » Material Sciences & Engineering | » Pediatrics & Therapeutics | » Thyroid Disorders & Therapy |
| » Medicinal Chemistry | » Petroleum & Environmental Biotechnology | » Tissue Science & Engineering |
| » Medical advancements in Genetic Engineering | » Pharmaceutica Analytica Acta | » Translational Medicine |
| » Medicinal & Aromatic Plants | » Pharmaceutical Biotechnology | » Transplantation Technologies & Research |
| » Medical Diagnostic Methods | » Pharmaceutics & Drug Delivery Research | » Trauma |
| » Medical Microbiology & Diagnosis | » Pharmacoepidemiology & Drug Safety | » Tourism & Hospitality |
| » Membrane Science & Technology | » Pharmacogenomics & Pharmacoproteomics | U |
| » Metabolic Syndrome | » Physical Chemistry & Biophysics | » Urology |
| » Microbial & Biochemical Technology | » Plant Pathology & Microbiology | V |
| » Molecular Biology | » Postgenomics: Drug & Biomarker Development | » Vaccines & Vaccination |
| » Molecular Biomarkers & Diagnosis | » Powder Metallurgy & Mining | » Veterinary Science & Technology |
| » Molecular Imaging & Dynamics | » Primatology | » Virology & Mycology |
| » Mycobacterial Diseases | » Primary Health Care | » Vitamins & Trace Elements |
| N | » Proteomics & Bioinformatics | W |
| » Nanomedicine & Biotherapeutic Discovery | » Psychology & Psychotherapy | » Women's health |
| » Nanomedicine & Nanotechnology | » Pulmonary & Respiratory Medicine | Y |
| | | » Yoga & Physical Therapy |

Contact us at: contact.omics@omicsonline.org

http://www



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.

on = data
geto = data
statement.execute
Set.next()

NANOSIGHT

seeing is believing



www.nanosight.com

Nanosight

NanoSight Ltd, is a company which designs and manufactures Nanoparticle Analysis Instruments. The company was founded in 1999 by Dr. Bob Carr to further develop a technique he invented to visualize nanoparticles suspended in liquid. The company has since developed the technique of Nanoparticle Tracking Analysis (NTA) and they produce a series of instruments to count, size and visualize nanoparticles in liquid suspension using this patented technology.



Products

NanoSight develops and produces products to visualize, characterize and measure virtually all nanoparticles. Their products can analyse particle size, concentration, aggregation and zeta potential simultaneously with a fluorescence mode allowing speciation of labeled particles.

The instruments comprise of a scientific camera, microscope and an LM12 sample viewing unit and are used in conjunction with a computer control unit which runs the Nanoparticle Tracking Analysis (NTA) software. The LM12 uses a 638 nm red laser diode to illuminate particles in liquid suspension which are held within the unit. NTA is used to analyze videos captured using the instrument, giving a particle size distribution and particle count.

Both the LM10 and the LM20 operate using a custom-designed software package, NTA. This software identifies and tracks individual nanoparticles which are moving under Brownian motion and relates the movement to a particle size. This is carried out for all particles in the laser scattering volume to produce a particle size distribution using the Stokes-Einstein equation, relating the Brownian Motion of a particle to a sphere-equivalent hydrodynamic radius.

NanoSight Limited

Minton Park,
London Road,
Amesbury
SP4 7RT
UK
Tel: +44 (0) 1980 676060
Fax: +44 (0) 1980 624703
Email: enquiries@nanosight.com

USA West Coast Office

Duncan Griffiths
NanoSight USA West
3027 Madeira Ave.
Costa Mesa, CA 92626
Tel: 714-747-9955
Email: duncan.griffiths@nanosight.com

USA East Coast Office

Jim Munhall
NanoSight East Coast Office
6660 N. High Street, Suite 2A
Worthington, Ohio 43085
Tel: (614) 888-0023
Fax: (614) 987-0045
Cell: (614) 264-3493
Email: jim.munhall@nanosight.com

USA East Coast Office

Malcolm Bailey
407 Keene Street
Duxbury
MA 02332
Tel: 603-490-2032
Email: mac.bailey@nanosight.com



Supporting Journals



2nd World Congress on Biomarkers & Clinical Research

12-14 September 2011 Baltimore, USA

Editors & Editorial Board



Krishnan VV California State University, USA	Godwin Okoi Ifere Clark Atlanta University, USA	Simon Langdon University of Edinburgh, UK
Jagjit S. Yadav University of Cincinnati, USA	Abdul Shakoor Chaudhry Newcastle University, UK	Jennifer Spratlin University of Alberta, Canada
Marco Falasca London School of Medicine & Dentistry UK	Babak Kateb International Brain Mapping & Intraoperative Surgical Planning Society, USA	Victor H Obungu Biotechnology Discovery Research Eli Lilly and Company, USA
Jin-ichi Inokuchi Tohoku Pharmaceutical University, Japan	Tiandao Li University of Iowa, USA	Nicolas Pallet Centre Universitaire des Saints Peres France
Teresa Coccini Scientific Institute of Pavia Toxicology Division, Italy	Hayley C. Whitaker Cambridge Research Institute, UK	Yang Yongliang Harvard University, USA
James V. Rogers Battelle Memorial Institute, USA	Huixiao Hong National Center for Toxicological Research USA	Chakravarty Tulane University Health Science Center USA
Wellington Pham Vanderbilt University, USA	Paolo Antonio Ascierio Unit of Medical Oncology and Innovative Therapy, Italy	Jamal Alruwaili University of Portsmouth, UK
Jianjun Cheng University of Illinois, USA	Mario Scartozzi Universita Politecnica delle Marche Ancona, Italy	Philipp Schuetz Harvard School of Public Health, USA
Sa A. Wang UT MD Anderson Cancer Center, USA	Murielle Mimeault University of Nebraska Medical Center, USA	Jiang He Center for Molecular & Functional Imaging, USA
C. Cameron Yin University of Texas, USA	Sunil Badve Indiana University School of Medicine, USA	Wen Jin Wu Division of Monoclonal Antibodies, USA



Journal of Molecular Biomarkers & Diagnosis is an open access scientific peer reviewed journal. It publishes the most exciting researches with respect to biomarker development and their diagnostic applications. This journal helps the people who are into emerging fields of biological and clinical business for global development.

Aims & Scope

Journal of Molecular Biomarkers and Diagnosis deals with biological indicators that signal a changed physiological state in drug discovery and clinical diagnosis by application areas and by technologies.

Journal of Molecular Biomarkers & Diagnosis - Open Access uses online manuscript submission, review and tracking systems of Editorial Manager® for quality and quick review processing.

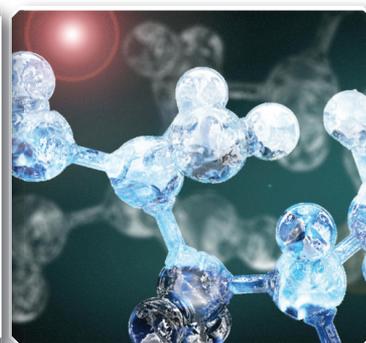
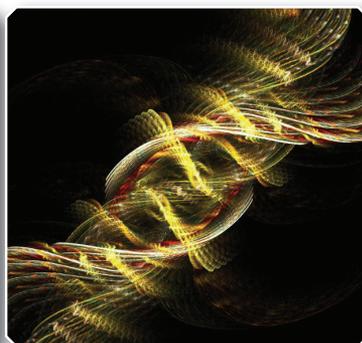
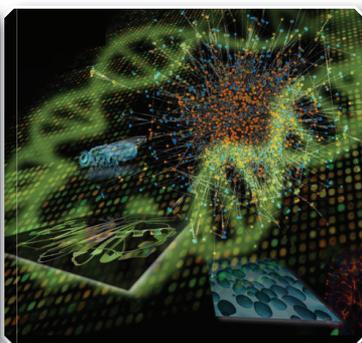
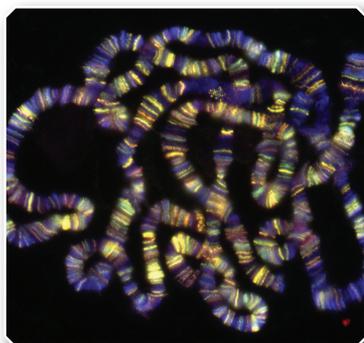
Submit your manuscript at
<http://www.editorialmanager.com/pharma/> (or)
 E-mail to editor.jmbd@omicsonline.org

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/jmbdhome.php>

Biomarkers are becoming a vital and indispensable part of clinical development. The importance of drug and biomarker development is to improve decision making, accelerate drug designing and reduce development costs mainly focusing on post-genomic processes.

Aims & Scope

Journal of Postgenomics: Drug & Biomarker Development (JPDBD) is an international, peer-reviewed scientific journal which provides a wide range of freely available online journals, review articles and research articles in the field of clinical, medical, biotechnological, pharmaceutical and other related life science areas.



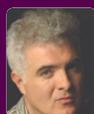
Editors & Editorial Board



Beata Lecka-Czernik
University of Toledo College
of Medicine, USA



Robert M. Snapka
The Ohio State University
USA



Ariel Fernandez
Rice University, USA



Jason P. Holland
Memorial Sloan-Kettering
Cancer Center, USA



Keqiang YE
Emory University School of
Medicine, USA



Peter L. Elkin
Mount Sinai School of
Medicine, USA



Natarajan Muthusamy
The Ohio State University
USA



Periasamy Selvaraj
Emory University, USA



Vineet Gupta
University of Miami, USA



Pengyu Hong
Brandeis University, USA

Jose Segovia BiophysicandNeurosciences, Cinvestav, Mexico	Takeki Uehara Developmental Research Laboratories, Japan
Sivanesan Dakshanamurthy Georgetown University Medical Center, USA	Satomi Onoue University of Shizuoka, Japan
Adin-Cristian Andrei University of Wisconsin-Madison, USA	Ramon Cacabelos Institute for CNS Disorders and Genomic Medicine, Spain
Irina Burd University of Pennsylvania, USA	Kaname Ohyama Nagasaki University, Japan
Shona Dalal Harvard School of Public Health, USA	Enrico Domenici GSK Medicines Research Centre, Italy
Steven Alan Enkemann H. Lee Moffitt Cancer Center and Research Institution, USA	Volker Daniel University of Heidelberg, Germany
Joseph Yeboah University of Virginia, USA	Andrea Kristina Horst University Medical Center Hamburg-Eppendorf, Germany
E. H. Yang Stevens Institute of Technology, USA	Sang Soo Hah Kyung Hee University, South Korea
Garry W. Buchko Pacific Northwest National Laboratory, USA	Bin Zhou Translational Research Informatics Center, Japan
Hiroyuki Kobori COE Tulane University Health Sciences Centre, USA	Monika Podhorecka Medical University of Lublin, Poland
Adebowale Adeyemo National Institutes of Health Bethesda, USA	Sharon Fontaine Terry University of Connecticut, USA
Francesco Marotta Texas University, Italy	Wang Kai Institute for Systems Biology, USA
Chad Bousman University of Melbourne, Australia	Linghui Li St Luke's Hospital, USA
Fumio Tsuji Santen Pharmaceutical Co., Ltd, Japan	Tao Jin Gothenburg University, Sweden
Friederike Teichert University of Leicester, UK	Sayed S. Daoud Washington State University, USA

Journal of Postgenomics: Drug & Biomarkers Development- 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.editorialmanager.com/omicsgroup> (or)

E-mail to editor.jpdbd@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/jpdbdhome.php>



Upcoming Conferences



2nd World Congress on Biomarkers & Clinical Research

12-14 September 2011 Baltimore, USA



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 Hovanesian
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



Mansour Mohamadzade
Northwestern University
USA



DEIVA Kumaran
University of Paris XI
France



Date & Venue

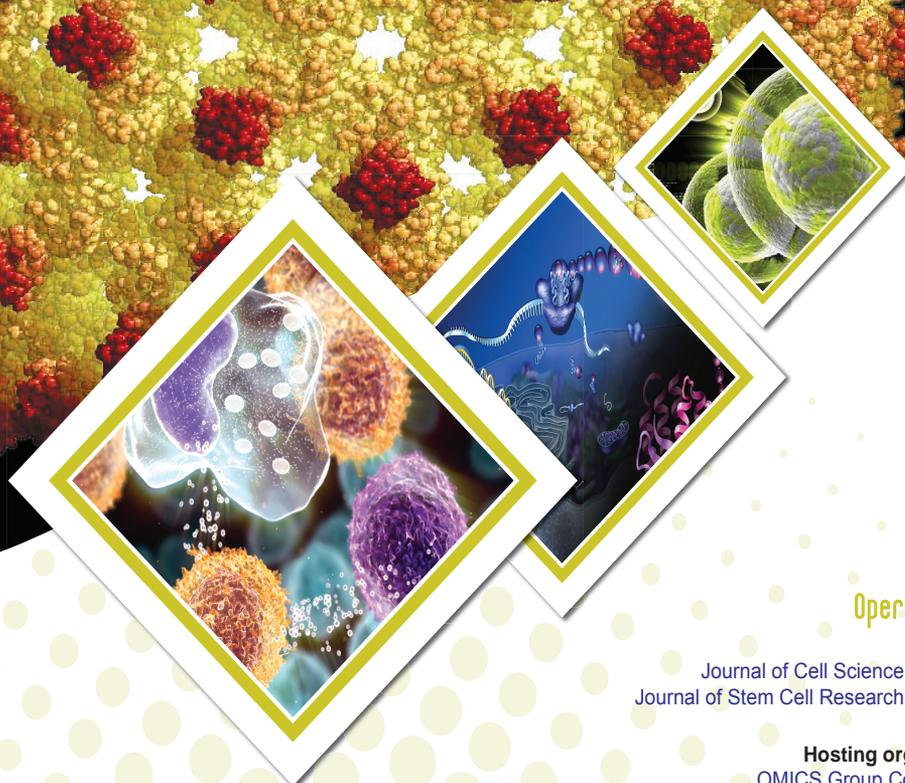
22-24 Nov 2011

Philadelphia, Marriott Hotel, USA

<http://www.omicsonline.org/vaccines2011>



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>

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>



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 Malese
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 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



George Perry
University of Texas at San Antonio, USA



Kenneth Blum
University of Florida College of Medicine, USA



Hareesh B. Nair
Texas Biomedical Research Institute San Antonio, USA



Burim N. Ametaj
University of Alberta Canada



Akhil Maheshwari
University of Illinois Chicago, USA



Neeraj Vij
John Hopkins University USA



X. Long Zheng
The University of Pennsylvania Medical Center, USA



Muhammad J. Javed
University of Illinois College of Medicine, USA



Duraisamy Balaguru
University of Texas, USA



Edward K.S. Chien
Gynecology Brown University, USA



Date & Venue

6-8 December 2011

Philadelphia, USA

<http://omicsonline.org/pediatrics2011>



2nd World Congress on Analytical & Bioanalytical Techniques



Operated by:
Editors

Journal of Analytical & Bioanalytical Techniques
Journal of Chromatography & Separation Techniques
Journal of Bioanalysis & Biomedicine

Hosting organization

OMICS Group Conferences
5716 Corsa Ave., Suite 110, Westlake Los Angeles CA 91362-7354, USA
Tel: +1-650-268-9 744, Fax: +1-650-618-1414, Toll free: 1-800-216-6499(USA & Canada)
E-mail: analytica2011@omicsonline.org

Organizing Committee

 <p>Halim Abdel-Baset Daichi Sankyo Pharma Development, USA</p>	 <p>Guo Lei Food and Drug Administration, USA</p>	 <p>Andrew Adamatzky University of the West of England, UK</p>	 <p>John Zhou London South Bank University, UK</p>	 <p>Edward Lai Carleton University, Canada</p>
 <p>Mirko Diksic McGill University, Canada</p>	 <p>Yoshihiro Mochimaru Tokyo Institute of Technology, Japan</p>	 <p>Pierre Guertin Laval University, Canada</p>	 <p>Roderiek Slavcev University of Waterloo, Canada</p>	 <p>Gilmar S. Erzinger University of the Region of Joinville, Brazil</p>



Date & Venue

16-17 December 2011

San Francisco Airport Marriott , USA

<http://www.omicsonline.org/analytica2011>

International Conference & Exhibition on Metabolomics & Systems Biology



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



Kazuyuki Nakamura
HUPO Council Member,
Japan



Miroslava Cuperlovic-Culf
National Research Council
of Canada, Canada



Bernd Lepenies
Max Planck Institute,
Germany



Gradimir Misevic
Gimmune GmbH
Switzerland



Guanyu Wang
George Washington
University, USA



Zhongming Zhao
Vanderbilt University, USA



Jimmy Efrid
University of North Carolina,
USA



Jagat R. Kanwar
Deakin University, Australia



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



Xue-Long Sun
Cleveland State University,
USA



Date & Venue

20-22 February 2012

San Francisco Airport Marriott, USA

2nd World Congress on Pharmaceutics & Novel Drug Delivery Systems



Operated by:

Editors

Journal of Pharmaceutics & Drug Delivery Research
Pharmaceutica Analytica Acta

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: pharmaceutica2012@omicsonline.org

Organizing Committee



Maryse Picher
Consultant Expert at Zinpro
Inc, USA



Yan Hu
University of Yamashashi
Takeda, Japan



Seyed Moien Moghimi
Chemistry University of
Copenhagen Denmark



Shivanand puthli
Mumbai India



Hideko Kaji
Jefferson University
USA



Alexander A. Kamnev
Microorganisms Russian
Academy of Sciences,
Russia



Sudip K. Das
Research Butler University
USA



Sudhakar Akulapalli
University of Nebraska, USA



Rakesh Srivastava
University of Kansas,
Kansas City



Ayman M. Noreddin
Hampton University, USA



Date & Venue

20-22 February 2012

San Francisco Airport Marriott, USA

2nd World Congress on Clinical Research Dermatology, Ophthalmology and Cardiology



Operated by:

Editors

Journal of Clinical & Experimental Dermatology
 Journal of Clinical & Experimental Ophthalmology
 Journal of Clinical & Experimental Cardiology

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: clinicalresearch2012@omicsonline.org

Organizing Committee

 Lucian Lozonschi University of Wisconsin School of Medicine, USA	 George Kroumpouzos Brown University, USA	 Michael W. Stewart Mayo Clinic, USA	 Jon C. George Deborah Heart and Lung Center, USA	 S.Wamique Yusuf University of Texas, USA
 Maria M. Tsoukas University of Chicago, USA	 Sudhakar Akulapalli Boys Town National Research Hospital, USA	 Larregina AT University of Pittsburgh, USA		



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



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/>



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

 Jiandi Wan Princeton University, USA	 Joachim Koetz University of Potsdam, Germany	 Rakesh K. Joshi University of Manchester U. K	 Yi Liu California Institute of Technology, USA	 Lev Solomon Ruzer Lawrence Berkeley National Laboratory, USA
 Wilson 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



Date & Venue

12-14 March 2012 Omaha, USA

Gastroenterology -2012

OMICS Group
Conferences
Accelerating Scientific Discovery

World Congress on Gastroenterology & Urology



Operated by:

Editors

Journal of Gastrointestinal & Digestive System
Urology: Current Research

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 Perakash
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. Kharbada
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>



3rd World Congress on Bioavailability & Bioequivalence

Pharmaceutical R & D Summit



Operated by:

Editors

Journal of Bioavailability and Bioequivalence
Journal of Bioanalysis and Biomedicine
Pharmaceutica Analytica Acta

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: babe2012@omicsonline.org

Organizing Committee



Bhaswat S. Chakraborty
Pharmaceuticals Ltd
Ahmedabad, India



George Perry
University of Texas
USA



Hareesh B. Nair
National Primate Research
Center Texas Biomedical
Research Institute, USA



Yulong Yin
Institute of Subtropical,
Changsha



Shivanand P. Puthli
Mumbai, India



Alexander A. Kamnev
Microorganisms Russian
Academy of Sciences,
Russia



Kiran Dip Gill
Institute of Medical
Education and Research,
India



Khalid M Alkharfy
King Saud University, Saudi
Arabia



Date & Venue

26-28 March 2012

Hyderabad Marriott Hotel, India

<http://www.omicsonline.org/BABE2012>



Key Note Forum



2nd World Congress on Biomarkers & Clinical Research

12-14 September 2011 Baltimore, USA



Dr. Abdel Halim

Daiichi-Sankyo Pharma Development, USA

Biomarkers in drug discovery: Potential use versus challenges

The role of biomarkers has been exponentially increasing in guiding decisions in every phase of drug development, from drug discovery into post-marketing studies. Also, biomarkers can predict patients' response to compound by identifying certain patient populations that are more likely to respond to the drug therapy or to avoid specific adverse events. This shift toward "personalized medicine is helping the drug industry achieve the goal of cost-effective and faster research, especially in poorly served areas such as neurodegenerative disorders and cancer.

Biomarkers assays range from esoteric type of assays performed on a fit-for-purpose basis to rigorously validated assays when a biomarker is used as a surrogate end point, for patient selection, or for randomization into different arms. Assay validation is essential, but of equal or even greater importance is the monitoring of assay performance and level of quality during production.

Despite all of the potential benefits of using biomarkers to advance pharmaceutical industry, discrepant results can pose a threat to development programs by triggering false decisions. Laboratory errors may be of pre-analytical, analytical, or post-analytical origin. Although clinical laboratory errors due to analytical problems have been, with momentous efforts, significantly reduced over time, the overall quality of clinical laboratory results can be compromised by the absence of true method-to-method or platform-to-platform standardization, or at least harmonization of test results.

This talk will highlight the following topics;

- Biomarkers and their potential utility in drug development.
- The major reasons behind discrepant results from biomarker laboratories and how to mitigate them.

Biography

Abdel Halim is a nationally recognized biomarker and clinical laboratory professional with more than 25 years of experience in all aspects of biomarker discovery, development, validation, and applications in patient management and pharmaceutical development. He is an expert in all biomarker techniques and platforms From safety lab POC till whole genome sequencing.

Abdel is leading the biomarker function within Daiichi-Sankyo pharmaceutical company and managing all safety and specialty biomarker aspects across different therapeutic areas in all phases of drug development.

Abdel holds Pharm D, and PhD in Clinical Biochemistry and Molecular Biology, and one of three lab professionals in the USA who are triple certified by the American Board in Clinical Chemistry, Molecular Diagnostics, and Toxicology.

Abdel is a member of 14 Clinical Laboratory Standard Institute (CLSI) subcommittees to establish guidelines promoting quality in clinical laboratories worldwide.



Mr. Jeremy Warren

NanoSight Ltd, United Kingdom

Seeing, counting and phenotyping exosomes as biomarkers using nanoparticle tracking analysis

Exosomes are 30-100nm nanovesicular bodies released from endosomes which originate in a wide variety of cells and can be found in most body fluids including blood, urine, saliva, breast milk etc.,. They are currently the subject of intense study, being increasingly recognized as playing multiple roles in intracellular communication and immune regulation. As well as displaying membrane proteins reflecting from their cellular origin, exosomes have now been shown to carry micro- and mRNA. It is increasingly accepted that exosomes are implicated in a multitude of pathological conditions and show much promise as diagnostics for many different diseases such as cancer, heart disease, diabetes, Alzheimer's, pre-eclampsia, etc. However, because of their small size, they are below the current detection limit of flow cytometry and the lack of methods for their detection and analysis is inhibiting progress in this field.

Nanoparticle Tracking Analysis is a relatively new method by which deeply submicron structures can be individually visualized and, through analysis of their Brownian motion, sized and counted in real time and with a rapid and robust microscopical methodology. Furthermore, fluorescently labeled exosomes can be successfully tracked and analysed allowing phenotyping of subpopulations in complex sample types which could form the basis of a new form of diagnostic test.

We will show results gained recently from the use of NTA in the development of a diagnostic test for pre-eclampsia and we will review other studies in which NTA has been most lately used to speciate and enumerate exosomes.

Biography

From a degree in Chemical Engineering from the University of Birmingham, UK, Warren worked for Unilever in chemical production where he qualified as a chartered engineer. He then set up a successful chemicals manufacturing business in Belgium, before completing an MBA at INSEAD in France. After a period in strategy consultancy with Booz.Allen, Warren began a series of CEO roles in SMEs centered on developing technology businesses. Warren joined NanoSight in 2005 as CEO and was directly involved in development of the company's multiparameter characterization technology. During the last two years emphasis has been on biological nanoparticles, with particular interest in the use of NanoSight as a platform for their detection and diagnostic application.



Dr. Jean Gabert

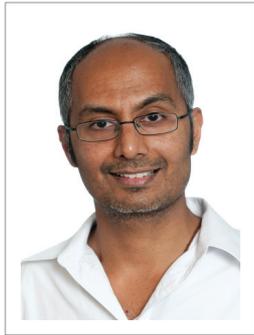
INSERM CRO2, Université de la Méditerranée, France

From research to the clinic: lessons from *BCR ABL* dosage in the tyrosine kinase inhibitors era

Standardisation and external quality controls are part of the routine in clinical biochemistry since years. International standards and external quality control rounds are absolutely warranted for any new biological marker for its worldwide use into the clinics. It is done for 40 years in biochemistry but such approach is still in its infancy for molecular biology tests. Taking the measurement of *BCR ABL* transcripts (M-BCR) as a model, we first developed a standardisation effort and external quality controls through the European Against Cancer (EAC) network then we developed freeze dried cells that can be sent worldwide at room temperature. *BCR ABL* is present mainly in patients having a chronic myeloid leukemia (CML). This naturally deadly disease has seen its prognostic revolutionized with the use of tyrosine kinase inhibitors targeting the BCR ABL protein. Now there is an international consensus to adapt the treatment based on the dosage of *BCR ABL* gene expression by real time PCR. We participated to the development of an international standard based on freeze dried cells which has been validated by the world Health Organization last year. During the meeting will be reported our efforts in this field at the regional, national and international levels and how biotech companies can participate to the effort of follow up improvement for health care patients.

Biography

Dr. Jean Gabert, Professor of Biochemistry and Molecular Biology, Faculty of Medicine, Méditerranée University, Marseille (France).



Dr. Crispin R. Dass

Victoria University, Australia

From research to the clinic: lessons from *BCR ABL* dosage in the tyrosine kinase inhibitors era

Cancer is a group of diseases characterized by uncontrolled growth of cells in the body. These lesions, if not treated, grow until they become life-threatening or fatal. Traditionally, surgery has been the main form of tumor control, though this is not performed where the growth is deep-seated in the body or located at a site where surgery could itself be life-threatening. Alternatives to, or assisting surgery are chemotherapy and radiotherapy. However, these two traditional forms of cancer therapy suffer due to harmful effects to the healthy parts of the body. To address this, there is a global push to find compounds that are effective against neoplastic cells, but less harmful against normal healthy cells of the body. Complementing this is the search for *in vitro* or *in vivo* assays that are more indicative of antitumor activity. Finally, there has been a growing push to find better drug delivery systems capable of more selective delivery of drugs to tumors in the body. This presentation discusses some of the cell-based assays and small animal models set up by our labs in the past decade, drug delivery systems we have tested so far, and biologicals (protein, nucleic acid, polysaccharide) trialed so far, some of which are undergoing clinical testing.

Biography

Crispin R. Dass has 17 years of cell and molecular biology research experience, mainly focusing on oncological R&D. His research is on systems at various levels – *in silico*, *in vitro*, *in vivo*, ADME/Tox, clinical, and also with biomedical education. He has worked on projects for Johnson & Johnson, GlaxoSmithKline, Amgen, and Novartis. His extensive experience is documented in his 120 papers to date, with publications in *Nature Medicine*, *Journal of the National Cancer Institute*, *Biomaterials*, *Nucleic Acids Research*, *Cancer*, and *Journal of Controlled Release*. He is currently on the editorial board of 3 other journals in his field, and has been invited to chair sessions and to give plenary lectures at national and international conferences. Based currently in St Albans (Melbourne, Australia), he has research links with Thailand, Fiji, USA, China, South Korea, Japan, Iran and India.



Scientific Tracks & Abstracts



2nd World Congress on Biomarkers & Clinical Research

12-14 September 2011 Baltimore, USA

1(i): Patient Segmentation and Stratification: Successful Integration of Diagnostic Tools

1(ii): Clinical Data Annotation: Classification Distribution Metrics, Pattern Recognition

Session Chair

Dr. Robert A. Warner

Tigard Research Associates, USA

Session Introduction

Title: Color-coded Z scores for the display and analysis of biomedical data

Dr. Robert A. Warner, Tigard Research Associates, USA



Title: Heat acclimation associated with decreased of urinary 8-hydroxydeoxyguanosine in navy boiler tender

Dr. Yung-Kai Huang, Taipei Medical University, Taiwan



Title: Dose time of presentation of patients of severe sepsis determines the clinical outcome?

Dr. Fahad Aziz, MSSM-Jersey City Campus, USA



Title: Biomarkers for novel diabetes therapies in early clinical development. Examples on markers of target activity, gene expression, efficacy and safety from an 11-beta HSD1 inhibitor program

Dr. Jan W Eriksson, University of Gothenburg, Sweden



Color-coded Z scores for the display and analysis of biomedical data

Robert A. Warner

Tigard Research Associates, USA

The ability to review and analyze large amounts of data reliably, rapidly and cost-effectively is important in research, industrial applications and clinical care. We hypothesized that converting raw digital data to standard scores (Z scores) and color-coding them based on their corresponding P values can be used to accomplish this. For each member of a population of data, the calculation of Z scores uses the formula:

$$Z \text{ Score} = (\text{Individual Data Point} - \text{Population Mean}) / \text{Population Standard Deviation}$$

We illustrate the use of the technique with continuously recorded data by showing the simultaneous changes that occur in five relevant parameters during acute myocardial infarction (MI). In addition, using digital electrocardiographic (ECG) data obtained from 1138 subjects, we used color-coded Z scores to develop criteria for prior inferior and anterior MI that gave diagnostic performances that were statistically significantly superior to those of two widely used commercial ECG diagnostic algorithms. Since each Z score is associated with a P value, color-coded Z scores indicate if an individual data point differs statistically significantly from the mean of a relevant population of data. Also, since the method expresses all parameters on the same scale (the standard deviation), it facilitates the meaningful simultaneous monitoring of multiple parameters. Our findings show that color-coded Z scores provide a highly intuitive, accurate, statistically meaningful and widely applicable method of interpreting data that is generated either by continuous recording or by individual tests.

Biography

Robert A. Warner received his MD from the State University of New York (SUNY) in Syracuse in 1969, completed training in cardiology at Duke University Medical Center in 1975 and is board-certified in both internal medicine and cardiology. He has served as Professor of Medicine at SUNY College of Medicine in Syracuse, NY, Chief of Medicine at the Syracuse VA Medical Center, Medical Director of Inovise Medical, Inc. and is the founder of Tigard Research Associates. Dr. Warner is the author of 70 scientific papers and 87 scientific abstracts.

Heat acclimation associated with decreased of urinary 8-hydroxydeoxyguanosine in navy boiler tender

Yung-Kai Huang, Chen-Chen Chang, Che-Yi Lai, Hsin-Hsiu Huang and Horn-Che Chiang

School of Oral Hygiene, Taipei Medical University

National Health Research Institutes, Taiwan

The physiological effects of heat are reviewed extensively elsewhere, but there is significant and poorly documented on heat tolerance in occupational exposure. Previous studies show that the hyperthermia has been induced reactive oxygen species and DNA damage. The aim of this study was to elucidate the association between heat acclimatization or body composition and urinary 8-hydroxydeoxyguanosine (U-8OHdG) level in navy boiler tender.

Data collections including a standardized questionnaire four repeated-measures (pre-sailing, after-sailing, per-work shift, and post-work shift) of urine sample were performed to measure the level of U-8OHdG and urinary electrolytes. The body composition of workers was provided by the body composition analyzer. The ion of sodium, potassium, and chlorine in urine and sweat was measured by electrolytic analyzer. U-8OHdG was measured by liquid chromatography with tandem mass spectrometry (LC/MS/MS). The Heat acclimation index $\Delta_{SL} Na$ and ΔNa calculated were the differences were calculated by subtracting the urinary sodium of before sealing from those of after sealing and before work shift from those of after work shift, respectively. Navy boiler tenders with better heat acclimation had a higher decreased of U-8OHdG than Navy boiler tenders with worse heat acclimation. Use of biologic markers may more accurately reflect total dose of exposure in populations. We used U-8OHdG as a biomarker to reflect the effect of health burden of DNA damage among naval personnel under environmental heat stress. U-8OHdG can be used as effective biomarker heat acclimatization in occupational medicine.

Dose time of presentation of patients of severe sepsis determines the clinical outcome?

Fahad Aziz

Resident Internal Medicine, Jersey City Medical Center, USA

The aim of this study was to compare the outcomes of patients with septic shock (SS) over a 12-month Period in a closed MICU setting, presenting during different times of the day.

Methods: Patients admitted to the medical intensive care unit (MICU) between January 2009 to January 2010 of a tertiary care center, who fulfilled the already reported consensus criteria for septic shock were included in this study.

Results: A total of 100 patients admitted to MICU with the diagnosis of SS were included in this study. Patients were divided into four groups on the basis of their presentation time (Group 1: 6AM-11:59 AM, Group 2: 12:00 PM- 5:59 PM, Group 3: 6PM-11:59PM & Group 4: 12:00 AM- 5:59 AM).

The mean age of cohort was 66.75 yr with 60% males. No significant differences were noted among the four groups with the respect to age, gender, hypertension, CAD, DM and COPD (P not significant).

The clinical out comes in the four groups were compared in terms of need for ventilator & inotropic support, number of deaths and length of stay of the patients in the MICU among different groups.

The patients in group A i.e. between 6 AM-11: 59 AM were found to have worse out come as compared to the patients in group B, C and D.

Discussion: The main finding of this retrospective study is that patients admitted to MICU in the morning hours have worse prognosis, as compared to the patients admitted during the rest of the days. A change in the organizational/staffing structure of a closed MICU during the early morning likely explains the increased mortality noted. It is likely that a number of factors in combination, including the morning rounds account for the higher risk of death during the morning hours.

Our study showed that the patients with septic shock follow the same circadian rhythm in respect to their all-clinical out comes. The patients presented in first quadrant i.e. between 6AM-11: 59 AM had worse out come as compared to the other patients presenting in the other quadrants.

Conclusion: The data suggests that septic shock patients presenting early in the day have worse prognosis as compared to the patients presenting late during the day.

Biography

Dr. Aziz is currently working as Internal Medicine resident at Jersey City Medical Center/ Mount Sinai School of Medicine. In addition to being an outstanding researcher, Dr. Aziz has authored several articles on different topics of his research and is working right now on many important research projects related to Critical Care medicine and Cardiology. These articles have also been cited hundreds of times by other researchers in the field. Dr. Aziz has presented his findings at various medical conferences and published in several internationally read peer-reviewed journals. In addition to that he is a member of editorial board of several well-recognized journal. His work has been well recognized both nationally and internationally.

Biomarkers for novel diabetes therapies in early clinical development. Examples on markers of target activity, gene expression, efficacy and safety from an 11-beta HSD1 inhibitor program

Jan W Eriksson

University of Gothenburg, Sweden and
AstraZeneca R&D, Sweden

Cortisol is produced by the adrenal cortex and by local regeneration via the enzyme 11-beta HSD1, eg in adipose tissue. This glucocorticoid hormone has strong insulin-antagonistic effects and it is suggested to play a role in the development of the metabolic syndrome, visceral obesity and type 2 diabetes. We studied the effect of the synthetic glucocorticoid, dexamethasone (Dex), on gene expression and glucose uptake capacity in human subcutaneous and omental adipose tissue aiming to identify new mechanisms and biomarkers for glucocorticoid-induced insulin resistance as well as for 11-beta HSD1 inhibitor treatment aiming for a reduction in local cortisol action. Moreover, phase I studies were done to characterize a novel selective 11-beta HSD1 inhibitor in healthy lean or obese male subjects, and subcutaneous adipose biopsies were performed. We assessed 11-beta HSD1 activity, genome-wide mRNA expression (microarray analysis) as well as circulating markers (novel markers based on gene expression data as well as established markers related to the cortisol axis).

Dex changed the expression of more than 500 genes in both subcutaneous and omental adipose tissue and pathway analysis of Dex-regulated genes showed a clear over-representation of functions and pathways related to inflammation. Single genes affecting lipolysis, glucose uptake and oxidation or adipocyte differentiation were changed after Dex incubation. The expression of the secreted peptides leptin and TIMP4 (metallopeptidase inhibitor 4) were increased by Dex in both depots. Dex dose-dependently impaired basal and insulin-stimulated glucose uptake in omental, and to a lesser degree in subcutaneous, adipocytes.

Repeated dosing of the novel 11-beta HSD1 inhibitor (AZD4017) in healthy subjects markedly reduced 11-beta HSD1 activity in the liver assessed by a prednisone challenge test and by the ratio of urinary cortisol:cortisone metabolites. 11-beta HSD1 inhibition was demonstrated also in adipose tissue after a single dose, but this effect seemed not to be sustained following repeated dosing for 9 days. Effects on circulating markers are being analysed and will be discussed.

A proposed strategy for use of translational and early clinical biomarkers in the development of novel diabetes treatments, as exemplified above, will be described.

Biography

MD, PhD, Full Professor in Internal Medicine. Board-certified specialist in Internal Medicine and Endocrinology. Currently part-time position as Professor, Dept of Molecular and Clinical Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden. Medical Science Director, Diabetes Disease Area, Cardiovascular/Gastrointestinal Clinical Development, AstraZeneca R&D, Mölndal, Sweden.

During more than 20 years several positions as senior consultant physician, mainly in diabetology and endocrinology at University Hospitals in Göteborg, Lund, Umeå in Sweden. These include senior leadership roles such as Head of Department and Head of Research Units. In the same time period leader of research projects in experimental and clinical diabetology and metabolism. Focus on mechanisms of insulin resistance, in particular translational aspects. Author of approx. 150 scientific papers.

Since 2007 Medical Science Director in Clinical Development, Diabetes (and Obesity) at AstraZeneca R&D. Leader of a large group of MDs, PhDs and other scientists that is responsible for translational and early clinical research in numerous drug projects. PI or co-PI for several internal and external scientific networks and collaborations, for example focusing on mechanisms and markers of insulin resistance and on markers of beta cell function and mass in diabetes.

2(i): Protein Biomarkers: Prognostic and C9 Protein Biomarkers

2(ii): Emerging Biomarkers in Breast Cancer

Session Chair

Dr. Georg F. Weber
University of Cincinnati, USA

Session Co-Chair

Dr. Geetika Chakravarty
Tulane University Health Science Center, USA

Session Introduction

Title: **A novel marker for breast cancer progression**

Dr. Georg F. Weber, University of Cincinnati, USA



Title: **Developing tissue biomarkers in early breast cancer**

Dr. Marina A. Guvakova, University of Pennsylvania, USA



Title: **Polycomb group genes as novel cancer biomarkers**

Dr. Francesco Crea, University of Pisa, Italy



Title: **SOX9: From biomarker to a therapeutic target in breast cancer**

Dr. Geetika Chakravarty, Tulane University Health Science Center, USA



Title: **Determinants and prognostic role of BNP in central Africans with congestive heart failure**

Dr. Longo-Mbenza Benjamin, Walter Sisulu University, South Africa



Title: **RNA helicase DDX20, a novel prognostic marker defines metastatic potential of breast cancer**

Dr. Alan Prem Kumar, National University of Singapore, Singapore



Title: **Septic encephalopathy: Relationship to serum and cerebrospinal fluid levels of adhesion molecules, lipid peroxides and S-100B protein**

Dr. Sherifa Ahmed Hamed, Assiut University Hospital, Egypt



Title: **Development of novel diagnostic and prognostic biomarker in breast cancer**

Dr. Gopal Kundu, National Center for Cell Science, India



A novel marker for breast cancer progression

Georg F. Weber

University of Cincinnati, USA

The early detection of tumor dissemination is a challenge in cancer diagnosis because biomarkers for invasiveness are largely lacking in clinical medicine. Osteopontin is frequently secreted by cancer cells and plays important roles in their ability to metastasize. According to a meta-analysis, Osteopontin is significantly associated with decreased patient survival. Osteopontin levels are also markers for stage, grade, and early tumor progression, reflecting a common molecular underpinning for distinct clinical measures (Weber et al. *Brit J Cancer* 2010;103:861). However, Osteopontin physiologically acts as an inducer cytokine for cellular immunity, which may protect from cancer through immune surveillance. The structural basis for the discrepant effects between tumor- and host-Osteopontin had long not been elucidated. Because we have identified the genetic basis of metastasis as aberrant expression or splicing of stress response genes, we have studied Osteopontin splice variants in malignant tumors. Osteopontin is subject to alternative splicing, which yields three messages, Osteopontin-a, -b and -c. The shortest form, Osteopontin-c is selectively expressed in invasive, but not in non-invasive, breast tumor cell lines, and it effectively supports anchorage independence. Osteopontin-c is present in 75-80% of breast cancers and 0% of normal breast tissues. Furthermore, Osteopontin-c detects a higher percentage of breast cancers than ER, PR, or HER2. In particular, a fraction of triple-negative breast cancers stains positively for Osteopontin-c (Mirza et al. *Int J Cancer* 122:889). Due to its absence from normal tissue, Osteopontin-c may be a superior biomarker for cancer progression. Its measurement in blood as a means of early detection is currently under investigation.

Biography

Georg F. Weber attended medical school in Wuerzburg, Germany. He worked at the Dana-Farber Cancer Institute, Harvard Medical School from 1990 through 1999 and is currently on the faculty at the University of Cincinnati. Georg F. Weber has published around 70 scientific reports, including many in the most respected professional journals, and various monographs, most recently a textbook on molecular oncology. He holds several patents. As a component of his mission to research cancer dissemination, Georg F. Weber is the founder and chief executive officer of MetaMol Theranostics, a company specialized in diagnosis and treatment of cancer metastasis.

Developing tissue biomarkers in early breast cancer

Marina A. Guvakova

University of Pennsylvania School of
Medicine, USA

We are interested in developing biomarkers (BM) to determine the likelihood that initial breast tumor remains contained in situ, as opposed to becoming invasive. In-tissue testing serves as a gold standard for breast cancer diagnostics, yet the power of high throughput technologies can be realized for diagnostic purposes if emerging technologies can be directly applied to samples obtained by the routine clinical procedure. Although a variety of quantitative methods exist for assaying biofluid-based BM, contemporary proteomic technologies remain impractical for application to archived formalin-fixed paraffin-embedded (FFPE) tissues that (being associated with clinical histories) provide a trove of information for BM discovery. Immunohistochemistry (IHC) remains the tool of choice to examine protein expression in tissue; however, it does not lend itself to the truly continuous measurements needed for BM study. We developed the analytic tools and algorithms – without use of sophisticated and expensive equipment – that allow measurements of protein expression in FFPE tissue on a continuous biologically relevant scale, while quantification of relative (rather than absolute) intensity of staining takes into account fluctuations of background staining. Using this approach, we have revealed that women with invasive breast cancer were 4 times more likely to have increased levels of insulin-like growth factor type I receptor and its target, Ras-related protein 1 than women with non-invasive tumors. To facilitate development of novel in-tissue BMs, we are taking advantage of digital multispectral imaging technology and developing pattern-recognition-based image analysis for the core-needle biopsies containing early form of breast cancer, i.e. carcinoma in situ.

Biography

Marina Guvakova received Ph.D. in cell biology from the Russian Academy of Sciences and post-doctoral training from Columbia and Thomas Jefferson University, USA. In 2001, she joined Faculty at the University Of Pennsylvania School Of Medicine; where she is now an Assistant Professor and a Senior Research Investigator at the Department of Surgery. She is an author of 20+ papers, recipient of Gordon Research Conferences awards, the New Investigator Award from the Endocrine Society, Breast Cancer Research Award. She serves as a reviewer for several journals, editorial board member of ISRN Endocrinology, and a CDMRP peer-review panel member.

Polycomb group genes as novel cancer biomarkers

Francesco Crea

Division of Pharmacology, University of
Pisa, Italy

Polycomb group genes (PcGs) are epigenetic effectors involved in gene silencing. PcG activity was first recognized as essential for stem cell maintenance during embryo development. Subsequently, several PcGs were shown to play a role in cancer initiation, progression, and chemotherapy resistance. For example, PcG member BMI1 is up-regulated in prostate cancer cells compared to normal counterparts, and mediates prostate cancer invasion and resistance to chemotherapy. Another PcG member (EZH2) is up-regulated in high grade and high stage breast, colorectal and brain tumors. At present, PcGs have been identified as negative prognostic markers in most human cancers. Easy-to-perform genetic analyses may pave the way to the emergence of PcGs as cancer biomarkers. For example, Germinal *EZH2* polymorphisms predict lung cancer risk and colorectal cancer prognosis. Somatic *EZH2* mutations were found to drive B-cell lymphoma progression. In addition, a small molecule inhibitor of EZH2 showed promising anti-tumor activity in breast, brain and prostate tumor models. Thus, PcGs may emerge as novel prognostic and predictive markers in Oncology. Despite the well-recognized role of PCGs in cancer cell biology, few researches explored the clinical potential of these genes. In this presentation, I will summarize current evidence on PcGs and cancer, with particular emphasis on what they can add to traditional oncology biomarkers. In addition, I will illustrate a paradigm for rational development of PcG-targeting anticancer regimens, suggesting specific therapeutic strategies. Hopefully, PcGs may emerge as novel prognostic and predictive biomarker, as well as viable targets to target cancer initiation and metastatic spreading.

Biography

Francesco Crea has completed his MD in 2006 and his PhD in 2010 (both cum *Laude*) at Scuola Superiore Sant'Anna, Pisa. He has spent 18 months at National Cancer Institute-Frederick (USA) as a Guest Scientist. He is currently Lecturer in Clinical Pharmacology at Pisa University. There, he is directing a research project on Polycomb genes in cancer. He has published more than 15 manuscripts on in peer-reviewed international journals, including the *Journal of Clinical Oncology*, *Trends in Pharmacological Sciences* and *Molecular Cancer Therapeutics*. He is Contributing Associate Editor-in Chief for the *World Journal of Gastroenterology*, and Editorial writer for *Epigenomics*.

SOX9: From biomarker to a therapeutic target in breast cancer

Geetika Chakravarty

Tulane Health Science Center, Tulane University, USA

Typically, there is a time gap of two to three weeks between a biopsy proven diagnosis of cancer and surgical intervention, at which time the physician has access to the same tumor tissue again. If a biomarker can differentially diagnose and predict the prognosis of the disease, the physician has the option of adding adjunct therapy to enhance the therapeutic efficacy of surgical intervention. Furthermore, if this biomarker can be targeted using a cocktail of drugs that induce differentiation of cancer cells (retinoids etc.) one may be able to monitor the therapeutic efficacy of this approach by analyzing the surgical specimen for markers of differentiation and compare the outcome with that of the initial biopsy specimen. In this talk I will summarize our work on one such novel biomarker: SOX9, our efforts to induce differentiation of poorly differentiated breast cancer cells through nuclear translocation of this biomarker with an HDAC inhibitor and modulation of its post translational function. I will conclude the talk with studies that show how monitoring of this biomarker is inexpensive, yet can yield much insight about the biology of the disease and how this information can be useful in choosing the right therapeutic approach.

Biography

Dr. Chakravarty completed her Ph.D from Tata Memorial Hospital, University of Mumbai, India and postdoctoral studies from Baylor College of Medicine, USA. She is looking for collaborators to test SOX9's biomarker potential. She is an Instructor in the School of Medicine, Tulane University. She has published in reputed cancer journals and is serving as an editorial board member of repute.

Determinants and prognostic role of BNP in central Africans with congestive heart failure

Longo-Mbenza B, Forka AC, Mouzenzo CM and Kianu Phanzu B

Walter Sisulu University, South Africa

B-type natriuretic peptide (BNP) is one of the most reliable biomarkers enabling a rapid bedside diagnosis and prognosis of congestive heart failure (CHF) in developed countries. Data related to BNP in sub-Saharan Africa is still lacking due to cost constraints. The aim of this study was to determine potential relationships between epidemiological features, symptoms, cardiometabolic risk factors, antioxidant biomarkers, white cell count, case fatality and BNP measurements. In univariate analysis, males, urban residences, excessive alcohol intake, coronary heart disease, dry cough, NYHA class 3-4 and mortality were defined by significant and higher BNP levels. In bivariate analysis, neutrophils ($r=0.286$; $P=0.047$), total bilirubin ($r=0.480$; $P<0.0001$), direct bilirubin ($r=0.465$; $P<0.001$), uric acid ($r=0.354$; $P=0.003$), systolic blood pressure ($r=-0.226$; $P=0.029$) BUN ($r=0.320$; $P=0.005$) and sodium ($r=-0.580$; $P=0.028$) showed significant correlations with BNP levels, respectively. In multiple linear regression analysis and after adjusting for confounding factors, the independent determinants explaining 99.1% of variations (adjusted R²) of BNP levels were BUN, neutrophils and uric acid. The optimal cut-off point of $BNP \geq 800$ pg/mL obtained by ROC curve ($AUC=0.819$ 95% CI 0.710-0.937, $SE=0.061$; $P=0.003$, sensitivity= 97.5% and specificity=75.8%, conferred a relative Risk of case fatality =16.9 95% CI 2.2-31.3; $P<0.001$). Thus in countries with limited resources, the equation $Y(BNP)=-4247 + 0.630 * BUN + 0.552 * \text{neutrophils} + 0.287 * \text{uric acid}$ and $BNP \geq 800$ pg/mL should be validated in large studies for the CHF management.

Biography

Benjamin B. Benjamin has received his MD, PhD in pathophysiology and MMed in Internal Medicine from the Bukarest Medical Institute (Romania), MSc in Cardiology and PhD in Cardiology at the Free University of Brussels (Belgium). He is a former Fulbright Scholar and visiting Professor in Clinical Pharmacology/Hypertension at the Institute of Lipid research, Baylor College of medicine, Houston (USA). He served for 30 years as chief of cardiology, Executive Dean of Faculty of Medicine and Deputy Vice-Chancellor at the University of Kinshasa, Democratic Republic of Congo. He is a member of 30 scientific societies, including: American Heart Association, American Diabetes Association, and American College of Cardiology, European Society of Cardiology and Pan-African society of Cardiology. He obtained a certificate in cardiovascular Epidemiology (Netherlands), Ethics (NIH), Bioethics (Oklahoma University) and Molecular genetics (Belgium, Italy). His original research was focused on elucidating the pathophysiological mechanisms of toxic myocarditis and immune-allergic cardiomyopathies. From 1980s until present, most of his research works are related to inflammatory states, oxidative stress, molecular biology, genetics, biomarkers and environmental impacts in Atherosclerosis, HIV/AIDS-related cardiac lesions, deafness (discovery of genes) and co-expression of genes in Pancreas. In addition to his role as clinician, lecturer, academic leader mentor, WHO expert and UN/Climate change Expert, he has been a very productive scientist: Supervisor of more than 10 PhD theses, 25 MSc theses, and 100 mini-dissertations, and over 300 papers published under his supervision. He is currently Research Champion professor at the Faculty of Health sciences, Walter Sisulu University, Mthatha, South Africa.

**RNA helicase
DDX20, a novel
prognostic marker
defines metastatic
potential of breast
cancer**

Alan Prem Kumar

Cancer Science Institute of Singapore;
National University of Singapore,
Singapore

Mortality from breast cancer is almost entirely the result of invasion and metastasis of neoplastic cells; therefore, understanding gene products involved in breast cancer metastasis is an important research goal. Prompted by a recent study showing increased expression of a DEAD-box family member, DDX20, in microarray data from lymphoma patients, a total of 194 breast tissue samples (97 breast cancers and 97 paired normal breast tissue) were retrieved. A high proportion of specimens show positive DDX20 (2+, 3+) expression in the tumor cores and negative (1+, 0) in their paired normal cores ($p < 0.001$). Since positive MMP9 expression is closely associated with poor prognosis, same cohort was stained for MMP9. When grouping patients with positive DDX20 expression to MMP9 expression, Kaplan-Meier correlation analysis show patients with positive DDX20 and MMP9 expression have poorer survival outcomes ($p = 0.029$). To explore a link between DDX20 and MMP9, we screened a panel of breast cancer cell lines for DDX20 and MMP9 expression. Interestingly, highly metastatic cell lines such as MDA-MB-231, BT549, and Hs578t have high expression levels of DDX20 and MMP9. Herein, we will present data for a functional consequence to decreased DDX20 in metastatic breast cancer cells. Together, our study identifies DDX20 as a new prognostic marker that is needed to identify patients who are at the highest risk for developing metastases, which might enable oncologists to begin tailoring treatment strategies to individual patients. This work is supported by grants from National Medical Research Council of Singapore (Grant R-713-000-119-275) and Cancer Science Institute of Singapore, Experimental Therapeutics I Program (Grant R-713-001-011-271) to APK.

Biography

Dr. Alan Prem Kumar earned his Ph.D. from University of North Texas, USA. From his Ph.D. work, he discovered a novel regulatory protein, PyrR for the pyrimidine biosynthetic pathway in *Pseudomonas*. Dr. Kumar then pursued Postdoctoral training in Cancer Research at Sidney Kimmel Cancer Center, California, USA. He was awarded a Postdoctoral Fellowship for his work on the role of nuclear receptors. Dr. Kumar relocated back to Singapore to join Cancer Science Institute of Singapore, National University of Singapore as an independent Principal Investigator to continue on his expertise on nuclear receptor and cancer pharmacology. His current research interest includes the role of nuclear receptors involved in the regulation of target genes and to elucidate mechanism and associated signal pathways. Another area of interest is aimed at developing new derivative drugs with hopefully fewer side effects. Over the years, Dr. Kumar and his laboratory have forged relationships with scientists in cancer research and with cancer advocacy groups in Singapore.

Septic encephalopathy: Relationship to serum and cerebrospinal fluid levels of adhesion molecules, lipid peroxides and S-100B protein

Sherifa A. Hamed

Departments of Neurology, University Hospital, Egypt

Severe septic illness is often associated with cerebral manifestations such as disturbed consciousness and delirium. Little was known about its effect on the CNS. This is the first study in children that assessed the direct mediators of brain inflammation and injury with sepsis. The serum and CSF concentrations of soluble intracellular adhesion molecule-1 (sICAM-1) (marker of endothelium-leukocyte interaction), nitric oxide (NO) and lipid peroxide (LPO) (markers for lipid peroxidation) and S-100B protein (marker of astrocytes activation and injury), were measured in 40 children with sepsis of whom 40% had moderate to severe septic encephalopathy. Serum from 25 normal children was used for comparison. Serum values of sICAM-1, NO, LPO and S100B were elevated in patients compared to controls. The greater elevation of CSF: serum albumin ratio suggests loss of blood-brain barrier integrity. After normalizing for CSF:serum albumin ratio, we demonstrated significant intrathecal synthesis of NO, LPO and S100B. Patients with encephalopathy had elevated serum and CSF levels of sICAM-1, NO, LPO and S100B compared to sepsis only. This study indicates that the brain is vulnerable in children with sepsis. It also suggests that coordinated interactions between immune system, vascular endothelial cells, blood-brain barrier, astrocytes and brain lipid peroxides, may contribute to septic encephalopathy.

Biography

Dr. Sherifa A. Hamed (M.D.) is an Associate Professor of Neurology and the director of the Neurogenetic unit in Assiut University, Egypt. She worked as a postdoctoral fellow (visiting scholar, 8/1998 to 8/2000) in USA [in Research Center for Genetic Medicine, Children's National Medical Center, Dept. Integrative Systems Biology, George Washington University School of Medicine and Health Sciences]. She was a part of a multidisciplinary research program concerning disease gene identification of muscular dystrophies. She served as a reviewer for 30 medical journals and has a least 70 international publications in the fields of Neurology, Neurogenetics and Neuropsychopharmacology.

**Development of
novel diagnostic
and prognostic
biomarker in breast
cancer**

Gopal C. Kundu

National Center for Cell Science, India

Cancer is a complex disease and most cancer treatments are limited to chemotherapy, radiation, and surgery. Recent evidences suggested that development of cancer progression and metastatic spread could be determined by the expression profilation of some proteins, considered as the markers. The discovery of cancer biomarkers has become a major focus of cancer research, which holds promising future for early detection, diagnosis, monitoring disease recurrence and therapeutic treatment efficacy to improve long-term survival of cancer patients. Breast cancer is the predominant malignancy where oncologists use predictive markers clinically to select treatment options with steroid receptors which are being used for many years. Osteopontin (OPN), a pro-inflammatory, chemokine like, calcified ECM associated protein plays important role in determining the oncogenic and angiogenic potential of various cancers including breast. During last several years, many groups including ours have demonstrated that OPN regulates tumor growth and metastasis in breast and other cancers. We have analyzed the expression of OPN in various grades of breast tumor tissues and the data revealed that OPN is a diagnostic and prognostic marker that may have value in a diagnostic panel along with other conventional breast cancer markers. Finally, our data as well as the data published by others suggested that OPN may act as early diagnostic and prognostic tissue and serum marker in breast cancer.

2(iii): Biomarkers for Human Diseases

2(iv): Blood Biomarkers: Serum Biomarkers & Blood Cells RNA Biomarkers

Session Chair

Dr. Tatjana Abaffy
University of Miami, USA

Session Co-Chair

Dr. Naoko Sueoka-Aragane
Saga University, Japan

Session Introduction

Title: Volatile signature of melanoma - A novel approach for early detection

Dr. Tatjana Abaffy, University of Miami, USA



Title: A non-invasive system for monitoring resistance to EGFR tyrosine kinase inhibitors with plasma DNA

Dr. Naoko Sueoka-Aragane, Saga University, Japan



Title: Centrosomal Nlp is an oncogenic protein that has a close relationship with tumorigenesis

Dr. Shao Shujuan, Dalian Medical University, People's Republic of China



Title: Next generation of biomarkers: Serum antibody repertoire profiling using next generation sequencing

Dr. Yuriy Ionov, Roswell Park Cancer Institute, USA



Title: Noninvasive Molecular Diagnosis of Human Visceral Leishmaniasis

Dr. Manisha Vaish, Banaras Hindu University, India



Title: Brain-derived neurotrophic factor as a biomarker of acute episodes in bipolar disorder: Meta-regression analysis

Dr. Brisa S. Fernandes, Federal University of Rio Grande do Sul – UFRGS, Brazil



**“Volatile signature
of melanoma - a
novel approach for
early detection”**

Tatjana Abaffy

Miller School of Medicine, University of
Miami, USA

The quest for melanoma biomarkers is paramount. The incidence of melanoma is increasing and mortality rates have not been significantly reduced. There is a need for reliable biomarkers that would help in the diagnosis of this aggressive disease. Our novel approach to detect and identify volatile metabolites released from melanoma tissue has the potential to discover novel biomarkers for detection of melanoma, as well as to increase our understanding of metabolic processes of this malignant cancer. In order to detect volatile metabolic signature of malignant melanoma, we are using Head Space Solid Phase Extraction Method (HS-SPME) and Gas Chromatography/Mass Spectrometry (GC/MS). The volatile metabolome exhibits significant natural variation and it may be very hard to find a variation caused by disease. To overcome this limitation, as a control, we are using perfectly matched, non-neoplastic, un-involved skin tissue from the same patient. Different histo-pathologic types and stages of melanomas are being analyzed. Different volatile signatures are identified indicating that a differential volatile profile of melanoma does indeed exist. A comprehensive volatile metabolomics study of melanoma on a large cohort of patients is underway.

Biography

Tatjana Abaffy, PhD is a Research Assistant Professor in the Department of Molecular and Cellular Pharmacology at the University of Miami, Miller School of Medicine, Miami - Florida, USA. She obtained her PhD from the University of Auckland, New Zealand studying complex physiology of glucose homeostasis. Her postdoctoral training was in the chemosensory field and involved studying taste and smell (olfactory) receptors and signal transduction. Currently, she is involved in a translational research related to skin cancer biomarkers detection.

A non-invasive system for monitoring resistance to EGFR tyrosine kinase inhibitors with plasma DNA

Naoko Sueoka-Aragane¹, Tomomi Nakamura¹, Kentaro Iwanaga^{1,2}, Akemi Sato¹, Kazutoshi Komiya¹, Tomonori Abe¹, Norio Ureshino^{1,2}, Shinichiro Hayashi¹, Toshiya Hosomi³, Mitsuharu Hirai³, Eisaburo Sueoka⁴ and Shinya Kimura¹

¹Department of Internal Medicine, Saga University, Japan

²Saga Prefectural Hospital Koseikan, Japan

³ARKRAY Inc., Takanna-cho, Nakagyo-ku, Japan

⁴Department of Transfusion Medicine, Saga University Hospital, Japan

EGFR tyrosine kinase inhibitors (EGFR-TKIs) have great response to lung adenocarcinoma with EGFR activating mutations. However, acquired resistance eventually developed, and the half of these patients has the gatekeeper T790M mutation of EGFR in lung cancer tissue. A non-invasive mutation detection system is desired considering the difficulty in obtaining tissue specimens during disease progression—the majority of lung cancer recurrences occur in distant sites. We report a novel non-invasive monitoring system, MBP-QP (mutation-biased PCR and quenching probe) method, to detect the mutation using plasma DNA. The MBP-QP method combines mutated-biased PCR and genotyping based on analysis of the melting curve of the probe DNA binding the target mutated site using a fluorescence quenching probe system. The detection limit was two copies of control plasmid, and 0.2 ng of genomic DNA isolated from a lung cancer cell line harboring T790M. 0.3 % mutant plasmid could be detected in the mixture of plasmids inserted with EGFR exon 20 with or without T790M. With this method, T790M mutations were detected in plasma DNA of 50% of patients who acquired resistance, but not in primary EGFR-TKI non-responders, patients responding to treatment, or patients not treated with EGFR-TKI, which is consistent with the clinical course. The non-invasive MBP-QP method enabled us to monitor T790M repeatedly and will be useful for determining appropriate lung cancer treatment strategies in practice.

Centrosomal Nlp is an oncogenic protein that has a close relationship with tumorigenesis

Shao Shujuan

Dalian Medical University, People's Republic of China

Disruption of mitotic events contributes greatly to genomic instability and results in mutator phenotypes. Indeed, abnormalities of mitotic components are closely associated with malignant transformation and tumorigenesis. Here we show that ninein-like protein (Nlp), a recently identified BRCA1-associated centrosomal protein involved in microtubule nucleation and spindle formation, is an oncogenic protein. Immunohistochemical and Western blot approaches showed that Nlp was overexpressed in approximately 80% of human breast and lung carcinomas analyzed. In human lung cancers, the results of RT-PCR, Southern blot and FISH confirmed that this deregulated expression was associated with NLP gene amplification. Further analysis revealed that Nlp exhibited strong oncogenic properties; for example, it conferred to NIH3T3 rodent fibroblasts the capacity for anchorage-independent growth in vitro and tumor formation in nude mice. Consistent with these data, transgenic mice overexpressing Nlp displayed spontaneous tumorigenesis in the breast, ovary, and testicle within 60 weeks. In addition, Nlp overexpression induced more rapid onset of radiation-induced lymphoma. Furthermore, mouse embryonic fibroblasts (MEFs) derived from Nlp transgenic mice showed centrosome amplification, suggesting that Nlp overexpression mimics BRCA1 loss. These findings demonstrate that Nlp abnormalities may contribute to genomic instability and tumorigenesis and suggest that Nlp might serve as a potential biomarker for clinical diagnosis and therapeutic target.

Biography

Shao Shujuan has completed her Ph.D and postdoctoral studies from Cancer Institute, Chinese Academy of Medical Sciences and Peking Union Medical College. She has been in charge of branches of the "National High Technology Research and Development Program (863 program)" and "National Basic Research Program of China (973 program)", 2 projects of National Natural Science Foundation of China (NSFC) and several projects supported by the Province and City. She has published 12 papers in reputed journals and highest IF score is more than 17. She has been awarded "State Council Expert for Special Allowance" in 2007.

Next generation of biomarkers: Serum antibody repertoire profiling using next generation sequencing

Yurij Ionov

Roswell Park Cancer Institute, USA

The promising idea of using serum antibodies for diagnosis of cancer is hampered by the heterogeneity of immune response against tumors and by low frequency of serum antibodies against particular autoantigens in cancer patients. The low diagnostic value of serum antibodies against tumor-associated autoantigens is the result of the limitations of the methods used for the detecting antibody responses. Current methods of antibody reactivity are designed for detecting high affinity and/or high titer antibodies. However, a growing tumor may induce a variety of low affinity and low titer autoantibodies which can not be detected by these methods.

We developed a strategy for serum antibody repertoire profiling, which allows detecting high affinity/high titer as well as low affinity/low titer autoantibodies in serum samples. This strategy, which we call virtual antigen array, is based on using random peptide phage display library panning on serum antibodies and NextGen sequencing of DNA from antibody bound phage. The iterative and amplificative nature of phage selection permits identification of antibodies with a broad range of affinities. The next generation sequencing of PCR amplified DNA from antibody bound phage permits detection of binding of a single antibody to a single peptide. The identity of the autoantigens recognized by serum autoantibodies is identified by using statistical analysis of BLAST homology search data for peptide sequences recognized by serum antibodies. The proposed strategy can be used for developing assays for early detection of cancer and prognosis of clinical outcomes and responses to therapies.

Biography

Yurij Ionov has completed his Ph.D at the Institute of Genetics and Selection of Industrial Microorganisms (Moscow, Russia). He did his postdoctoral studies at California Institute of Biological Research where he has made his contribution to the discovery of microsatellite instability in colon cancer. He is the Assistant Professor of Oncology at Roswell Park Cancer Institute in Buffalo NY.

Noninvasive molecular diagnosis of human visceral leishmaniasis

**Manisha Vaish, Jaya
Chakravarty and Syam Sundar**

Institute of Medical Sciences, Banaras
Hindu University, India

Visceral leishmaniasis is a vector borne disease which affects 0.5 million people around the world per annum. Its accurate diagnosis and definitive cure still requires attention. The gold standard procedure of diagnosis of symptomatic VL is parasite demonstration in spleen biopsy, which carries risk of intra abdominal hemorrhage. Bone marrow aspirates is often done but due to its low sensitivity and highly painful procedure fails to make it better choice for diagnosis. The detection of Leishmania DNA by polymerase chain reaction (PCR) in splenic, bone marrow or blood samples is an important advance in molecular diagnosis of Visceral Leishmaniasis (VL). We for the first time introduce use of noninvasively obtained buccal swab samples in molecular diagnosis of VL. In this study we performed PCR from buccal swabs; multicopy rRNA (Small Subunit Unit, SSU) gene was used as the target region for amplification of *L. donovani*. The PCR assay was optimized and sensitivity was determined in 307 subjects including 148 parasitological confirmed VL patients, 39 healthy controls from non endemic region, 92 endemic healthy controls and 28 subjects of different diseases such as malaria, tuberculosis etc. The results were encouraging, buccal swab samples were positive in 123 out of 148 patients (sensitivity 83.11%, 95% CI, 76.25-88.29). The developed assay was 100% specific as none of the non endemic healthy control samples amplified. The specificity in healthy controls of endemic region was 86% (95% CI, 77.31-91.55) and in different disease group it was 92.85%. Molecular diagnosis using buccal cells provide new tool for absolutely specific, highly sensitive and easy diagnosis for all type of symptomatic VL cases. This assay can also open new prospects for epidemiological studies in endemic population.

Biography

Manisha Vaish has completed her PhD in Biotechnology from one of most prestigious institution of India, Banaras Hindu University in year 2011 at age of 27. She has four publications in international journals during her PhD.

She has already developed the idea of working as a researcher in early youth. She maintained excellent academic records throughout with Biology being my favorite subject. It then became a significant point of turn, when she opted to participate in examination for admission in biotechnology. She made it in first attempt and was placed in one of top rated places, Allahabad Agricultural Institute Deemed University, India. Meanwhile she got a national fellowship (GATE) to carry on research in India.

Brain-derived neurotrophic factor as a biomarker of acute episodes in bipolar disorder: meta-regression analysis

Brisa S. Fernandes

Federal University of Rio Grande do Sul,
RS, Brazil

Brain-derived neurotrophic factor (BDNF) plays a central role in synaptic plasticity and neurogenesis. Bipolar disorder (BD) is among the most disabling of all psychiatric disorders and is associated with poor outcomes. Some studies suggest that BDNF levels decrease during mood states and remain normal during euthymia, but other studies have contradicted this paradigm. Therefore, the aim of this study was to perform a meta-analysis of all studies that measured peripheral BDNF levels in adults with BD. We conducted a systematic review using electronic databases. Inclusion criteria were studies that measured BDNF in plasma or serum in vivo in adult patients with BD. The resulting studies were compiled to measure the effect sizes (ESs) of the differences in BDNF levels between BD patients in different mood states and controls. Thirteen studies were included with a total of 1113 subjects. The BDNF levels were decreased in both mania and depression when compared to controls (ES -0.81, 95% CI -1.11 to -0.52, $p < 0.0001$ and ES -0.97, 95% CI -1.79 to -0.51, $p = 0.02$, respectively). The BDNF levels were not different in euthymia when compared to controls (ES -0.20, 95% CI -0.61 to 0.21, $p = 0.33$). Meta-regression analyses in euthymia showed that age ($p < 0.0001$) and length of illness ($p = 0.04$) influenced the variation in ES. There was also an increase in BDNF levels following the treatment for acute mania (ES -0.63, 95% CI -1.11 to -0.15, $p = 0.01$). In conclusion, BDNF levels are consistently reduced during manic and depressive episodes and recover after treatment for acute mania. In euthymia, BDNF decreases with age and length of illness. These data suggest that peripheral BDNF could be used as a biomarker of mood states and disease progression for BD.

Biography

Dr. Brisa S. Fernandes has completed his M.D. at the age of 23 years from Federal University of Health Sciences of Porto Alegre, Brazil. She is a psychiatrist and currently a full time researcher as a doctoral student at the Laboratory of Calcium Binding Proteins in the Central Nervous System and Department of Biochemistry, Federal University of Rio Grande do Sul (UFRGS). She has published 20 papers in reputed journals and received nine research awards or honors, including the Samuel Gershon Award for Junior Investigators (SGAJI) from the International Society for Bipolar Disorders (ISBD) in 2010. Her main focus of research is biomarkers in psychiatric diseases, particularly bipolar disorder and schizophrenia, and its pathological and clinical implications.

Session Chair

Dr. Jagat R. Kanwar
Deakin University, Australia

Session Co-Chair

Dr. Renaud Seigneuric
University of Burgundy, France

Session Introduction

Title: **Angiogenic activities of YKL-40 in cancer development: A potential biomarker and target for cancer diagnosis and therapy**

Dr. Rong Shao, University of Massachusetts, USA



Title: **Genetic biomarkers for metastatic Melanoma**

Dr. Stanley P. L. Leong, University of California, USA



Title: **Proteomic approaches for profiling cancer signaling pathways**

Dr. Fei ye, Mount Sinai School of Medicine, USA



Title: **Ultra-sensitive detection of BRAF V600E and G469A mutations by Ice COLD-PCR and BLOcker-Sequencing**

Dr. Yanggu Shi, Transgenomic Inc., USA



Title: **From bench to bedside**

Dr. Gargi Basu, Caris Life Sciences, USA



Title: **Cancer biomarkers: From discovery to clinical implementation**

Dr. Renaud Seigneuric, University of Burgundy, France



Title: **Label-free optical bio-sensors for proteomic analysis: current applications and future development in cancer research**

Dr. Valentina Donzella, Piazza Martiri della Libertà, Italy



Title: **Secretome analysis of large cell lung cancer cell lines using two-dimensional electrophoresis coupled to mass spectrometry**

Dr. Zahra Mojtahedi, Shiraz University of Medical Sciences, Iran



Title: **Copro-antiapoptotic protein survivin and lactoferrin biomarkers for improved detection and nanodelivery to colon cancer**

Dr. Jagat R. Kanwar, Deakin University, Australia



Title: **Cancer bioinformatics, A potential way for prediction of chemotherapeutic responses in clinics**

Dr. Da Yong Lu, Shanghai University, PR China



Angiogenic activities of YKL-40 in cancer development: A potential biomarker and target for cancer diagnosis and therapy

Rong Shao

Pioneer Valley Life Sciences Institute,
University of Massachusetts, USA

Accumulating evidence has shown that elevated serum levels of a secreted glycoprotein YKL-40 are associated with a worse prognosis from a variety of advanced human cancers, including breast cancer, colorectal cancer, ovarian cancer, and brain tumor. Furthermore, these increased levels correlate with poorer survival of cancer patients, suggesting that serum levels of YKL-40 might be a prognostic biomarker. Yet the role of YKL-40 activity in these cancers is poorly understood. To explore a functional role of YKL-40 in tumor development, we engineered cancer cells with YKL-40 cDNA to express ectopic YKL-40. Over-expression of YKL-40 in these cancer cells led to larger tumor formation with an extensive angiogenic phenotype than did control cancer cells in mice. Affinity purified recombinant YKL-40 protein promoted vascular endothelial cell angiogenesis *in vitro*, the effects of which are similar to the activities observed using cancer cell conditioned medium after transfection with YKL-40. Immunohistochemical analysis of human breast cancer revealed a correlation between YKL-40 expression and blood vessel density. YKL-40 levels were positively correlated with tumor grade and *Her2/neu*, but negatively correlated with estrogen and progesterone receptor. In complementary approaches, we found that blockade of YKL-40 by YKL40 siRNA gene knockdown and a YKL-40 neutralizing antibody restrained tumor growth, angiogenesis, and progression. Taken together, these findings have shed light on the mechanisms by which YKL-40 promotes tumor angiogenesis and progression; thus pointing to a valuable cancer diagnostic and prognostic biomarker as well as a target for cancer therapy.

Biography

Dr. Rong Shao has been working on identification of key molecules that mediate tumor angiogenesis and metastasis since he received a postdoctoral training at the Dept of Pharmacology and Cancer Biology, Duke University in 2004. He is a scientist and assistant professor at Pioneer Valley Sciences Institute, University of Massachusetts Amherst, MA. He has published more than 20 papers in prestigious journals. He also serves as an editorial board member of two peer-reviewed journals and a reviewer of more than ten journals. Recently, Dr. Shao's research work has received a number of federal funding agencies including NIH (NCI) and DoD.

Genetic biomarkers for metastatic melanoma

Stanley P. L. Leong¹, Botoul Maqsoodi², Wilson Lew², Yunqing Ma², RaziKhan², Takuro Yaoi², John C. Moretto¹, Brigitte Robert¹, George Bers², Mohammed Kashani-Sabet¹ and Gary K. McMaster²

¹California Pacific Medical Center, Center for Melanoma Research and Treatment, USA

²Affymetrix, Inc., Santa Clara, USA

We hypothesize that the heterogeneous outcomes of melanoma are genetically determined. Sixty two melanoma-related genes have been categorized from the literature to compare the functional genes between metastatic melanoma and their skin controls. The 62 gene transcripts were tested against 20 frozen metastatic melanoma samples and their skin counterparts with normalization to five housekeeping genes, following approval by the institutional IRB. RNA expression was quantified directly from tissue homogenates by the QuantiGene[®] Plex branched DNA assay. Seven genes demonstrating the most significant difference in expression differences (p-values 1.28E-09 -1.93E-06) between melanoma and normal skin when analyzed by Cluster Analysis and Principal Component Analysis were studied using Formalin Fixed Paraffin Embedded (FFPE) tissues by the branched DNA *in situ* RNA expression technology QuantiGene[®] ViewRNA. Of these 7 genes, 4 genes were upregulated in the melanoma metastases versus normal skin tissues. These 7 candidate genes gave signal differences both in intensity and/or spatial recognition between melanoma and normal skin tissue microenvironments relating to angiogenesis, immune response/inflammation, DNA replication, cell proliferation/motility, tissue invasion/progression, epidermis development, cell communication and morphogenesis. We conclude that a novel set of melanoma-associated genes was found in this discovery phase. Future studies may include *in situ* QuantiGene[®] ViewRNA assay from FFPE sections in a large cohort of melanoma patients with detailed clinical outcomes to determine the significance of these genes.

Biography

Dr. Stanley P.L. Leong received his MD and MS degrees from Tulane University. He completed a surgical oncology fellowship at the NCI. He is currently Chief of Cutaneous Oncology, Associate Director of the Center for Melanoma Research and Treatment at the California Pacific Medical Center and Senior Scientist at the California Pacific Medical Center Research Institute as well as Professor Emeritus of Surgery at the University of California, San Francisco. He has published over 140 peer-reviewed articles and 12 books and serving on several editorial boards of repute. His research interests include cancer metastasis, sentinel node biology and cancer immunology.

**Proteomic
approaches for
profiling cancer
signaling pathways**

Fei Ye

Department of Pathology, Mount Sinai
School of Medicine, USA

After human genome is decoded, the characterization of the proteins is the next challenging task. Unlike genomic studies where individual changes may not have functional significance, protein expression is closely aligned with cellular function and activity. The proteomic profiling of functionally important regulatory proteins in cancer cells may shed light on the understanding of the molecular mechanisms of cancer development and metastasis. Uncovering the underlying protein signaling network changes in cancer aids in understanding the molecular mechanism of carcinogenesis and identifies the characteristic signaling network signatures unique for different cancers and specific cancer subtypes. The identified signatures can be used for cancer diagnosis, prognosis, and personalized treatment. During the past several decades, several proteomic approaches have been adopted to identify some signaling proteins and to help us understand their structure, function, and clinical significances in various cancers. We recently developed a powerful proteomic approach called Protein Pathway Array (PPA) analysis that allows identifying the important, but low abundance proteins and phosphoproteins in various cancers. In recent years, using proteomic approaches, we and others have identified various cancer biomarkers in diagnosis, prognosis and therapeutic target identification in various cancers. This presentation summarizes the usage of proteomics in recent years as an important technique in defining the proteome of cancer, which has helped in elaborate understanding of the diseases and has provided new avenues for developing better therapeutics and prognosis.

Biography

Fei Ye has completed her Ph.D at the age of 31 years from Norman Bethune University of Medical Sciences (NBUMS) in China and postdoctoral studies from Tongji Medical University in China. She is the assistant director of Molecular Pathology Division and assistant professor of Department of Pathology at Mount Sinai School of medicine. She has published more than 30 papers in reputed journals and serving as a reviewer of several reputed journals including Cancer Letters and Cancer Investigation.

**Ultra-sensitive
detection of BRAF
V600E and G469A
mutations by
Ice COLD-PCR
and BLOCKer-
Sequencing**

**Yanggu Shi, Benjamin Legendre,
Jr., Tyler Borczyk, Phil Eastlake
and Katherine Richardson**

Transgenomic Inc., USA

BRAF, a serine/threonine kinase, mediates the RAS/RAF/MAPK signal transduction pathway. Over 90% of BRAF mutations are V600E (c.1796T>A); this activates mitogenic cascades leading to tumorigenesis. This mutation is present in 70% melanoma, 100% hairy cell leukemia, 40% papillary thyroid cancer and, less frequently, other cancer types. V600E mutation status is valuable for determining clinical diagnosis, companion diagnostic tests, treatment guidance and outcome prediction. Ice COLD-PCR (Improved & Complete Enrichment CO-amplification at Lower Denaturation temperature) is technology that enriches mutated DNA sequences in an excess of wild-type DNA through selective amplification of the mutant DNA population using LNA-modified oligonucleotides (RS-oligo) complementary to wild-type sequence. After Ice COLD-PCR enrichment, V600E mutations could be detected at 0.05% as confirmed by standard Sanger sequencing. For the BRAF mutation G469A (c.1406G>C), limit of detection was 0.01%. We combined Ice COLD-PCR enrichment and dye terminator sequencing using a novel sequencing methodology, BLOCKer-Sequencing (BLOCKing Oligonucleotide Cycle Sequencing). Wild-type strand sequencing is blocked by a BLOCKer-oligo but mutant DNA is concurrently sequenced with one primer and amplified with a 5' phosphate primer. Lambda exonuclease selectively removed all products resulting from incorporation of the primer containing the 5' phosphate. BLOCKer-Sequencing after standard PCR increased the limit of V600E detection from 20% for standard Sanger sequencing to 1%. This compares favorably with other commercially available non-sequencing based mutation detection systems. The results presented here will demonstrate enhanced limits of detection when BLOCKer-Sequencing is used following Ice COLD-PCR amplification.

Biography

Dr. Yanggu Shi completed his Ph.D. from New York University and postdoctoral studies from Columbia University College of Physicians and Surgeons. He is a Sr. Scientist at Transgenomic, Inc. Prior to this he was a Sr. Scientist at Human Genome Sciences, Inc.

From bench to bedside

Gargi D Basu

Caris Life Sciences, USA

A major goal of cancer research is to test cancer tissue at the molecular level and make therapeutic predictions. Personalized medicine is a rapidly advancing aspect of health care that is based on each person's unique clinical, genetic, genomic and environmental information. It depends on providing a comprehensive understanding of personalized medicine from scientific discovery at the laboratory bench to the implementation of these novel pathways of understanding human biology at the bedside. One of the most widely used molecular profiling services with the most accepted methods is Caris Target Now. The goal of Target Now is to identify clinically relevant and patient specific biomarkers from the patients' tumor and help inform more effective and targeted treatment options. A variety of tests are performed on each tumor sample including immunohistochemistry, fluorescent in situ hybridization, microarray analysis and DNA sequencing. The profiled biomarkers are then reported out with drug associations. In a pilot study, treatment recommended by Target Now molecular profiling has been shown to increase progression free survival among some patients. Caris Target Now combines comprehensive molecular pathology and tumor profiling with an exhaustive evidence-based review of the latest clinical literature on biomarkers and their correlation to potential drug response. This provides treating physicians with the information needed to personalize cancer treatment. Some of the Target Now tests performed on common tumor types and their association with therapy will be discussed in detail.

Biography

Gargi Basu had completed her Ph.D from All India Institute of Medical Sciences in 1999 and then joined Mayo Clinic for postdoctoral studies. She is currently working at Caris Life Sciences in the Biomarker Evidence Team as a scientist. She has published over 25 papers in reputed journals and her work has appeared in Dr. Robert Weinberg's book on "The Biology of Cancer" and also on the cover of AACR journal. Her work on breast cancer has been featured on Breast Cancer Net News Release and on AACR Press Release.

**Cancer biomarkers:
from discovery
to clinical
implementation**

Renaud Seigneuric

Heat Shock Proteins and Cancer, INSERM
U866 ; 7, Boulevard Jeanne d'Arc, France
University of Burgundy, France
ICB, CNRS, UMR 5209, France

New biomarkers make sense if they provide better or different information compared to existing ones. There is a high interest in identifying, validating and eventually using biomarkers as they may help detecting a disease (e.g.: cancer) or its relapse earlier, assess treatment efficacy or toxicity, improve treatment follow-up or contribute to patient selection.

In oncology, investigated biomarkers may be as diverse as: proteins, circulating tumour DNA, circulating tumour cells, mRNA transcripts, polysomes, miRNAs, metabolites or autoantibodies for instance. Cancer biomarkers may be investigated by ELISA tests, immunohistochemical analyses, western blots, mass spectrometry or 'omics' among others.

However, many early claims of candidate biomarkers are in fact not substantiated, since they need to fulfil several stringent criteria along the way. Beyond this wide diversity in biomolecules and assays, several common pitfalls and challenges have been identified. Based on experience from the lab and the clinics as well as from the literature, some reasons for spurious findings are reviewed, with examples from transcriptomics, proteomics and heat shock proteins. This may contribute to provide more solid ground for the long and challenging endeavours to clinical implementation.

Biography

Renaud Seigneuric holds a French and a Canadian PhD in Biomedical Engineering. He completed his postdoctoral fellowship at the Maastricht lab, one of the 5 Siemens centres of excellence (Maastricht, the Netherlands). He patented, together with clinicians, lists of biomarkers leading towards more individualized cancer therapies. He was appointed in 2007 as assistant professor in biophysics (University de Bourgogne, Faculty of Medicine and Pharmacy, Dijon, France). Working at different scales, his translational research is devoted to cancer detection and treatment. He was recently nominated by the Who's Who in Medicine and Healthcare (2011-2012).

**Label-free optical
bio-sensors for
proteomic analysis:
current applications
and future
development in
cancer research**

Valentina Donzella

Scuola Superiore Sant'Anna, Piazza Martiri
della Libertà, Italy

Molecular tests based on specific protein quantification from body fluids or tissues have remarkably improved clinical practice. In oncology, they can be useful for early disease detection, treatment tailoring and prognosis prediction. Available technology does not always allow a comprehensive evaluation of proteomic alterations in patients.

To move towards analysis parallelization, a technological breakthrough is needed; it can be represented by Laboratories-on-a-Chip (LOCs). Those devices can integrate and automate all needed sample process functionalities into an inexpensive, portable and disposable, thumb-size object. Involved processes range from biological fluid handling and driving, heating, cooling, separating, molecule detection and signal processing. Which means integrating on the same chip optics, electronics, and micro-fluidics. The component dedicated to protein detection is the bio-sensor, where target bio-molecules are somehow 'trapped' producing a proper output signal. A bio-sensor is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element (biochemical receptor), which is in direct spatial contact with a transduction element. The recognition elements can be composed of antibodies, enzymes, hormones, receptors, etc. Optical signal use for binding detection offers several advantages, e.g. it is immune from electromagnetic interference and is separated from electrical signals (needed for fluid stream control and for driving electronics). In addition, unlabelled detection requires no preventive sample preparation or alteration. Thus, label-free optical biosensors integrated in LOCs may pave the way to the discovery and detection of novel biomarkers, offering the advantages of low-cost, easy use and small volume requirements.

Biography

Valentina Donzella, B.Sc. (2003) and M.Sc. (2005) in Electronic Engineering, received her Ph.D cum laude in Engineering (Innovative technologies) in 2010, from Scuola Superiore Sant'Anna, Pisa (SSSUP, Italy). In 2009, she spent 8 months as visiting Ph.D. student of Engineering Physics at McMaster University, ON, CA. She is a postdoctoral fellow, IEEE member, working on integrated optical biosensors for biological markers as well as on silicon photonics. She is proposal reviewer for Technology Foundation (STW, NWO) in Utrecht, the Netherlands and Guest Editor for Micro and Nanosystems, Bentham Science Publisher. She is lecturer for the International Master on Communication Networks Engineering, at SSSUP.

**Secretome
analysis of large
cell lung cancer
cell lines using
two-dimensional
electrophoresis
coupled to mass
spectrometry**

Zahra Mojtahedi

Shiraz University of Medical Sciences, Iran

The secretome of cancer cells is a valuable source of biomarkers that can ultimately reach the serum or other body fluids. Cancer biomarkers can facilitate early disease detection and monitoring, contribute to our understanding of the biology of cancer, and support the development of more efficient therapies. Recently, high-throughput proteomic analysis of the conditioned media of cancer cell lines has shown potential to identify novel biomarkers in cancer. We used two-dimensional electrophoresis coupled to liquid chromatography tandem mass spectrometry to identify the proteomes of the large cell lung cancer cell lines QU-DB and Mehr-80. A total of 130 distinct protein species were identified. Of these, 79 were previously found in serum or other body fluids, the membrane compartment or conditioned media of other cancer cell lines. Some of the proteins that we identified, e.g. IL-6, ubiquitin-carboxyl-terminal hydrolase isozyme L1 (PGP9.5), α -enolase, peroxiredoxin-1 are known putative serum markers for lung cancer, whereas others might be candidate markers for further validation in lung cancer body fluids such as epidermal fatty acid-binding protein, peptidyl-prolyl cis-trans isomerase A, chloride intracellular channel protein 1 and 4.

Biography

Zahra Mojtahedi has completed her medical doctor in 1998 and Ph.D in 2008 from Shiraz University of Medical Sciences. She has published more than 20 articles, and she is the director of Proteomics Lab in Shiraz Institute for Cancer Research, in Shiraz, Iran.

Copro-antiapoptotic protein survivin and lactoferrin biomarkers for improved detection and nanodelivery to colon cancer

Jagat R Kanwar, Ganesh Mahidhara, Rupinder K Kanwar and Chun Hei Antonio Cheung¹

Institute for technology research and innovation (ITRI), Deakin University, Australia

¹National Institute of Cancer Research, National Health Research Institutes (NHRI), Taiwan

We and others have found that survivin, a member of the family of inhibitor of apoptosis proteins that is overexpressed in several human tumours. Lactoferrin is also known to express in inflammatory diseases such as inflammatory bowel disease and Crohn's disease. We assessed the differential expression of survivin, other apoptotic biomarkers and lactoferrin in stool and serum samples of colorectal cancer (CRC) patients. We compared serum and stool samples from CRC patients and samples from healthy volunteers using an in vitro enzyme-linked immunosorbent assay to evaluate the survivin and lactoferrin response in patients. The sensitivity of the anti-survivin and lactoferrin response from patients with CRC was 65% and 70%, the specificity was 62% and 75% respectively with good predictive positivity and predictive negativity. Combined detection using survivin and lactoferrin produced better sensitivity (65%) and specificity (90%), respectively. In conclusion a positive association between survivin and lactoferrin concentrations in sera and stool samples of patients with CRCs was established. Our results suggest that analysis of both parameters would assist in screening patients with CRC. Our findings also suggest that the reduction in the serum survivin and copro-lactoferrin levels of advanced CRC patients after chemotherapy can be used as a predictor of response to the chemotherapy but not that of survival. In addition, we developed dominant negative mutant of survivin (SurR9-C84A) and loaded into Alginate enclosed chitosan- calcium phosphate nano carriers (ACSC-NCs), in order to improve the oral bioavailability and to protect the peptide from the locale of gastro intestinal tract. These CSC-NCs loaded with SurR9-C84A were tested in a xenograft mice model of colon cancer. We found all tumor bearing mice regressed tumors significantly. Anti-tumor activity was mediated by inducing apoptosis and necrosis in tumours. There was significant decrease in angiogenesis and vasculature in the CSC NCs-SurR9-C84A as compared to empty CSC-NCs ingested control tumor mice. In the present study we developed a safe, nontoxic, mucoadhesive, completely biodegradable, compatible and sustain released CSC-NCs as a proof of concept in colon cancer which can be used for other cancer types. Thus these CSC-NCs can be exploited for oral administration to protect from variable pH in intestinal track and resistance to gastric enzymes which otherwise digest proteins in gastrointestinal tract.

Biography

Associate Professor Jagat Kanwar is an immunologist and molecular biochemist. He is group leader of the Laboratory of Immunology and Molecular Biomedical Research has an international reputation in investigating fundamental and applied molecular aspects of cancer and chronic inflammation. He is an immunologist, molecular biologist and cell biologist. He has extensive training and expertise in studying the molecular mechanisms and devising treatments for human diseases like cancer and chronic inflammatory diseases such as asthma, atherosclerosis, inflammatory bowel disease (IBD), arthritis and multiple sclerosis in both in vivo and in vitro models. The research approach employed monotherapy (gene therapy, immunotherapy) or combinational therapy with commercially available chemotherapeutic agents including peptides. From 2002-2006, within Lactopharma his main research project involved the identification of milk bioactive molecules/ fractions for the treatment of cancer and employed monotherapy (gene therapy, immunotherapy or anti-angiogenic molecules) or combinational therapy with milk and natural plant bioactives and the results obtained have generated 3 patents and two provisionals are to be submitted. He is working on nanotechnology based peptide, siRNA and miRNA delivery for targeting survivin (currently most attractive cancer target), HIF-1 α and apoptotic cell signalling molecules expression in the cancers and inflammations. For commercial funded grants his research group carries out research in the areas of dairy/grain bioactives as immunomodulators, their role in bone and muscle development, osteoarthritis and wound healing. Presently his 7 PhD students are working on various cancer biomarkers and nanobiotechnological oral delivery systems for gene transfer technology and proteins in cancers. For commercial funded grants his research group carries out research in the areas of bioactives as immunomodulators, their role in bone, muscle development and osteoarthritis. His publications have added to the body of knowledge in the fields of nanobiotechnology, cancer gene therapy, cell biology and immunology. Kanwar's research work generated in total of 12 patent/PCTs with two provisionals in preparation. Five of these patents have been licensed for commercialization to biotech companies Antisoma, NeuronZ, Neuren Pharmaceuticals and Fonterra. He was invited as a speaker in more than 30 conferences and chaired sessions in Immunology, Nanotechnology, Nanomedicine and Biotechnology.

Cancer bioinformatics, a potential way for prediction of chemotherapeutic responses in clinics

Da-Yong Lu¹, Ting-Ren Lu² and
Xue-Liang Chen³

¹School of Life Sciences, Shanghai
University, China

²College of Science, Shanghai University,
China

³Dept of Oncology and Thermo-therapy,
Central Hospital of Jing-An District, China

Cancers are different etiological diseases with same characteristics of unlimited cell reproductions caused by the abnormalities of genetic molecules in human cells. Bioinformatics plays important role in revealing these abnormalities of genetic molecules for the importance of cancer diagnostics, prognostics and most important, therapeutics. It is a way of profound significance not only with quickness and high-throughput, but also of potential quantitative value of prediction for drug responses and use details. It is the fastest-growing area in recent cancer research. However, many technical and economic drawbacks impede us from reaching the goal of therapeutic benefits in clinics at current stage and will continual to be in the case in nearly future. We in several years before suggest a way of combination of drug sensitivity tests and mathematical computation, bioinformatics to make it more adequate and available. Adhering to this policy, improving of bioinformatics systems is especially important for the benefits of future individual therapy. In general, presently bioinformatics requires rigorous discipline and reasonable routine to make it real work in future clinical practices. Their gaining of popularity and new breakthrough are largely dependent on the progression of these disciplines. After introducing the general backgrounds of current bioinformatics application in cancer research, here we represent our insights and suggestions into the approach, especially their relations with genome-wide analysis, drug sensitivity tests and mathematics-related problems.

Biography

LU Da-Yong, oc/professor; ad/1288 Shangda Rd, 95-202, Shanghai200444, PR China; ed/ph D Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 2005, MS, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 1986, BS, Shanghai Medical University (Now Fudan University affiliated), 1982; Now School of Life Sciences, Shanghai University, Shanghai200444, PR China. Undergo the studies of cancer pathology, biochemistry pharmacology and clinical therapeutics from 1982 and some hypotheses in AIDS and neural science in 2007. More than 20 scientific articles have been published in international journals.

- 3(i): Cancer Science & Therapy
- 3(ii): Cardiovascular Diseases: Research & Therapy
- 3(v): Central Nervous System
- 3(vi): Biomarkers for Multiple Sclerosis

Session Chair

Dr. Sule AKIN

Baskent University School Of Medicine, Turkey

Session Co-Chair

Dr. Yasuhiro Nihon-Yanagi

Hachinohe City Hospital, Japan

Session Introduction

- | | |
|---|---|
| <p>Title: Development and prospective evaluation of a 20-gene model for molecular nodal staging of bladder cancer</p> <p>Dr. Alexander S. Baras, Johns Hopkins University, USA</p> |  |
| <p>Title: Utility of β-2 microglobulin as a housekeeping gene in human cancerous colorectal tissue</p> <p>Dr. Yasuhiro Nihon-Yanagi, Hachinohe City Hospital, Japan</p> |  |
| <p>Title: Myocardial CXCR4 interaction with β2-adrenergic receptor: a potential therapeutic approach for congestive heart failure</p> <p>Dr. Sima T. Tarzami, Mount Sinai School of Medicine, USA</p> |  |
| <p>Title: Influence of total PSA, BNP, GAMMA-GT, haemoglobin, blood urea nitrogen, glucose, triglycerides and renal failure on D-DIMER levels among central Africans with congestive heart failure</p> <p>Dr. Longo-Mbenza Benjamin, Walter Sisulu University, South Africa</p> |  |
| <p>Title: Biomarkers of brain function in children with uncomplicated epilepsy</p> <p>Dr. Sherifa Ahmed Hamed, Assiut University Hospital, Egypt</p> |  |
| <p>Title: Therapeutic hypothermia for postresuscitation syndrome and lactate levels</p> <p>Dr. Sule AKIN, Baskent University School Of Medicine, Turkey</p> |  |
| <p>Title: The roles of human apurinic/aprimidinic endonuclease/redox effector factor (APE1/Ref-1) in tumor diagnosis and related mechanism study</p> <p>Dr. Nan Dai, Third Military Medical University, China</p> |  |
| <p>Title: "Molecular characterization and current treatment strategy of glioblastoma multiforme"</p> <p>Dr. Xiang Zhang, Fourth Military Medical University, PR China</p> |  |

13 September 2011 (Tuesday)

Track 3(i) 3(ii) 3(v) 3(vi)

Title: Individualized cancer chemotherapy

Dr. Da Yong Lu, Shanghai University, PR China



Title: Prognostic value of troponin i & pro-brian natriuretic peptide in patients with sever sepsis: A closed unit experience

Dr. Fahad Aziz, MSSM-Jersey City Campus, USA



Title: Sulphonylureas: Do we need to introspect safety again?

Dr. Devindra Sehra, Sehra Medical Centre, India



Title: Blood-based test for multiple sclerosis – Biomarkers for disease detection and monitoring of treatment

Dr. Victor Levenson, Rush University Medical Center, USA



Development and prospective evaluation of a 20-gene model for molecular nodal staging of bladder cancer

Alexander Baras

Department of Pathology, Johns Hopkins University, USA

Background: Neoadjuvant chemotherapy prior to cystectomy confers a small yet significant survival benefit in bladder cancer. Yet, it has not been widely adopted, since most patients do not benefit and we are currently unable to predict those that do. We propose that tools identifying patients with advanced disease prior to surgical management would be useful in selecting patients for neoadjuvant chemotherapy.

Methods: We developed a gene expression model (GEM) predictive of pathological node status for use on primary tumor tissue from clinically node negative (cN0) patients. From a subset of transcripts, we developed both the GEM and cutoffs identifying patient strata with elevated and decreased risk of nodal involvement using two separate training cohorts (N=90 and N=66). We then independently evaluated the GEM and cutoffs to predict node positive disease in tissues from a Phase III trial cohort (AUO-AB-05/95, N=185).

Findings: A 20-gene GEM was developed and the stratification schema from it identified subjects with high (RR 1.74, [1.03-2.93]) and low (RR 0.70, [0.51-0.96]) relative risk of node positive disease. Multivariate logistic regression demonstrated the GEM predictor was independent of age, gender, pathologic stage, and lymphovascular space invasion (P=0.019).

Interpretations: This study proves the principle that molecular staging before surgery can be faithfully achieved and could change the way we view urothelial cancer management and practice. Selecting patients for neoadjuvant chemotherapy based on the risk of node positive disease has the potential to benefit high-risk patients while sparing others toxicity and delay to cystectomy.

Biography

Alexander Baras is a young investigator with interests in surgical pathology, personalized medicine, and computational biology. He completed his combined M.D. & Ph.D at the age of 29 in 2011 from the University of Virginia under the Medical Scientist Training Program. He has published 18 manuscripts in various journals and he has recently started reviewing manuscripts for BMC Biochemistry and Cancer. He has served as a bioinformatics consultant for Novartis in the past and is currently a resident physician in the department of Pathology at Johns Hopkins University.

**Utility of β -2
microglobulin as a
housekeeping gene
in human cancerous
colorectal tissue**

Yasuhiro Nihon-Yanagi
Hachinohe City Hospital, Japan

Internal controls are used for the estimation of gene expression by techniques such as quantitative real-time PCR. However, recent studies have shown these the expression levels of these housekeeping (HK) genes differ among various tissues or between normal and diseased tissue status. Some investigators reported low expression of β -2 microglobulin (B2M) in colorectal cancer. Other investigators emphasize that since the expression levels of different HK genes depend on the tissue type or experimental conditions, researchers should use several control genes in parallel for certain tissues.

To study mRNA expression levels of Toll-like receptor (TLR) 2 and 4 in sporadic human colorectal cancer tissue and non-cancerous colorectal tissue, we chose three HK genes, β -glucuronidase (GUS), β -actin (BA) and B2M as internal controls. Relative quantification was performed using these three genes separately and simultaneously. Then TLR2 and 4 expression levels were compared between the cancerous colorectal tissue and non-cancerous colorectal tissue specimens.

Our findings demonstrate that consistent data were obtained in most cases when GUS and BA were used as internal controls. When B2M was used as an internal control, analysis of TLR2 and 4 expression showed higher expression in cancerous colorectal tissue than in non-cancerous colorectal tissue. These results may be related to the low level of B2M in cancerous colorectal tissue.

Myocardial CXCR4 interaction with β 2-adrenergic receptor: a potential therapeutic approach for congestive heart failure

Sima T. Tarzami

Cardiovascular Research Center, Mount Sinai School of Medicine, USA

Chemokines are small secreted proteins with chemoattractant properties that play a key role in inflammation, metastasis, and embryonic development. We previously demonstrated a nonchemotactic role for one such chemokine pair, stromal cell-derived factor-1 α and its G-protein coupled receptor, CXCR4. Stromal cell-derived factor-1/CXCR4 are expressed on cardiac myocytes and have direct consequences on cardiac myocyte physiology by inhibiting contractility in response to the nonselective β -adrenergic receptor (β AR) agonist, isoproterenol. As a result of the importance of β -adrenergic signaling in heart failure pathophysiology, we investigated the underlying mechanism involved in CXCR4 modulation of β AR signaling. Our studies demonstrate activation of CXCR4 by stromal cell-derived factor-1 leads to a decrease in β AR-induced PKA activity as assessed by cAMP accumulation and PKA-dependent phosphorylation of phospholamban, an inhibitor of SERCA2a. We determined CXCR4 regulation of β AR downstream targets is β 2AR-dependent. We demonstrated a physical interaction between CXCR4 and β 2AR as determined by coimmunoprecipitation, confocal microscopy, and BRET techniques. We assessed the effect of cardiac overexpression of CXCR4 during TAC using a cardiotropic adeno-associated viral vector (AAV9) carrying the wildtype CXCR4 gene (AAV9.CXCR4^{WT}). Cardiac overexpression of CXCR4^{WT} in mice with pressure overload prevented ventricular remodeling and maintained function as determined by echocardiography and in vivo hemodynamics. The CXCR4 interaction with β 2AR will provide further insight into how CXCR4 modulates calcium homeostasis and chronic pressure overload responses in the cardiac myocyte. Together these results suggest that AAV9.CXCR4 gene therapy is a potential therapeutic approach for congestive heart failure.

Biography

Dr. Sima Tarzami received her B.Sc. and M.Sc. degrees from Hofstra University, New York, and her Ph.D. from Albert Einstein School of Medicine, New York, all in USA from 1992-2002. She has been a faculty in Mount Sinai School of Medicine since 2007, first as a Research Instructor and then promoted to an Assistant Professor of Medicine. Her major area of research is related to myocardial expression, signaling and function of chemokine receptor-4 in the animal models of heart disease. She currently holds a Grant in Aid from the American Heart Association, and KO2 from the NIH. She is an author of 14 peer reviewed papers and 10 published abstracts. She is a member of editorial board of international journal of clinical and experimental medicine (IJCEM) and also a manuscript reviewer of number of major journals including AHA.

Influence of total PSA, BNP, GAMMA-GT, haemoglobin, blood urea nitrogen, glucose, triglycerides and renal failure on D-DIMER levels among central Africans with congestive heart failure

Longo-Mbenza B, Ntima Mamona G, Forka AC, Vangu Nzita M and Kianu Phanzu B
Walter Sisulu University, South Africa

Objectives: To investigate the independent determinants of D-dimer variations in congestive heart failure (CHF)

Methods: A cross-sectional study among 102 black Congolese patients managed for CHF at LOMO medical centre, Kingshasa, DRC.

Results: In not considering biomarkers in all bivariate analysis, renal failures, pulmonary tuberculosis, age($r=-0.291$), Heart rate($r= 0.0224$), AST($r= 0.176$), haemoglobin ($= -0.222$), neutrophils ($r = 0.304$), and Lymphocytes($r= -.0288$), showed significant correlation with D-dimer levels. After considering biomarkers in all, 68% of all the variations (adjusted R²) of D-dimer levels were explained significantly and independently by Gamma GT, total PSA, Haemoglobin(Hb), BUN, BNP,Glucose (FPG) and Triglycerides (TG) in the equation $Y(\text{D-Dimer})= 4314.4 + 0.216 \text{ Gamma GT} + 0.186\text{PSA}- 0.199\text{HB} + 0.167 \text{ BUN} + 0.232 \text{ BNP} + 0.157\text{FPG}-0.141\text{TG}$ In patients with renal failures, 66.1% of variations (adjusted R²) of D-dimer levels were explained by Gamma GT and thyroxin(T4) as follows: $Y(\text{D-dimer})=4349.7 + 0.786 \text{ Gamma GT}-0.303 \text{ T4}$. However, in patients without renal failures, only 7% of variations (adjusted R²) of D-dimer levels were explained Hb as follows:

$Y(\text{D-dimer}) = 3884.7-0.288\text{Hb}$.

Conclusion: Biomarkers related to oxidative stress, inflammation, hypothyroidism, anaemia, renal function and diabetes mellitus may add significant value in the interpretation of D-dimer levels in Central Africans with CHF.

Biography

Benjamin B. Benjamin has received his MD, PhD in pathophysiology and MMed in Internal Medicine from the Bukarest Medical Institute (Romania), MSc in Cardiology and PhD in Cardiology at the Free University of Brussels (Belgium). He is a former Fulbright Scholar and visiting Professor in Clinical Pharmacology/Hypertension at the Institute of Lipid research, Baylor College of medicine, Houston (USA). He served for 30 years as chief of cardiology, Executive Dean of Faculty of Medicine and Deputy Vice-Chancellor at the University of Kinshasa, Democratic Republic of Congo. He is a member of 30 scientific societies, including: American Heart Association, American Diabetes Association, and American College of Cardiology, European Society of Cardiology and Pan-African society of Cardiology. He obtained a certificate in cardiovascular Epidemiology (Netherlands), Ethics (NIH), Bioethics (Oklahoma University) and Molecular genetics (Belgium, Italy). His original research was focused on elucidating the pathophysiological mechanisms of toxic myocarditis and immune-allergic cardiomyopathies. From 1980s until present, most of his research works are related to inflammatory states, oxidative stress, molecular biology, genetics, biomarkers and environmental impacts in Atherosclerosis, HIV/AIDS-related cardiac lesions, deafness (discovery of genes) and co-expression of genes in Pancreas. In addition to his role as clinician, lecturer, academic leader mentor, WHO expert and UN/Climate change Expert, he has been a very productive scientist: Supervisor of more than 10 PhD theses, 25 MSc theses, and 100 mini-dissertations, and over 300 papers published under his supervision. He is currently Research Champion professor at the Faculty of Health sciences, Walter Sisulu University, Mthatha, South Africa.

Biomarkers of brain function in children with uncomplicated epilepsy

Sherifa A. Hamed

Department of Neurology, Assiut University Hospital, Egypt

Many studies reported cognitive and behavioral abnormalities with recurrent seizures in adult brains. Similar evidences from the pediatric population are few and controversial. We aimed to investigate the effect of recurrent seizures on the developing brains. Included were 42 children with recurrent untreated uncomplicated epilepsy (generalized or focal) with mean age of 14.1 years and 30 healthy children for comparison. Intelligence (IQ) and cognition were examined using Wechsler Intelligence Scale for Children (WISC-III) and Stanford Binet subsets test (SBST4). Serum levels of neuron-specific enolase (NSE) and S100B proteins, sensitive markers of neuronal and glial cells damage were measured. Compared to controls, patients had lower mean score of full scale IQ (FSIQ) of WISC-III ($P=0.045$) particularly performance IQ (PIQ) scores ($P<0.01$), and comprehension, pattern analysis, quantitation, bead memory and memory for sentences of SBST4 ($P=0.045$; $P=0.013$, $P=0.007$, $P=0.002$; $P=0.035$), but not for NSE or S100B. Significant correlation was observed between FSIQ and duration of illness ($r=-0.430$, $P=0.035$) and number of seizures ($r=-0.580$, $P=0.005$) but not with S100B or NSE levels. Lower intelligence and poor cognitive performance are common with recurrent childhood epilepsy. Dysfunction in brain connectivity but not structural brain injury may likely be the cause.

Biography

Dr. Sherifa A. Hamed (M.D.) is an Associate Professor of Neurology and the director of the Neurogenetic unit in Assiut University, Egypt. She worked as a postdoctoral fellow (visiting scholar, 8/1998 to 8/2000) in USA [in Research Center for Genetic Medicine, Children's National Medical Center, Dept. Integrative Systems Biology, George Washington University School of Medicine and Health Sciences]. She was a part of a multidisciplinary research program concerning disease gene identification of muscular dystrophies. She served as a reviewer for 30 medical journals and has a least 70 international publications in the fields of Neurology, Neurogenetics and Neuropsychopharmacology.

Theurapeutic hypothermia for postresuscitation syndrome and lactate levels

Sule AKIN

Baskent University School Of Medicine,
Turkey

Therapeutic hypothermia (TH) is recommended therapy that reduces ischemic injury after low blood flow. It should be initiated soon in patients with ischemic injury and mild hypothermia (32-35°C for 12-24 hours). Postresuscitation Syndrome (PRS) is a pathology that is performed after return of spontaneous circulation following successful cardiopulmonary resuscitation (CPR). The pathophysiology is referred to global ischaemia and reperfusion injury due to cardiac arrest and CPR. It is a kind of "septic inflammatory response syndrome". TH is an accepted and valuable treatment option for PRS presented with neurological and cardiovascular impairment and multi-organ dysfunction. Indication of TH for both initial rhythms of cardiac arrests including shockable and non-shockable rhythms are still underinvestigation.

Lactic acidosis contributes to the pathophysiology of PRS including neurologic impairment. However, lactate levels are also elevated during TH applications. Lactic acidosis injures and inactivates mitochondria. Increased lactate levels (3-5 mmol/L) associated with reperfusion and hypothermia may be treated by efficient oxygen delivery. While administering TH after CPR, hemodynamic values, organ function markers, lactat levels and neurologic status should be evaluated. During TH, at the point that reaches to goal temperature, lactate blood levels' stable or decreasing values are predictive for good neurologic outcomes. At that point still increasing values reveal worsening neurologic outcomes or mortality.

It is evident that TH is one of the important therapy of PRS. In my presentation, I will also represent our clinic's experience and studies about lactate levels and importance of follow up as a good biomarker of neurologic functions after CPR.

Biography

Sule Akin has completed her medical education in Cukurova University Medical School and also Anesthesiology and Reanimation Department. She is an Associated Professor in Baskent University Anesthesiology and Critical Care Medicine Department and works as a consultant. Her interests in the area are neuroanesthesia, anesthesia for orthopedics, thoracic surgery and organ transplantation, neuro and surgical-critical care and cardiopulmonary resuscitation. She works and teaches in these fields. She also has many national and international publications about the interested areas. She is the instructor and course-director of "European Resuscitation Council" and reviews for articles for national journals.

**The roles of
human apurinic/
apyrimidinic
endonuclease/redox
effector factor
(APE1/Ref-1) in
tumor diagnosis and
related mechanism
study**

Nan Dai

Daping Hospital and Research Institute of
Surgery, Third Military Medical University,
China

Apurinic/apyrimidinic endonuclease/redox effector factor (APE1/Ref-1) is the major AP endonuclease in mammalian cells. It is a multifunctional protein which functions not only in DNA repair but also as a reduction-oxidation factor. Recently studies have showed that alteration of expression levels, cellular location and/or patterns of APE1/Ref-1 may consider as a good candidate in cancer screening and auxiliary diagnosis.

Interestingly, we found that expression of APE1/Ref-1 was significantly increased in tumor patients' serum. So we measured serum APE1/Ref-1 protein level in 210 healthy and 200 lung cancer patients by sandwich ELISA. Serum APE1/Ref-1 protein level was skewed distribution and significant increased in cancer patients ($P < 0.05$). We also detected serum APE1/Ref-1 antibody in 345 lung cancer patients, 350 healthy donors and 91 monitor patients before and after chemotherapy by indirect ELISA. Serum APE1/Ref-1-Abs level of lung cancer patients was significantly higher than that of healthy donors and after chemotherapy ($P = 0.000$). Both of APE1/Ref-1 protein and antibody combined with CEA, CA125 and CA242 can elevate the diagnostic sensitivity and correct rate. These results indicated that detection of APE1/Ref-1 in serum may be helpful in early diagnosis of malignant tumors and evaluating chemosensitivity. To explore the genetic association between SNP of APE1/Ref-1 and lung cancer susceptibility, we investigated a population based case control study among Chinese Han people in Chongqing City. Logistic regression analysis indicated that APE1 -141G/G genotype were reduced 38% risk of lung cancer compared with APE1 -141T/T genotype. APE1-141T/148Glu haplotype may serves as an important genetic susceptibility factor for lung cancer.

**Molecular
characterization
and current
treatment strategy
of glioblastoma
multiforme**

**Xiang Zhang, Wei Zhang, Wei-
dong Cao, Gang Cheng, Yong-
qiang Zhang, Bo-lin Liu and
Jin-xiang Cheng**

Department of Neurosurgery, Xijing
Hospital, China
Fourth Military Medical University, China

Glioblastoma multiforme (GBM) is the most frequent and aggressive primary brain tumor in human and is classified by the WHO in the group of diffusely infiltrative astrocytomas, representing the most malignant subtype of them. The aberrant genetic events and signaling pathways have been clearly demonstrated. They are cellular, highly anaplastic, and morphologically highly heterogeneous tumors. Understanding the genetic alterations, specific molecular biomarkers and proliferative pathways might promote therapeutic development for the management of GBM. In this article, we review the molecular characterization of GBM cells and current treatment strategy, including gross or near-total resection of the tumor, followed by radiotherapy and concurrent chemotherapy, stereotactic brachytherapy and new targeted therapies. The multimodal approaches for the treatment of GBM improve the prognosis.

Individualized cancer chemotherapy

Da-Yong Lu and Ting Ren Lu

Department of Neurosurgery, Xijing
Hospital, Fourth Military Medical
University, China

A major obstacle to control cancer growth and metastasis in patients is the widespread inappropriate use of anticancer drugs. As increasing numbers and types of anticancer drugs has been developed, clinicians become more and more likely to misuse them in their practice. We have known that cancers are different etiological diseases with the same pathologic characteristics of unlimited growths. With this type of heterogenous characters, it means responses to same anticancer drugs can be various from patient to patient even though they all develop from same organs of humans, or even represent with same histological tissues or phenotype. Owing to all these reasons, individualized cancer chemotherapy will be a future trend to improve the anticancer drug applications in clinics. In this article, we will document, review, discuss and highlight this issue.

Biography

LU Da-Yong, oc/professor; ad/1288 Shangda Rd, 95-202, Shanghai200444, PR China; ed/ph D Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 2005, MS, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 1986, BS, Shanghai Medical University (Now Fudan University affiliated), 1982; Now School of Life Sciences, Shanghai University, Shanghai200444, PR China. Undergo the studies of cancer pathology, biochemistry pharmacology and clinical therapeutics from 1982 and some hypotheses in AIDS and neural science in 2007. More than 20 scientific articles have been published in international journals.

Prognostic value of troponin i & pro-brian natriuretic peptide in patients with sever sepsis: A closed unit experience

Fahad Aziz

Resident Internal Medicine, Jersey City Medical Center, USA

Introduction: Myocardial dysfunction is a common complication in patients with sepsis. Cardiac troponins and natriuretic peptides are biomarkers that were previously introduced for diagnosis and risk stratification in patients with acute coronary syndrome and congestive heart failure, respectively. However, their prognostic and diagnostic impact in critically ill patients warrants definition.

Materials And Methods: Patients admitted to the intensive care unit (ICU) between January 2009 to January 2010 of a tertiary care center, who fulfilled the already reported consensus criteria for septic shock were included in this study.

Results: Sixty-eight patients with septic shock meeting entry criteria were retrospectively studied. 64.7% patients were found to have positive troponins (Troponin I > 0.05). Twenty-four (35.29%) patients had troponin I < 0.05 ng/ml and compromised the troponin I negative group. The mean (S.D) serum troponin I value in troponin I –positive group was 2.55 ± 1.67 ng/ml. None of the patient had progressive EKG changes.

Clinical Outcomes In Terms Of Troponins:

The Troponin I-positive group had higher APACHE II score (30 ± 6

Vs 22 ± 4.7) on admission. Twenty-eight patients died in the total study and among them twenty patients (71.42%) had elevated troponin I. Left ventricular dysfunction was more common in troponin-I positive group (EF= 38 ± 10) than in Troponin I-negative group (EF= 52 ± 6.5). 63.63 % of the patients with elevated Troponin I required mechanical ventilation as compared to 50% patients with normal Troponin I levels. The patients with elevated troponin I levels had longer MICU stay (7.45 vs 5.28 days)

Clinical Outcomes In Term Of Probnp: Among Twenty-eight deaths in this study, 66.66 % patients had elevated Pro BNP. Left Ventricular dysfunction was more common in patients with elevated Pro-BNP (EF= 42 ± 8.2 vs EF = 52 ± 10). 76.67 % patients who needed mechanical ventilation had elevated Pro-BNP. Similarly 67.82 % patients on inotropic support had elevated Pro-BNP. Elevated Pro-BNP was also found to be associated with increase in MICU stay (6.72 vs 4.35 days)

Conclusion: To date, it is unclear whether clinically unrecognized myocardial cell injury accompanies, causes, or results from this decreased cardiac performance. These findings suggest that in septic shock, clinically unrecognized myocardial cell injury is a marker of LV dysfunction.

Biography

Dr. Aziz is currently working as Internal Medicine resident at Jersey City Medical Center/ Mount Sinai School of Medicine. In addition to being an outstanding researcher, Dr. Aziz has authored several articles on different topics of his research and is working right now on many important research projects related to Critical Care medicine and Cardiology. These articles have also been cited hundreds of times by other researchers in the field. Dr. Aziz has presented his findings at various medical conferences and published in several internationally read peer-reviewed journals. In addition to that he is a member of editorial board of several well-recognized journal. His work has been well recognized both nationally and internationally.

Sulphonylureas: Do we need to introspect safety again?

Devindra Sehra¹, Sudhish Sehra¹ and Shiv Tej Sehra²

¹Sehra Medical Centre, India

²Mt. Auburn Hospital, USA

Introduction: Sulphonylureas (SUs) are commonly prescribed medications for type 2 diabetes mellitus (T2DM) worldwide. Differences among SUs for kinetic and adenosine triphosphate sensitive potassium (KATP) channels selectivity and consequential extra pancreatic effects, though recognized in literature, are not considered by treatment guidelines.

Areas Covered: The role of SUs in various systems related adverse effects have not been well understood. Inconsistencies in literature and lack of clinical trials assessing the long-term effects of monotherapy or combination therapy with SUs add to the concern. This review provides insights in issues concerning safety of SUs based on literature published between 1980-2011. A comprehensive search was carried out on PubMed, Embase & Cochrane databases using search terms viz. sulphonylureas, sulphonylureas and KATP channels, sulphonylureas & cardiovascular effects, sulphonylureas side effects etc.

Expert Opinion: SUs have been linked to CV events, growth hormone (GH) disorder, malignancy, weight gain and CNS adverse effects. These adverse effects generally get masked as they are thought to be related to diabetes per se. The current article will allow the fraternity to ponder and undertake further research on the ill effects of largely prescribed anti-diabetic medication.

Blood-based test for multiple sclerosis – biomarkers for disease detection and monitoring of treatment

Victor V. Levenson

Rush University Medical Center, USA

Detection of multiple sclerosis (MS) is a challenging process, which usually requires repeated imaging over time. The absence of unequivocal detection tests delays initiation of treatment thus increasing potential for significant brain damage. Similarly, the absence of biomarkers that reflect disease activity complicates treatment of clinically-defined MS and trials of disease-modifying medications. In this presentation novel biomarkers based on methylation of cell-free circulating DNA in blood will be described. These biomarkers reflect the presence of relapsing-remitting MS (RRMS) even when the patient is in remission. Moreover, they can differentiate patients in relapse and in remission thus opening the possibility to detect asymptomatic relapses, which constitute over 90% of relapses in RRMS. Treatment-related changes in DNA methylation-based biomarkers suggest that methylation of cell-free circulating DNA can be used to monitor treatment thus providing an objective measure of success for clinical trials. To illustrate the potential of methylation patterns I will use data produced by our MetDet-56 technique, which is designed to evaluate methylation patterns of 56 promoters in each clinical sample. Current version of the assay evaluates methylation on a genome-wide scale but still requires only 1 ng of DNA or 0.5 ml of blood plasma. This presentation will concentrate on technical aspects of methylation pattern development and assessment as applied to solving well-defined clinical problems of multiple sclerosis.

Biography

Victor V. Levenson has received his MD from the 2nd Moscow Medical Institute and his Ph.D from the Institute of Molecular Biology (Moscow, USSR). His laboratory developed a unique and currently unmatched process for methylation detection in extremely small clinical samples (biopsies, cytological samples and cell-free-circulating DNA from blood). He has published more than 35 peer-reviewed papers in reputed journals.

4(i): Transcription Profiling and Transcriptomic Analysis

4(ii): DNA Diagnosis

4(iv): Clinical Array-based Karyotyping

Session Chair

Dr. Jean Gabert

Université de la Méditerranée, France

Session Co-Chair

Dr. Irina Smolina

Boston University, USA

Session Introduction

Title: From research to the clinic: lessons from BCR ABL dosage in the tyrosine kinase inhibitors era

Dr. Jean Gabert, Université de la Méditerranée, France



Title: PNA technology for diagnosis of infectious and genetic diseases

Dr. Irina Smolina, Boston University, USA



Title: Molecular diagnostic system for gliomas based on gene expression profiling

Dr. Mitsuaki Shirahata, The TazukeKofukai Medical Research Institute Kitano Hospital, Japan



Title: Direct detection of circulating tumor cells (CTCs) in blood using digital cast PCR for early detection of lung cancer

Dr. Caifu Chen, Life Technologies, USA



Title: Biotransformation of citral by *Saccharomyces cerevisiae* and *Aspergillus niger*

Dr. Akbar Esmaeili, Islamic Azad University, Iran



From research to the clinic: lessons from *BCR ABL* dosage in the tyrosine kinase inhibitors era

Jean Gabert¹, Nathalie Beaufils²

¹INSERM CRO2, Université de la Méditerranée, France

²Biochemistry and Molecular Biology laboratory, Hôpital Nord, France

Standardisation and external quality controls are part of the routine in clinical biochemistry since years. International standards and external quality control rounds are absolutely warranted for any new biological marker for its worldwide use into the clinics. It is done for 40 years in biochemistry but such approach is still in its infancy for molecular biology tests. Taking the measurement of *BCR ABL* transcripts (M-BCR) as a model, we first developed a standardisation effort and external quality controls through the European Against Cancer (EAC) network then we developed freeze dried cells that can be sent worldwide at room temperature. *BCR ABL* is present mainly in patients having a chronic myeloid leukemia (CML). This naturally deadly disease has seen its prognostic revolutionized with the use of tyrosine kinase inhibitors targeting the *BCR ABL* protein. Now there is an international consensus to adapt the treatment based on the dosage of *BCR ABL* gene expression by real time PCR. We participated to the development of an international standard based on freeze dried cells which has been validated by the World Health Organization last year. During the meeting will be reported our efforts in this field at the regional, national and international levels and how biotech companies can participate to the effort of follow up improvement for health care patients.

Biography

Dr. Jean Gabert, Professor of Biochemistry and Molecular Biology, Faculty of Medicine, Méditerranée University, Marseille (France).

**PNA technology
for diagnosis of
infectious and
genetic diseases**

Irina Smolina

Department of Biomedical Engineering,
Boston University, USA

We have developed the robust DNA-targeted PNA-based assays which make it possible to detect DNA signature sequences within genomes avoiding global DNA denaturation. Although many natural proteins are capable of targeting duplex DNA (dsDNA) in a sequence-specific manner, our ability to design de novo proteins with desired sequence specificity are very limited, at best. That is why the ability of Peptide Nucleic Acid (PNA) of sequence specific recognizing dsDNA has attracted considerable interest. The basic understanding of the process of dsDNA invasion by pyrimidine bis-PNAs and various applications of the phenomenon have been elucidated during the past two decades. As a result, novel approaches for detecting short (about 20-bp-long) signature sites on genomic DNA under non-denaturing isothermal condition within fixed cells without nucleic acid extraction have been developed. In particular, a PD-loop-based method of pathogen detection has been developed in our laboratory, which makes it possible to distinguish not only different bacterial species but also to discriminate drug sensitive versus drug resistant strains. The next step would be to extend the approach to human cells, which would open the way for even more promising applications. Some encouraging data in this direction will be presented. Featuring both high specificity and high sensitivity as well as amenability to automation PNA-based DNA diagnostics thus being capable of expedient detection of DNA analytes directly in clinical specimens and environment. Progress in this direction may ultimately result in the numerous highly effectual unconventional medical and environmental diagnostic assays.

Biography

Irina Smolina is the Research Assistant Professor at the Department of Biomedical Engineering at Boston University. She received her M.Sc from the Moscow Institute of Physics and Technology (Russia) and completed her Ph.D from Institute of Bioorganic Chemistry (Russian Academy of Science, Moscow). She was a postdoctoral fellow at Boston University and at Harvard Medical School and has published more than 15 papers in reputed journals that span the range from fundamental human genome studies to applied diagnostic analysis, and from analytical chemistry to biotechnology research.

Molecular diagnostic system for gliomas based on gene expression profiling

Mitsuaki Shirahata¹,
Shigeyuki Oba², Yoshitaka
Narita³, Yoshihiro Muragaki⁴,
Motohiko Maruno⁵, Ryo
Matoba⁶, Susumu Miyamoto⁷,
Kikuya Kato⁸

¹The TazukeKofukai Medical Research
Institute Kitano Hospital, Dept. of
Neurosurgery

²Kyoto University Graduate School of
Informatics, Dept. of Systems Science,
Integrated Systems Biology Laboratory

³National Cancer Center, Dept. of
Neurosurgery

⁴Tokyo Women's Medical University, Dept.
of Neurosurgery

⁵Osaka Medical Center for Cancer
and Cardiovascular Diseases, Dept. of
Neurosurgery

⁶DNA Chip Research Inc.

⁷Kyoto University, Dept. of Neurosurgery

⁸Research Institute, Osaka Medical Center
for Cancer and Cardiovascular Diseases

Background: As the histological diagnosis of glioma is often difficult, the patients outcome will fail to match the predicted biological behavior. Therefore, it is clinically important to identify the molecular prognosis predictors for gliomas.

Purpose: Our aim was to identify prognostic gene signature for gliomas based on gene expression profiling.

Materials and Methods: We selected 3456 genes expressed in gliomas, including 3012 genes found in a glioma expressed sequence tag collection. The expression levels of these genes in 152 gliomas (100 glioblastomas, 21 anaplastic astrocytomas, 19 diffuse astrocytomas, and 12 anaplastic oligodendrogliomas) were measured using adaptor-tagged competitive polymerase chain reaction, a high-throughput reverse transcription-polymerase chain reaction technique. We applied unsupervised and supervised principal component analyses to elucidate the prognostic molecular features of the gliomas. The prognostic gene scores (PGS) were determined by expression levels of 58 prognostic genes identified by Cox regression analysis. The prognosis predictability of the PGS was tested in independent sample sets.

Results: The global gene expression data matrix was significantly correlated with the histological grades, oligo-astro histology, and prognosis. Using 110 gliomas, we identified PGS based on the expression profile of 58 genes, resulting in a scheme that reliably classified the glioblastomas into two distinct prognostic subgroups. The prognosis predictability of PGS was then tested with another 42 cases. Multivariate Cox analysis of the glioblastoma patients using other clinical prognostic factors, including age and the extent of surgical resection, indicated that the PGS was a strong and independent prognostic parameter.

The clinical utility of the PGS was demonstrated in another 55 cases of anaplastic glioma.

Conclusion: The gene expression profiling identified clinically informative prognostic molecular features in astrocytic and oligodendroglial tumors that were more reliable than the traditional histological classification scheme.

Direct detection of circulating tumor cells (CTCs) in blood using digital cast PCR for early detection of lung cancer

Caifu Chen, David Deng, Fawn Wang, Yun Bao, David Merrill, and Pius Brzoska

Genomic Assays R&D, Life Technologies, USA

Enumeration and molecular characterization of circulating tumor cells (CTCs) in human blood holds great potential in cancer diagnosis, survival prognosis, and treatment guidance. However, current methods require extensive process to isolate rare CTCs in blood. We reported a new approach for direct CTC analysis in blood without cell sorting by using digital sample enrichment and reverse transcription competitive allele-specific TaqMan qPCR (RT-qCastPCR) for rare mutations and RT-qPCR for cancer cell-specific marker genes. CastPCR is capable of detecting 1 mutant in 1,000,000 wild-type molecules. Blood samples from lung cancer patients or normal individuals with spiked-in known lung cancer cell lines were partitioned in aliquots of 5 - 50 μ L onto 96-well plates, such that each well contained either one cancer cell or none in the presence of 50 - 500 thousand normal white blood cells. Genetic mutations and panel of cancer-specific markers including CK19 and CEA for CTC identification and enumeration were determined by using both castPCR and RT-qPCR assays. The sample partition process resulted in a digital enrichment of 20 - 200 folds (the relative ratio of CTC to normal cells) in a CTC-positive well. Digital castPCR accurately identified known mutation and CK19 in spiked-in samples of ~10 - 60 cells per mL whole blood by two cell lines, but there was no positive well in the absence of spiked-in cells. Furthermore, cell type specific markers (CK19) and known EGFR mutations were identified in the same sample wells, indicating that identified mutation was specifically derived from cancer cells. In five blood samples from lung cancer patients of stage I - IV, EGFR mutation (p.L858R) was detected in all samples. CTC numbers in 3 early-stage lung cancers (I and II) were 11 - 32 cells/mL blood. In contrast, > 96 CTCs/mL were detected in stage IV patients. In conclusion, our data suggest that combination of digital sample enrichment with castPCR and RT-qPCR could be used to directly enumerate CTCs and detect cancer mutations in whole blood samples of lung cancer patients.

**Biotransformation
of citral by
*Saccharomyces
cerevisiae* and
*Aspergillus niger***

Akbar Esmaeili

Department of Chemical Engineering,
Islamic Azad University, Iran

The objective of this research was to study the pathways involved during biotransformation of citral by the free cell method (FCM) and the immobilized cell method (ICM) using *Saccharomyces cerevisiae* and by the sporulated surface cultures method (SSCM) using *Aspergillus niger*. The culture preparation was done using such variables as different growth mediums and incubation periods to obtain maximum cells of *S. cerevisiae* and *A. niger* for citral biotransformation. Further analysis was performed using fourier-transform infrared (FT-IR), ultraviolet analysis (UV), gas chromatography (GC) and gas chromatography/mass spectroscopy (GC-MS). All three methods produced citronello; SSCM additionally yielded hydroxycitronellal and acetone as major products. ICM was the most effective method, its major product being citronellol.

Biography

Akbar Esmaeili has completed his Ph.D at the age of 35 years from Islamic Azad University. He is the Associate Prof. Department Chemical Engineering North Tehran Branch, Islamic Azad University. He has published more than 40 papers in reputed journals, more 5 books, referee for more 30 paper's and serving as three editorial board member of repute.

5(i): Proteomics & Genomics

5(ii): Molecular Informatics and Inflammation

5(iii): Biomarkers: Toxicology

Session Chair

Dr. Moonsoo M. Jin
Cornell University, USA

Session Co-Chair

Dr. Tao Chen
US Food and Drug Administration, USA

Session Introduction

Title: Investigation of novel biomarkers for Alzheimer's disease using lipid-coated nanoparticles

Dr. Hitoshi Sohma, Sapporo Medical University Center for Medical Education, Japan



Title: Development of a microRNA assay for evaluating genotoxicity of agents

Dr. Tao Chen, US Food and Drug Administration, USA



Title: Biomarkers in the age of integromics

Dr. Hakima Amri, Georgetown University Medical Center, USA



Title: Quantitative imaging of inflammation toward diagnosis of systemic inflammation and tumor growth

Dr. Moonsoo M. Jin, Cornell University, USA



Title: Genome annotation, with implications for biomarkers

Dr. Mark Gerstein, Yale University, USA



Investigation of novel biomarkers for Alzheimer's disease using lipid-coated nanoparticles

Hitoshi Sohma^{1,2}, Mami Yamaguchi¹, Michitoshi Kimura¹, Shin-ichi Imai¹, Kayo Matsumoto¹, Norio Takei¹ and Yasuo Kokai¹

¹Department of Biomedical Engineering, Sapporo Medical University School of Medicine, Japan

²Department of Educational Development, Sapporo Medical University Center for Medical Education, Japan

Objective: Alzheimer's disease (AD) differs from other forms of dementia in its relation to amyloid beta peptide (Abeta42). Abeta42, a proteolytic product of amyloid precursor proteins (APP), has a toxic effect on neuronal cells. This effect implies that protein expression is changed in neuronal cells by Abeta42, which provides a molecular marker for this disease. In the present study, we used the mice primary culture neurons and investigated the proteins in the supernatant after incubation with or without Abeta₄₂.

Methods: In view of the appearance of an acidic phospholipid (phosphatidylserine (PS)) on the outer plasma membrane of an apoptotic cell, we used PS as a probe and proteins bound to PS-coated magnetic nano-beads in a Ca²⁺-dependent manner were identified using a proteomic approach.

Results: Of a number of proteins identified, we focused on annexin A5 and milk fat globule-EGF-factor 8 (MFG-E8) that is involved in the clearance of apoptotic cells. Both annexin A5 and MFG-E8 were found to be increased significantly in the culture supernatant by Abeta42. Tg2576 mice (AD mouse model), which overexpress mutant human APP, showed significant increase of annexin A5 in both the brain cortex and plasma, compared with control. The level of annexin A5 significantly increased in a greater proportion of AD patients as compared to that in a control group (*p*-value of less than 0.0001 in the logistic regression analysis).

Conclusions: Both annexin A5 and MFG-E8 are novel plasma biomarker candidates for AD.

Biography

Hitoshi Sohma completed his Ph.D. in biochemistry at Hokkaido University, Japan, focusing on Ca²⁺-signaling in cell-cell communications, and his postdoctoral studies at the National Institute of Mental Health, NIH. He is a professor in the Department of Educational Development, Sapporo Medical University Center for Medical Education, Sapporo, Japan. He is now involved in both pathobiochemical research and the management of medical education at the university. He has published more than 50 papers in the biomedical field.

**Development of a
microRNA assay
for evaluating
genotoxicity of
agents**

Tao Chen

National Center for Toxicological
Research, US FDA, USA

MicroRNAs (miRNAs) are a class of small RNAs and play an important role in carcinogenesis. miR-34a has been suggested as a tumor suppressor miRNA and its expression is directly controlled by the p53 gene to respond to DNA damage and cell apoptosis. In this study, alternation of miR-34a expression by genotoxins was evaluated to determine whether this miRNA could be used as an indicator for genotoxic damage in vivo and in vitro. In our in vivo study, it was found that miR-34a was up-regulated by N-ethyl-N-nitrosourea (ENU), a direct acting mutagen, in mouse liver and spleen, by aristolochic acid, a human genotoxic carcinogen, in rat kidney and liver, by riddelliine and comfrey, genotoxic botanical carcinogens, in rat liver; while no such change was detected in tissues of mice treated with non-genotoxic carcinogens. In our in vitro study, miR-34a expression in TK6 human cells was significantly increased by treatment of different genotoxins, ENU, cisplatin, etoposide, mitomycin C, methyl methane sulfonate, and toxal in a dose dependent manner. In contrast, treatment of cells with usnic acid, a non-genetic toxin, did not dysregulate miR-34a. The fold-changes of miR-34a expression for the treatments over the controls generally were large, for example, 22-fold in comfrey treatment and 12-fold in AA treatment. Therefore, miR-34a expression responds sensitively and specifically to genotoxic insults of chemicals. Thus, miR-34a expression has the potential to become a biomarker for genotoxin exposure.

Biography

Dr. Chen is an expert on genetic and genomic toxicology in U.S. Food and Drug Administration. He is also an adjunct professor in two universities. Dr. Chen serves as an editor or reviewer for a number of journals in toxicology, molecular biology and bioinformatics. He has served as a consultant for the World Health Organization and as a reviewer for research proposals for US National Science Foundation. He has been invited to present a number of seminars, keynote speeches and planetary lectures in national and international scientific meetings, and to write many review papers or book chapters on carcinogenesis and mutagenesis. He has published more than 100 manuscripts and abstracts in peer-reviewed journals and books, and scientific meetings. Dr. Chen's research addresses on defining different biomarkers for carcinogenesis like gene expression, microRNA expression, DNA adducts, mutations, and tumors.

Biomarkers in the age of integromics

Hakima Amri

Georgetown University Medical Center,
Department of Biochemistry, Cellular and
Molecular Biology, USA

Despite the rapid technological advances in the omics high throughput data generation, mining the data biomarkers or biological significance remain challenging. This is attributed to the lack of adequate analytical tools that take into consideration the biological heterogeneity, and to the confusion stemming from the imposition of a pathology-type immunohistochemical (IHC) biomarker concept on omics data. In most cases, the characteristics of the IHC biomarkers are not compatible with and cannot be compared to those from omics datasets. An omics biomarker cannot be assigned and validated without prior modeling and subtyping of the disease to reveal the extent of its heterogeneity, ontogenic classes, and omics' clonal aberrations (driver changes) underlying its subtypes and pathways' complexity.

In the age of integromics, a systems biology method such as parsimony phylogenetic analysis is better suited for data analysis, where disease modeling and the unraveling of clonal from non-expanded mutations should precede biomarker delineation. The analytical paradigm is based on phylogenetic principles, which aim to identify groups of patients (clades) that share clonal aberrations, and models these clades into a tree-like diagram termed cladogram. The cladogram is our dynamic tool of disease modeling; it spans a hierarchical arrangement of the normal, the transitional (at risk), and the diseased phenotypes. It offers a multidimensional systematic approach that is dynamic and highly predictive, and permits the recognition of biomarkers at various levels of the hierarchical classification--within and between clades. The universality of the data parsing approach offers a suitable platform for omics data integration and biomarkers discovery.

Biography

Hakima Amri holds a Ph.D. in Biochemistry and MS in Reproductive Biology from Pierre and Marie Curie University, Paris, France. After completing her post-doctoral training in Molecular Endocrinology, she joined the department of Biochemistry and Cellular and Molecular Biology at Georgetown University to research natural therapeutics for cancer. Dr. Amri's background in developmental biology and her interest and work in cancer research led to the creative application of phylogenetics to mutation-based diseases, such as cancer. This multi-disciplinary background provides Dr. Amri with a profound understanding of the disease biochemical pathways and the limitations facing biomedical research. Most recently, she has been advocating the application of phylogenetics analysis to high-throughput omics data. Dr. Amri shows that parsimony phylogenetics is a multidimensional dynamic analytical tool that is useful for disease modeling, profiling, and subtyping as well as biomarker discovery.

**Quantitative
imaging of
inflammation toward
diagnosis of systemic
inflammation and
tumor growth**

Moonsoo M. Jin

Department of Biomedical Engineering,
Cornell University, USA

Department of Radiology, Department of
Surgery, Weill Cornell Medical College,
USA

Dysregulated host inflammatory response causes many diseases, including cardiovascular and neurodegenerative diseases, cancer, and sepsis. Sensitive detection of the site of inflammation will, therefore, produce a wide-ranging impact on disease diagnosis and treatment. We hypothesized that nanoprobe designed to mimic the molecular interactions occurring between inflamed leukocytes and endothelium may possess selectivity toward diverse host inflammatory responses. To incorporate inflammation-sensitive molecular interactions, superparamagnetic iron oxide nanoparticles were conjugated with integrin lymphocyte function-associated antigen (LFA)-1 I domain, engineered to mimic activated leukocytes in physiology. Whole body optical and magnetic resonance imaging in vivo revealed that leukocyte-mimetic nanoparticles localized preferentially to the vasculature within and in the invasive front of the tumor, as well as to the site of acute inflammation. This study presents the first demonstration of in vivo detection of tumor-associated vasculature with systemically injected inflammation-specific nanoparticles, presenting a possibility of tumor detection by inflamed tumor microenvironment.

Biography

Moonsoo Jin received his doctoral degree at MIT, followed by his postdoctoral training in what can be broadly defined as protein engineering and design at Harvard Medical School. In 2006, he joined Cornell University as a faculty in the department of Biomedical Engineering. His lab uses multi-scale, interdisciplinary approaches to developing proteins for therapy and diagnosis applications. He has received numerous prestigious awards including Scientist Development Grant from the American Heart Association and NIH Transformative R01 Grant. He also started a biotech company, Nanomedik, Inc., which aims to translate nanotechnology to clinics.

Genome annotation, with implications for biomarkers

Mark Gerstein

Yale University, USA

A central problem for 21st century science is annotating the human genome and making this annotation useful for the interpretation of personal genomes. My talk will focus on this problem. I will describe an overall framework for data integration that brings together different evidence to annotate features such as binding sites and ncRNAs. Much of this work has been carried out within the ENCODE and modENCODE projects, and I will describe my approach interchangeably both in human and various model organisms (e.g. worm). I will further explain how many different annotations can be inter-related to characterize transcription in the intergenic space, build regulatory networks, and identify fusion genes. This work has clear implications for biomarker discovery.

Biography

Mark Gerstein is the Albert L Williams professor of Biomedical Informatics at Yale University. He is co-director the Yale Computational Biology and Bioinformatics Program, and has appointments in the Department of Molecular Biophysics and Biochemistry and the Department of Computer Science. He received his AB in physics summa cum laude from Harvard College and his PhD in chemistry from Cambridge. He did post-doctoral work at Stanford and took up his post at Yale in early 1997. Since then he has published appreciably in scientific journals. He has >400 publications in total, with a number of them in prominent journals, such as Science, Nature, and Scientific American. His research is focused on bioinformatics, and he is particularly interested in large-scale integrative surveys, biological database design, macromolecular geometry, molecular simulation, human genome annotation, gene expression analysis, and data mining.

6(i): Biomarkers in Drug Discovery

6(ii): Applications in New Drug Development

6(iii): Translational Medicine

Session Chair

Dr. Crispin R. Dass
Victoria University, Australia

Session Co-Chair

Dr. Michael Holinstat
Thomas Jefferson University, USA

Session Introduction

Title: Biomarkers in drug discovery: Potential use versus challenges

Dr. Abdel Halim, Daiichi-Sankyo Pharma Development, USA



Title: 12-Lipoxygenase regulation of platelet-mediated hemostasis and thrombosis

Dr. Michael Holinstat, Thomas Jefferson University, USA



Title: The search for safe compounds, robust assays and better drug delivery systems for improved anticancer activity

Dr. Crispin R. Dass, Victoria University, Australia



Title: Potential application of Nitrate reductase as biomarker in identifying novel inhibitors against M.tuberculosis

Dr. Dhiman Sarkar, National Chemical Laboratory, India



Title: Bromotyrosine derivatives isolated from marine sponges as antiparasitary

Mr. Elkin Galeano, Universidad de Antioquia, Colombia



Biomarkers in drug discovery: potential use versus challenges

Abdel Halim

Director, Clinical Biomarkers, Daiichi-Sankyo Pharma Development, USA

The role of biomarkers has been exponentially increasing in guiding decisions in every phase of drug development, from drug discovery into post-marketing studies. Also, biomarkers can predict patients' response to compound by identifying certain patient populations that are more likely to respond to the drug therapy or to avoid specific adverse events. This shift toward "personalized medicine is helping the drug industry achieve the goal of cost-effective and faster research, especially in poorly served areas such as neurodegenerative disorders and cancer.

Biomarkers assays range from esoteric type of assays performed on a fit-for-purpose basis to rigorously validated assays when a biomarker is used as a surrogate end point, for patient selection, or for randomization into different arms. Assay validation is essential, but of equal or even greater importance is the monitoring of assay performance and level of quality during production.

Despite all of the potential benefits of using biomarkers to advance pharmaceutical industry, discrepant results can pose a threat to development programs by triggering false decisions. Laboratory errors may be of pre-analytical, analytical, or post-analytical origin. Although clinical laboratory errors due to analytical problems have been, with momentous efforts, significantly reduced over time, the overall quality of clinical laboratory results can be compromised by the absence of true method-to-method or platform-to-platform standardization, or at least harmonization of test results.

This talk will highlight the following topics;

1. Biomarkers and their potential utility in drug development.
2. The major reasons behind discrepant results from biomarker laboratories and how to mitigate them.

Biography

Abdel Halim is a nationally recognized biomarker and clinical laboratory professional with more than 25 years of experience in all aspects of biomarker discovery, development, validation, and applications in patient management and pharmaceutical development. He is an expert in all biomarker techniques and platforms From safety lab POC till whole genome sequencing.

Abdel is leading the biomarker function within Daiichi-Sankyo pharmaceutical company and managing all safety and specialty biomarker aspects across different therapeutic areas in all phases of drug development.

Abdel holds Pharm D, and PhD in Clinical Biochemistry and Molecular Biology, and one of three lab professionals in the USA who are triple certified by the American Board in Clinical Chemistry, Molecular Diagnostics, and Toxicology.

Abdel is a member of 14 Clinical Laboratory Standard Institute (CLSI) subcommittees to establish guidelines promoting quality in clinical laboratories worldwide.

12-Lipoxygenase Regulation of Platelet-Mediated Hemostasis and Thrombosis

Michael Holinstat

Thomas Jefferson University, USA

Platelet activation plays a central role in regulating hemostasis and thrombosis. Following platelet activation, metabolism of phospholipids such as arachidonic acid (AA) by 12-lipoxygenase (12-LOX) may play a significant role in regulating the degree and stability of platelet reactivity. Although 12-LOX has been described as mediating both pro- and anti-thrombotic effects in the platelet, the underlying mechanism for these actions has remained elusive. Using both inhibitors of 12-LOX as well as its metabolites, we investigated the mechanisms by which this enzyme regulates platelet function. To assess the role of 12-LOX in platelet activation and thrombosis, granule secretion and integrin activation were measured by flow cytometry and confirmed by aggregation in the presence or absence of 12-LOX activation or exogenous addition of eicosanoid metabolites. Inhibiting 12-LOX resulted in a complete inhibition of dense granule secretion and repression of platelet activation. Addition of 12-HETE, resulted in a significant increase in dense granule secretion and addition of 12-HETrE, resulted in complete inhibition of thrombin-mediated platelet activation, giving support to DGLA metabolism (the substrate for 12-HETrE) as a negative regulator of platelet activity while AA metabolism appears to act as a positive regulator of platelet function. Understanding the role of 12-LOX and its metabolites in platelets will enable us to delineate its contribution in regulation of platelet reactivity as well as a readily available biomarker indicating the potential for thrombosis and stroke.

Biography

Michael Holinstat is an assistant professor of Medicine at Thomas Jefferson University in Philadelphia. He received his Ph.D. in Pharmacology from the University of Illinois at Chicago and postdoctoral training at Vanderbilt University in the Department of Pharmacology. His research focuses on identifying novel approaches to anti-platelet therapy with a special emphasis on regulation of platelets through the lipoxygenase pathway leading to a number of oxidized fatty acids which may play a central role in regulating unwanted platelet activation. Additionally, the lab studies regulation of platelet signaling through PAR1 and PAR4.

**The search for
safe compounds,
robust assays
and better drug
delivery systems for
improved anticancer
activity**

Crispin R. Dass

School of Biomedical and Health Sciences,
Victoria University, Australia

Cancer is a group of diseases characterized by uncontrolled growth of cells in the body. These lesions, if not treated, grow until they become life-threatening or fatal. Traditionally, surgery has been the main form of tumor control, though this is not performed where the growth is deep-seated in the body or located at a site where surgery could itself be life-threatening. Alternatives to, or assisting surgery are chemotherapy and radiotherapy. However, these two traditional forms of cancer therapy suffer due to harmful effects to the healthy parts of the body. To address this, there is a global push to find compounds that are effective against neoplastic cells, but less harmful against normal healthy cells of the body. Complementing this is the search for in vitro or in vivo assays that are more indicative of antitumor activity. Finally, there has been a growing push to find better drug delivery systems capable of more selective delivery of drugs to tumors in the body. This presentation discusses some of the cell-based assays and small animal models set up by our labs in the past decade, drug delivery systems we have tested so far, and biologicals (protein, nucleic acid, polysaccharide) trialed so far, some of which are undergoing clinical testing.

Biography

Crispin R. Dass has 17 years of cell and molecular biology research experience, mainly focusing on oncological R&D. His research is on systems at various levels – *in silico*, *in vitro*, *in vivo*, ADME/Tox, clinical, and also with biomedical education. He has worked on projects for Johnson & Johnson, GlaxoSmithKline, Amgen, and Novartis. His extensive experience is documented in his 120 papers to date, with publications in *Nature Medicine*, *Journal of the National Cancer Institute*, *Biomaterials*, *Nucleic Acids Research*, *Cancer*, and *Journal of Controlled Release*. He is currently on the editorial board of 3 other journals in his field, and has been invited to chair sessions and to give plenary lectures at national and international conferences. Based currently in St Albans (Melbourne, Australia), he has research links with Thailand, Fiji, USA, China, South Korea, Japan, Iran and India.

**Potential Application
of Nitrate reductase
as biomarker in
identifying novel
inhibitors against
*M.tuberculosis***

Dhiman Sarkar

National Chemical Laboratory (CSIR),
India

Mycobacterium tuberculosis, the most important life-threatening bacterial pathogen is responsible for three million deaths annually. Latency in tubercle bacilli has been found as principal cause for long duration of treatment as well as development of resistance. Identification of dormant stage inhibitors could demonstrate desirable effect on eradication of tuberculosis. For past few years, we are involved in developing novel screening tools using respiratory type nitrate reductase (NarGHJI) as biomarker. A significant increase in NarGHJI activity is observed during transition from aerobic to anaerobic dormant stage. We had earlier developed an *in vitro* whole cell based high throughput assay for anti-tubercular screenings. A similar pattern of bacilli dependent conversion of nitrate to nitrite was found to occur during its residence within human Thp1 macrophages. Nitrate reduction by *M. tuberculosis* represents the count of viable bacilli within the host. This screening protocol is also validated on a small set of in-house library. We are able to screen a small in-house library to evaluate these protocols. One of the scaffolds identified from these screens belong to 1,2,4 trozole class of compounds. Altogether, the host cell based assay provides advantage of picking up pro-drug like molecules simultaneously keep apart the false actives which can be easily metabolized. This presentation discusses the developments of whole cell based assays by using nitrate reductase, screenings, identifying novel inhibitors and their target.

Biography

Dhiman Sarkar completed his Ph.D from Jadavpur University and then joined AstraZeneca R & D Bangalore, India. As Research Scientist, he was associated with different projects on anti-tubercular and anti-malarial developments in AstraZeneca (1996 to 2002). He joined National Chemical Laboratory (CSIR-NCL) as senior scientist with the responsibility of developing a screening facility and currently, he is Principal Scientist and Head, Repository of Small Molecules at National Chemical Laboratory, a premier laboratory within CSIR, India. He has published more than 14 papers in peer reviewed journals.

Bromotyrosine derivatives isolated from marine sponges as antiparasitary

Elkin Galeano¹, Olivier P. Thomas², Sara Robledo³, Diana Muñoz³ and Alejandro Martínez¹

¹Universidad de Antioquia, Colombia.

²Université de Nice-Sophia Antipolis, Parc Valrose, France

³Universidad de Antioquia, Colombia

Tropical diseases caused by single-celled parasites are of particular importance: malaria, leishmaniasis and Chagas disease, it represents three most important diseases caused by parasitic protozoa. It is estimated that these three diseases are responsible for more than 110,000 deaths every year. In the absence of a long-term protecting vaccine, the control of these parasitic infections is based on a few chemotherapeutic agents, most of which nowadays have parasitic resistance, severe adverse effects and variable efficacy according to the phase of the disease. For this reasons development of new, safe and effective antiprotozoal agents are urgent needs. By these reasons, we are evaluating the potential of Colombian sponge as source of antiparasitic compound. Urabá Gulf is located in the Northwest Colombian Caribbean Sea, on the border with Panama. We are isolated 14 different bromotyrosine derivatives from marine sponges; structural determination of isolated compounds was assigned using one- and two-dimensional NMR, MS and other spectroscopy data. All compounds were evaluated in vitro, against the most important tropical parasitic: *Leishmania panamensis*, *Plasmodium falciparum* and *Trypanosoma cruzi*. The selectivity indices were realized comparing the activity against the toxicity of the compounds over the human promonocytic cell line U937. Four evaluated compounds showed high selective indices as antiparasitic *in vitro* at concentrations between 10 and 20 μ M.

Biography

Elkin GALEANO is Pharmaceutical Chemist, M. Sc. in Pharmaceutical Science and last year doctoral students in Pharmaceutical Science. He works in the Marine Natural Products Research Group at University of Antioquia, Colombia. He has published more than 10 papers in journals and recently, a review on marine natural products in drug development and new perspectives.

7(iii): Molecular Imaging and Dynamics

7(iv): Statistics in Biomarker Research

Session Chair

Dr. Jeremy Warren
NanoSight Ltd., UK

Session Co-Chair

Dr. Anka N. Veleva
North Carolina State University, USA

Session Introduction

Title: Protease finger printing for biomarker discovery

Dr. Kalyani Jambunathan, Center for Drug Discovery (CADRE) SRI International- Shenandoah Valley, USA



Title: Novel peptides targeting circulating cellular biomarkers for molecular imaging of tumor Angiogenesis

Dr. Anka N. Veleva, North Carolina State University, USA



Title: Seeing, counting and phenotyping exosomes as biomarkers using nanoparticle tracking analysis

Mr. Jeremy Warren, NanoSight Ltd., UK



Title: Compare bayesian evaluation of biomarkers as surrogate endpoints with the frequency form

Dr. Shohreh Jalaie, Tehran University of Medical Sciences, Iran



Title: Effect of carvacrol on D-galactosamine-induced mitochondrial enzymes and DNA damage by single-cell gel Electrophoresis

Dr. Balakrishnan Aristatile, King Saud University, Saudi Arabia



Protease finger printing for biomarker discovery

Kalyani Jambunathan, Douglas S. Watson and Amit K. Galande

Center for Drug Discovery (CADRE) SRI International, USA

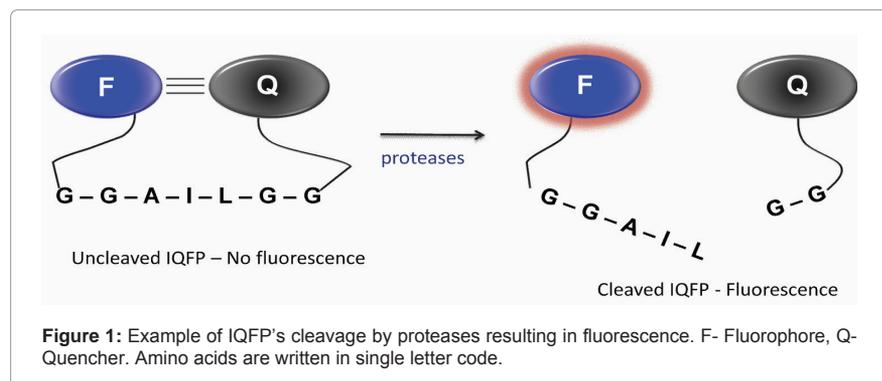
Fluorescence resonance energy transfer (FRET) is a distance-dependent interaction between two chromophores in which excitation is transferred from a donor molecule (fluorophore) to an acceptor molecule (quencher) without photon emission. Removal of the acceptor molecule from donor's proximity results in quantifiable fluorescence (Figure 1). FRET is an important technique and can be utilized in monitoring peptide substrate cleavage by proteases in different biological samples.

We report a simple, sensitive, specific FRET based platform for detection of proteases profiles in different biological samples by screening against a combinatorial library of internally quenched peptide probes (IQFP's). The library was utilized to determine the proteolytic profile of two clinically relevant biological fluids, serum and bronchoalveolar lavage fluid. Both fluids displayed a distinct and quantifiable proteolytic signature.

The library was further utilized to distinguish between the protease profiles of different *Aspergillus* species and also to identify peptide probes that are indicative of invasive aspergillosis (IA) in a guinea pig model.

Substrate specificity of biologically relevant recombinant enzymes such as prolyl oligopeptidase (POP) and fibroblast activation protein (FAP) both of which are implicated in number of human diseases was also determined using the IQFP library screen.

The approach provides a comprehensive finger print of the proteolytic activity of complex biological fluids as well as individual proteases. The technology is currently being applied to identify proteases as biomarkers in a variety of disease states for subsequent development of in vitro diagnostics.



Biography

Kalyani Jambunathan is a researcher at SRI International's Center for Advanced Drug Research (CADRE), at present working on NIAID funded project to develop FRET based assay to detect fungal derived proteolytic activity during invasive Aspergillosis. She graduated with a BSc in chemistry from Madras Christian College (MCC, India), MSc in chemistry from Indian Institute of Technology-Madras (IIT-M) and PhD in chemistry under the guidance of Dr. H. Mario Geysen in Department of Chemistry at University of Virginia. Her areas of specialization include but not limited to peptide science, molecular biology, assay design and development.

**Novel peptides
targeting circulating
cellular biomarkers
for molecular
imaging of tumor
angiogenesis**

Anka N. Veleva

Department of Biomedical Engineering,
North Carolina State University, USA

Malignant tumors acquire new blood vessels either locally by remodeling pre-existing mature capillaries or by recruiting circulating cells derived from the bone marrow. Recent laboratory and clinical evidence validate the role of circulating bone marrow derived pro-angiogenic, tumor homing cells as biomarkers of the tumor angiogenic status. Peptide sequences specific for these circulating biomarkers represent a new approach in angiogenic medicine and can be used for several different applications that will benefit the diagnosis and treatment of cancer.

In this investigation we report on the discovery of high affinity peptide ligands that are specific for bone marrow derived tumor homing cell populations. We screened a peptide phage display library and devised a novel selection approach that combines in vitro and in vivo protocols. To assess the utility of the novel high affinity, high specificity peptides we examined the ability of the peptide ligands to direct imaging reagents in vivo and monitored the process by noninvasive positron emission tomography (PET) scans. For this purpose we developed a labeling platform employing the phage that displays the cell specific peptide as a molecularly targeted imaging agent. These proof-of-principal experiments demonstrate the ability of the peptide to deliver payload (radiolabeled phage conjugates) in vivo to angiogenic tumors. The novel peptides provide molecular tools with which to monitor noninvasively the status of tumor angiogenesis on a cellular and molecular level.

Biography

Dr. Anka (Dobrev) Veleva is a faculty member at the Joint UNC/NCSU Department of Biomedical Engineering. Dr. Veleva is also a Principal Investigator at the McAllister Heart Institute at the University of North Carolina at Chapel Hill. Her multidisciplinary research program integrates aspects and utilizes methodologies from disciplines such as high-throughput molecular screening, vascular stem cell biology, medical engineering, and high-resolution imaging. She is an author of 40+ peer reviewed articles in reputed journals and a number of patent applications. Dr. Veleva serves as a manuscript reviewer for various journal including *Molecules* among others.

**Seeing, counting
and phenotyping
exosomes as
biomarkers using
nanoparticle
tracking analysis**

Jeremy Warren and Bob Carr

NanoSight Ltd, Amesbury, UK

Exosomes are 30-100nm nanovesicular bodies released from endosomes which originate in a wide variety of cells and can be found in most body fluids including blood, urine, saliva, breast milk etc.,. They are currently the subject of intense study, being increasingly recognized as playing multiple roles in intracellular communication and immune regulation. As well as displaying membrane proteins reflecting from their cellular origin, exosomes have now been shown to carry micro- and mRNA. It is increasingly accepted that exosomes are implicated in a multitude of pathological conditions and show much promise as diagnostics for many different diseases such as cancer, heart disease, diabetes, Alzheimer's, pre-eclampsia, etc. However, because of their small size, they are below the current detection limit of flow cytometry and the lack of methods for their detection and analysis is inhibiting progress in this field.

Nanoparticle Tracking Analysis is a relatively new method by which deeply submicron structures can be individually visualized and, through analysis of their Brownian motion, sized and counted in real time and with a rapid and robust microscopical methodology. Furthermore, fluorescently labeled exosomes can be successfully tracked and analysed allowing phenotyping of subpopulations in complex sample types which could form the basis of a new form of diagnostic test.

We will show results gained recently from the use of NTA in the development of a diagnostic test for pre-eclampsia and we will review other studies in which NTA has been most lately used to speciate and enumerate exosomes.

Biography

From a degree in Chemical Engineering from the University of Birmingham, UK, Warren worked for Unilever in chemical production where he qualified as a chartered engineer. He then set up a successful chemicals manufacturing business in Belgium, before completing an MBA at INSEAD in France. After a period in strategy consultancy with Booz.Allen, Warren began a series of CEO roles in SMEs centered on developing technology businesses. Warren joined NanoSight in 2005 as CEO and was directly involved in development of the company's multiparameter characterization technology. During the last two years emphasis has been on biological nanoparticles, with particular interest in the use of NanoSight as a platform for their detection and diagnostic application.

Compare bayesian evaluation of biomarkers as surrogate endpoints with the frequency form

Shohreh Jalaie¹, Soghrat Faghihzadeh², Farzad Eskandari³ and M.Reza Meshkani⁴

¹Tehran University of Medical Sciences, Iran

²Tarbiat Modares University, Iran

³Allameh Tabataba'i University, Iran

⁴Shahid Beheshti University, Iran

In medical and pharmaceutical research, interest in using biomarkers as surrogate endpoints for target clinical endpoint has stemmed from various reasons. Because of importance of statistical evaluation of surrogate marker, very different methods are suggested.

Alonso et al. proposed the “likelihood reduction factor” (LRF) as a unified approach when neither the biomarker nor the true endpoint is normally distributed. This measure of individual-level association can be used under any generalized linear model for a single trial or meta-analysis.

Flowing of these criteria for surrogate evaluation, in this study, we have explored the Bayesian approach to the evaluation of the validity of a surrogate at the individual level, based on the Bayes factor for choosing the best model in the context of generalized linear modeling.

It is suggested that the Bayesian LRF denoted by LRFB which benefits from the prior knowledge on the situation under study would perform yet better in comparison to other criteria.

By a Theorem we proof, for large sample size, $\text{Lim LRF}_B = \text{LRF}$. The relation between the Bayesian likelihood reduction factor (LRF_B) and its frequentist counterpart (LRF) have been shown by a small scale simulation also.

We have simulated different trials with different priors in the logistic regression models by R software. The results show that LRF can be viewed as a special case of LRFB relative to a certain prior. Hence, the importance of prior knowledge and Bayesian analysis for surrogate's validation is shown.

Biography

Shohreh Jalaie has completed her Ph.D in Biostatistics from Tarbiat Modares University in 2008. She passed a scholarship in Melbourne University. She is faculty member of Tehran University of Medical Science. She has published more than 20 papers in reputed journals.

**Effect of carvacrol
on D-galactosamine-
induced
mitochondrial
enzymes and
DNA damage
by single-cell gel
Electrophoresis**

**Balakrishnan Aristatile¹, Khalid
S. Al – Numair², Abdullah. H.
Al – Assaf¹ and Kodukkur
Viswanathan Pugalendi^{3*}**

¹College of Food and Agricultural Science,
King Saud University, Saudi Arabia

²College of Applied Medical Sciences,
King Saud University, Saudi Arabia

³Faculty of Science, Annamalai University,
India

In the present study, we investigate the effect of carvacrol on the activities of serum hepatic marker enzymes, mitochondrial enzymes and the DNA damage in D-galactosamine (D-GalN)-induced hepatotoxic rats. The hepatic marker enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and γ -glutamyl transpeptidase (GGT) activities are elevated in (D-GalN)-induced rats. In addition, the activities of hepatic mitochondrial enzymes (such as isocitrate dehydrogenase, α -ketoglutarate dehydrogenase, succinate dehydrogenase, malate dehydrogenase, NADPH dehydrogenase and cytochrome c-oxidase) are significantly decreased in D-GalN- hepatotoxic rats. Oral administration of carvacrol brought these hepatic markers and mitochondrial enzymes activities to near normal levels. In D-GalN-induced hepatotoxic rats, the hepatic mitochondrial thiobarbituric acid reactive substances (TBARS) significantly increased and the activities of enzymatic antioxidants such as superoxide dismutase (SOD), glutathione peroxidase (GPx) and non-enzymatic antioxidants such as vitamin C, vitamin E and reduced glutathione (GSH) decreased significantly in the liver and mitochondria. Administration of carvacrol restores the enzymatic activities and non-enzymatic antioxidants levels towards normal. DNA damage was observed in D-GalN-hepatotoxic rats and treatment with carvacrol significantly decreased the DNA damage. These results suggest that carvacrol is having hepato-protective and antioxidant properties and can also protect the liver mitochondrial damage in D-GalN-induced rats.

Session Chair

Dr. Anita Kamra Verma
University of Delhi, India

Session Introduction

Title: Biopolymer nanotherapeutics: Enabling oncology drug development by nanoconjugates & nanoparticles

Dr. Anita Kamra Verma, University of Delhi, India



Title: Urinary microRNAs as noninvasive biomarkers for drug-induced liver injury

Dr. Xi Yang, National Center for Toxicological Research, USA



Title: Biomarkers: Evolving regulatory landscape for drug development and diagnostics

Dr. Orest Hurko, Biologics Consulting Group, Inc., USA



Title: Utilization and cost of prostate-specific antigen (PSA) as a biomarker among prostate cancer patients: Results from Taiwan national health insurance research database

Dr. Yi-Hsien Lin, Cheng Hsin General Hospital, Taiwan



Biopolymer Nanotherapeutics: Enabling oncology drug development by Nanoconjugates & nanoparticles

Anita Kamra Verma

Dept. of Zoology, K. M. College,
University of Delhi, India

In the recent years the nanobiotechnology/ Translational nanotechnology has witnessed an increase in interest towards the nanoparticles and their biological effects and applications. These include bottom-up and molecular self assembly, bio-efficacy of naked nanoparticles and nano-safety, drug encapsulation and nanotherapeutics for use in microscopy, imaging and diagnostics. The nanotechnology market is predicted to be valued at \$2 trillion by 2012, so the likelihood of exposure to synthesized nanomaterials will exponentially increase. The last decade has seen successful clinical application of nanoparticles and polymer-anticancer drug conjugates. Three dimensional structures of sugars help in binding to target proteins and are attractive non-toxic therapeutic agents to modulate blood coagulation, cancer metastasis, or cell growth. The potential of nanotechnology to improve human health may be fully realized when aspects of transport (epithelial, endothelial, and cellular) are better understood along with how the physical/chemical characteristics of nanoparticles influence their stability, biodistribution, and toxicology.

The focus of the talk will be the recent advances in this field involving conventional anticancer drugs, stimulation of the immune system by the nanoparticles and nanoconjugated drugs relative to free drugs, altered biodistribution and Pharmacokinetics including the recently reported immunological response to nanoparticulate delivery for development of protein vaccines against tuberculosis.

Biography

Anita Kamra Verma, Associate Professor, at K.M.College, University of Delhi, has over 20 years of teaching experience and has worked in National Institute of Immunology, New Delhi. She has done her post graduation in 1982 from Univ. of Delhi, and Ph.D in 1988. She was a Senior Scientist at the School of pharmacy, University of Manchester for two years. She has two Patents on Anti-Cancer Drugs and over 25 publications to her credit. She has been awarded the Charles Darwin Gold medal in 2009. Her research interests include '*Developing Novel Polymer Therapeutics as Nano-medicines*', making in-vivo models for quantifying nanoparticulate drug delivery for cancer and Diabetes, developing rationale designs, based on whole body and cellular pharmacokinetics-pharmaco-dynamic profile of drugs.

**Urinary microRNAs
as noninvasive
biomarkers for
drug-induced liver
injury**

Xi Yang

Food and Drug Administration (FDA),
National Center for Toxicological
Research, USA

Several recent studies measured elevated levels of circulating plasma microRNAs (miRNAs) after toxicant-induced liver injury, most likely due to leakage from damaged hepatocytes. miRNAs have also been detected in urine with some of them being derived from organs outside of the urinary system, opening up their potential use as noninvasive biomarkers of disease or injury. Despite this potential, changes in urine miRNA profiles have not been investigated as biomarkers for drug-induced liver injury. In this study, an innovative method for collecting, processing, and analyzing urinary miRNA was used to examine miRNA profiles from rats treated with a single oral dose of acetaminophen (APAP), carbon tetrachloride (CCl₄), or non-hepatotoxicant (penicillin/PCN). The APAP and CCl₄ increased clinical pathology and histopathological indices of liver injury at 24 hours; however, there was no hepatotoxicity caused by PCN. For the APAP study, urinary miRNA levels correlated best with the degree of liver centrilobular glycogen depletion. In contrast to the high inter-animal variability noted for serum alanine and aspartate aminotransferases and centrilobular liver necrosis, urinary miRNA levels were consistently elevated in all high dose animals. APAP and CCl₄ both increased the urinary levels of select miRNAs; whereas, PCN caused slight decrease of the significantly changed miRNAs. In addition, 10 of the increased miRNAs were common between APAP and CCl₄; and the clustering analysis revealed a distinct miRNA pattern from hepatotoxicant-treated groups. These results suggest that specific miRNAs in the urine could reflect the severity of drug-induced liver injury and therefore have the potential to be used as noninvasive preclinical and clinical biomarkers.

Biomarkers: Evolving regulatory landscape for drug development and diagnostics

Orest Hurko

Biologics Consulting Group, Inc., USA

Ever since 2006, biomarkers have been advocated by the FDA Critical Path Initiative as a way of making development more efficient. Despite an enormous uptake by industry, their utility in registration packages is far from clear. Unraveling the complexity requires recognition of several types of biomarkers, each with distinct regulatory implications. These are biomarkers for (1) dose-selection, (2) selection of patients, (3) efficacy, and (4) toxicity. Use of biomarkers from the first two classes is encouraged by the FDA. Dose-selection biomarkers do not require recognition as surrogates by regulatory agencies, inasmuch as sponsors are given considerable latitude in the choice of dosing regimens, bounded only by the need for acceptable safety margins defined by preclinical and Phase 1 studies. Similarly, trial sponsors may define entry criteria as narrowly as they like. However, they do so with the responsibility to provide a companion diagnostic, which itself must meet regulatory standards for reliability.

In contrast, validation of efficacy or toxicity biomarkers to the level required for surrogacy in traditional registrations has been very limited. The most significant distinction is afforded by the FDA's Accelerated Approval process, which allows the use of an efficacy biomarker as a primary endpoint in pivotal trials, even if it had not been validated sufficiently for use in traditional approvals. The Government Accountability Office has tabulated 64 NDA's and BLA's approved on the basis of surrogate biomarkers. Other uses of efficacy or toxicity biomarkers for internal decision-making, including biomarker adaptive designs, will be discussed.

Biography

Orest Hurko completed his M.D at the Harvard Medical School after graduate studies at MIT. Postdoctoral studies were conducted at the NIH and Johns Hopkins, where he served on the faculty for 17 years. After 12 years industrial experience at SmithKline Beecham, GSK, Wyeth and Pfizer, where he was responsible for biomarker development, he now serves as Senior Clinical Consultant at BCG, Inc, a regulatory consultancy that has contributed to 10 of the 12 BLA's most recently approved by the FDA. He has published more than 200 papers and is co-author of two books, including *McKusick's Mendelian Inheritance in Man*.

Utilization and cost of prostate-specific antigen (PSA) as a biomarker among prostate cancer patients: Results from Taiwan national health insurance research database

Yi-Hsien Lin^{1,2}

¹Division of Radiotherapy, Cheng Hsin General Hospital, Taiwan

²School of Medicine, National Yang-Ming University, Taiwan

Prostate-specific antigen (PSA) is a major biomarker in the early diagnosis and monitoring of prostate cancer. However, the statistics of use and cost of PSA test is limited. Taiwan National Health Insurance covered over 99% residents and comprehensive medical services, including the PSA test among prostate cancer patients. This cross-sectional study used a sampled NHI research database containing one-million beneficiaries. Claims of the year of 2009 were analyzed. Postate cancer patients were identified by diagnosis codes. A total of 1235 prostate cancer patients using medical services in 2009 consisted this cohort. Among them, 1061 patients (85.9%) received 3247 PSA tests (average 3.06 tests per user) in 2009, including 3088 tests in outpatient services and 159 tests in inpatient services. The total cost of PSA test was US\$36897, accounting 0.8% of the total cost of this cohort. The average PSA test per user was 1.8, 3.0, 3.3, 3.2, and 2.8 in patients at age of < 50, 50's, 60's, 70's and > 80 years, respectively. In conclusion, our results demonstrated the frequency of use and the cost of PSA test among prostate cancer patients is low in Taiwan. Further investigation of the cost-effectiveness of PSA test was warranted.

Biography

Yi-Hsien Lin has completed his M.D at the age of 25 and Ph.D at the age of 37 years from National Yang-Ming University, Taiwan, Taipei. He is now the attending physician of Division of Radiotherapy and the executive secretary of Cancer Committee of Cheng Hsin Hospital, Taipei, Taiwan. He has published more than twenty papers in reputed journals. Dr. Lin has a wide variety of research interests including radiation therapy, traditional medicine and health economics.



Posters



2nd World Congress on Biomarkers & Clinical Research

12-14 September 2011 Baltimore, USA

**¹⁸⁸Re-Lanreotide:
Determination of radiopharmacokinetic parameters in rats**

Eva M. Molina-Trinidad^{1,2},
Consuelo Arteaga de Murphy³,
Helgi Jung-Cook⁴, Eduardo
Murphy Stack⁵, Martha Pedraza-
López³, José Luis Morales-
Márquez¹, Guadalupe Vertiz
Serrano⁴

¹Universidad Nacional Autónoma de México, México

²Área Académica de Farmacia. Ex-Hacienda la Concepción Tlilcuautila, Hidalgo

³Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México

⁴Universidad Nacional Autónoma de México, México

⁵School of Medicine, Westhill University, México

Background: We used ¹⁸⁸Re-lanreotide to determine its radiopharmaceutical parameters in a model of Wistar rats with induced hepatocellular carcinoma, after a single intravenous dose. The rat model is useful to determine the pharmacokinetic parameters and the tumor/organ ratios of ¹⁸⁸Re-lanreotide to be used for calculating the personal dose following the methodology *MIRDOSE* and later in the diagnosis and therapy of cancer.

Objective: We used ¹⁸⁸Re-lanreotide to determine radiopharmaceutical parameters in a model in rats Wistar.

Methods: ¹⁸⁸Re labeled by a modified direct method. AS-30D hepatoma cells were obtained from ascites of a Wistar rat with hepatoma. Healthy and tumor induced hepatocellular carcinoma Wistar rats were used for distribution and radiopharmacokinetic studies. ¹⁸⁸Re-lanreotide, ≈1.8 MBq in 0.1 mL was injected in the peritoneal cavity and in the dorsal left side of healthy rats. The rats were sacrificed at 0.083, 0.25, 0.5, 1.16, 3 and 24 h post injection. The activity (%IA/g) of all the blood samples in the following times: 0.25, 0.5, 1.1, 3, 5, 8, 12, 15, 18, and 24 h for healthy rats and 0.25, 0.5, 1.16, 3, and 24 h for hepatoma induced rats.

Results: The radiopharmacokinetic parameters were calculated following a two-compartment, first-order elimination model of ¹⁸⁸Re-lanreotide in healthy rats and for rats with induced tumor using the *WinNonlin* program.

Conclusion: A pharmacokinetic profile of ¹⁸⁸Re-lanreotide in healthy and hepatoma tumor induced rats follow model two-compartment. With mean residence time and the mean half life we will be calculate the therapeutic dose following *MIRDOSE* methodology.

Relationship between total PSA, free PSA, free PSA/total PSA ratio and cardiometabolic risk among central Africans cardiac patients without prostate diseases

Forka Ac, Longo-Mbenza B, Kutupa Ezer E, Buassa-Bu-Tsumbu B, Kianu Phanzu B

Walter Sisulu University, South Africa

Objective: To identify epidemiologic and cardiometabolic factors correlated with Total PSA, Free PSA and Free PSA/Total PSA ratio. Independent determinants of total PSA were also investigated.

Methods: A cross-sectional study conducted among 70 black hypertensives without prostate diseases at LOMO Medical center, Kinshasa, DRC.

Results: In bivariate analysis, age ($r=0.290$; $P=0.47$), waist circumference ($r=-0.245$; $P=0.41$), number of cigarettes smoked ($r=0.289$; $P=0.015$) and serum creatinine ($r=0.408$; $P=0.001$) were significantly correlated with Total PSA. Low socio-economic status (67.6% vs. 32.4%), ethnic groups from West (56.4% vs. 36%), excessive alcohol intake (75% vs. 43.3%), smoking (100% vs. 24.5%) and family history of prostate cancer (85.7% vs. 42.9%) were significantly ($P<0.05$) associated with elevated Total PSA ≥ 4 ng/mL. However, Free PSA was not correlated with any variable. There was a significant correlation between waist circumference ($r=-0.114$; $P=0.004$), number of cigarettes smoked ($r=-0.215$; $P=0.021$), HDL-cholesterol ($r=-0.225$; $P=0.018$); GGT ($r=-0.318$; $P=0.007$), fasting plasma glucose ($r=-0.326$; $P=0.008$) and Free PSA/Total PSA ratio. In multiple linear regression analysis, 46.1% (Adjusted R²) of variations of total PSA were explained by Total cholesterol (TC), Ferritin (Fer), and GGT in this equation $Y(\text{Total PSA}) = -24.3 + 0.306TC + 0.343Fer + 0.241GGT$.

Conclusion: Prevention of oxidative stress, dyslipidemia and life style changes might prevent both Cardiovascular Disease and prostate cancer in these Central Africans hypertensives.

Efficient drug carrier nanofibers contained PEG-POSS loading insulin nanoparticles for oral delivery of protein drugs

Kyu Oh Kim, Byoung-Suhk Kim, Ick Soo Kim

Shinshu University, Japan

In a recent year, nanotechnology has been utilized to develop new therapies and next generation nanosystems for “smart” drug delivery. A variety of organic/inorganic nanomaterials and devices have been often used as delivery vehicle to enhance the therapeutic activity by prolonging drug half-life, improving solubility of hydrophobic drugs, reducing potential immunogenicity, and/or releasing drugs in a sustained or stimuli-triggered fashion. Current treatment methods involve regular injections of insulin, which can be both painful and inconvenient, thus leading to low patient compliance. In order to overcome this problem, the oral route is considered to be the most convenient and comfortable means of drug administration for patients. In this work, novel drug carrier nanofibers with core-shell poly(ethylene glycol) (PEG)-polyhedral oligosilsesquioxane (POSS) nanoparticles were used to encapsulate insulin as new drug delivery carriers via electrospinning. The morphologies of fiber and particles, particle size and ζ potential of the pure nanostructured core-shell PEG-POSS and the corresponding insulin-loaded PEG-POSS nanoparticles were investigated by transmission electron microscopy (TEM) and laser diffraction particle sizer. Insulin release test showed that insulin was well-protected inside PEG-POSS nanoparticles at gastric pH for 2hrs, and was released at intestinal pH (pH 6-7) where the absorption and activation of the drug are necessary. We therefore believe that such nanofibers contained PEG-POSS nanoparticles could be useful as a potential carrier for insulin drug delivery systems.

Biography

Ms. Kyu Oh Kim have joined at department of Bioscience and Textile Technology, Nano Fusion Technology Research Group, Shinshu University at Japan, since 2009- now as a Doctor's degree (Advisor: Prof. Ick-Soo Kim). Her research interests are “Biocompatible Organic/inorganic nanofiber using a polyhedral oligosilsesquioxane (POSS) and designing the fibrous scaffolds for tissue engineering application”. She received her bachelor and master degree in polymer system engineering from Dankook University at Korea in 2009 (Advisor: Prof. Kee-JongYoon).

Human epididymis protein 4 (HE4) plays a key role in ovarian cancer cells proliferation and motility

Lin Guo

Fudan University Shanghai Cancer Center,
China

The Human Epididymis Protein 4 (HE4) is a novel biomarker for epithelial ovarian cancer (EOC). We previously ascertained the serum HE4 level was significantly elevated in the majority of all ovarian cancers but not in benign diseases or health control, therefore, it is useful for application in clinical diagnosis, even for the malignant ovarian carcinoma patients at early stage. Although the molecular mechanism of the HE4 protein is unknown, the *HE4 (WFDC2)* gene is amplified at high levels in ovarian cancers. We therefore performed experiments to explore preliminary the functions of HE4 in ovarian cancer cells. Here, we reported that HE4 was specially overexpressed in human ovarian cancer SKOV3 cells. And, we showed that HE4 secreted by ovarian cancer cells enhances cell adhesion and motility. At the molecular level, HE4 promotes epidermal growth factor receptor activation, increases the expression of cell adhesion molecules on the cell surface. Moreover, stable transfection of cells with plasmid expressing HE4-pcDNA3.1 promoted cell migration and adhesion. Correspondingly, HE4 enhanced migration of cells was also inhibited by HE4-shDNA expression. Interestingly, following down-regulation of HE4, the phosphorylations of JNK and ERK were dramatically decreased. This study suggested that expression of HE4 was associated with cancer cell proliferation and migration through MAPK signaling pathway. Taken together, our results provide the first evidence of the cellular and molecular mechanisms that may underlie the motility-promoting role of HE4 in EOC. In addition, these results underscore the important functional implications of HE4 processing in ovarian cancer progression. Therefore, it might be taken into consideration in future studies that examine the role of HE4 as a target for gene-based therapy.

Molecular analysis of idiopathic cryptorchidism in the Mexican population

Rosa María Viguera^{1,4}, Juan C. Gutiérrez¹, Ismael Zamora¹, Osvaldo Cuevas², Julio Rojas¹, Oscar Gutiérrez^{1,4}, Emiy Yokoyama³, Lucía Taja⁵, Margarita Chávez-Saldaña¹

¹Laboratorio de Biología de la Reproducción

²Servicio de Urología;

³Departamento de genética Humana; Instituto Nacional de Pediatría S.S.

⁴Facultad de Medicina Veterinaria y Zootécnia, UNAM

⁵Lab. Genética Molecular y Farmacogenética, Instituto Nacional de Cancerología; México

Cryptorchidism (CO) may occur as an isolated manifestation (idiopathic) or associated with a congenital malformation syndrome. CO is an important factor for male infertility and testicular malignancy on adulthood, itself might be considered a complex disease in which multiple genes are involved in the testicular descent. In this study we analyzed some single nucleotide polymorphisms (SNPs) in the *INSL3* and *RXFP2* genes, which could contribute as risk factors or susceptibility for the idiopathic CO in Mexican patients. 85 patients were included with idiopathic CO and 100 children on the control group, where 12 SNPs were analyzed. 100% from patients but also from the control group were out normal homozygous for the p.R102C and p.R105H from the gene *INSL3* variables, while the p.R102H variable was detected in only one patient in heterozygous state. Two alterations were detected by sequencing: p.R105R and the p.T86M. The frequency of the analyzed variables in the *RXFP2* gene is similar to other populations, comparing the frequency of these variables with the patients and the control group, the c.51869A-G variable showed differences, since the GG genotype or at risk, is more common on idiopathic CO patients, while realizing the genotype-phenotype correlation, it shows that the c. 30704C-T variable, the TT genotype or at risk is more common on bilateral CO patients. Knowing the type and distribution from the allelic variables in our population, will allow the improvement of risk prevention methods and susceptibility for this malformation and in the future the infertility and testicular cancer preventive care.

Computational and molecular analysis of HIV release by 'Viral Protein-U' at the time of pregnancy

Supriya Singh, Shashi Khare,
Sudha Prasad, RL Ichhpujani,
DS Rawat, LS Chauhan, Arvind
Rai

National Centre for Disease Control
(NCDC), India

Maulana Azad Medical College, India

Introduction: The so-called accessory genes of HIV have recently been found to be of significance with roles in viral replication and pathogenesis. The trans-membrane viral protein U of HIV causes CD4 down-regulation and is also involved in release of the virus (as a counter protein to overcome the host restriction by tetherin). The present study was carried out to determine the genetic characteristics of the trans-membrane and cytoplasmic domain of the vpu protein of HIV during pregnancy. In addition we also studied BST-2 m-RNA expression at the time of pregnancy and post-partum (preliminary results).

Materials and Methods: Blood samples were obtained from 53 HIV sero-positive patients (28 from antenatal risk group; 22 from other risk groups; 3 samples post partum). Amplification of vpu gene was followed by sequencing. Sequence analysis was performed with the help of MEGA and Bioedit. Homology modeling using Swift Modeler was used to construct models from the deduced amino acid sequences. VMD (Visual Molecular Dynamics) version 1.9 was used to understand the molecular features of the membrane protein. Phylogenetic analysis based on sequence and structural homology was carried out. Sequence variability was also determined using Entropy tool from Los Alamos Database. I-Mutant 2.0 and Membrane Protein Explorer were used to study the effect of mutations, stability and hydrophobicity of the trans-membrane protein. The mRNA expression levels of BST-2 were examined using Real Time PCR.

Results: Significant decrease in sequence variability in the pregnant risk group was observed. Phylogenetic results confirmed that our isolates belonged to subtype C. Multiple structural alignments of sequences from antenatal risk group revealed increased entropy in the trans-membrane domain, whereas the cytoplasmic domain was much conserved. Structural homology based on Qres values indicated a higher structural similarity in the trans-membrane region as compared to the cytoplasmic domain. The post partum group exhibited mRNA expression of BST-2, in contrast to its absence in other risk groups.

Conclusions: Pregnancy being an interferon depressed physiology, vpu doesn't have to put much effort to antagonize tetherin. It maintains a significantly conserved amino acid sequence with the trans-membrane domain being comparatively more variable than the cytoplasmic domain, but none of the variations in the amino acid sequence of the trans-membrane region alter the protein structurally and therefore allows an optimum viral extrication. The host restriction protein BST-2 is able to counteract for the action of vpu post-partum. The expression seems to coincide with the beginning of the interferon induced physiology i.e. labor and post partum, a host strategy to control virus release and alleviate the possibility of virus transmission at the time of delivery when the fetus is in contact with maternal secretions, and also during breastfeeding.

Identification of surface markers during proliferation and differentiation of mouse adipose-derived mesenchymal stem cells

Vandana Panwar and Umesh Kr. Shandilyas

National Dairy Research Institute, India

Embryonic stem (ES) cells and genetically modified stem cells are being widely used in basic research in the field of regenerative medicine. However, clinical application of these cells is currently difficult in view of ethical issues. On the other hand, cells derived from bone marrow, adipose tissue or other tissues have attracted attention as clinically applicable sources of autografting cells, because these cells can differentiate into various types of cells, including adipocytes, osteocytes, chondrocytes, smooth muscle cells, endothelial cells and neuronal cells. Since, adipose tissue yields mesenchymal stem cells (MSCs) 500 fold greater than bone marrow, isolated with minimal invasive procedure and moreover, it is contaminated with lesser number of hematopoietic stem cells, it could be a better source for mesenchymal stem cells. Surface markers are now increasingly used for identification of these cells and their differentiation. Even these markers are being exploited for obtaining homogenous cell preparation. Many surface antigens which are known for mouse bone marrow MSCs but their presence or absence in mouse adipose tissue has not been established. Comparatively, identification of markers on adipose derived MSCs from human is actively pursued. So far, presence or absence of 36 well studied surface markers on human adipose derived MSCs is established, albeit some of them being doubtful. In contrast, presence of only 6 markers and absence of 10 markers in mouse adipose derived MSCs has been established.

Biography

Ms. Vandana is pursuing PhD from National Dairy Research institute which is a premier institute of INDIA in Dairy Research sector. She has completed Master of sciences from Maharshi Dayanad University, Rohtak, India. She has a very good academic record and awarded Institute Fellowship from, Indian Council of Agricultural Research, INDIA.

Development of high sensitivity bioluminescent enzyme immunoassay for oxytocin as biomarkers for psychiatric disorder

Yoshihiro Sano¹, Shiomi Ohta¹, Hiroshi Ohkuma², Haruhumi Tsuge² and Hidetoshi Arakawa¹

¹School of Pharmacy, Showa University, Japan

²Biochemical Research Laboratory, Eiken Chemical Co. Ltd., Japan

Autistic spectrum disorder (ASD) is known as a disease of wide prevalence in children. DSM-IV is currently used as the diagnosis of ASD in clinical psychiatry. However, it is difficult to provide a definitive diagnosis of ASD. As the reason, characteristics of ASD are very similar to that of schizophrenia or social anxiety disorder. Therefore, if children develop ASD until in early childhood and cannot be received treatment, they will have a high risk secondary disorder, depression etc. As a result, development of simple clinical laboratory test for ASD is necessary for early detection and rapid cure of that disorder. Recently, it has been suggested that ASD patients have low level of OXT in their plasma. Therefore, OXT might be able to be used as one of the biomarker for ASD, psychiatric disorder.

In this report, we developed highly sensitive bioluminescent enzyme immunoassay (BLEIA) for OXT utilizing the Luciferin/luciferase detection system.

On this assay, the detection limit was 1 pg/assay (B0-3SD). Additionally, in the result of the cross reactivity examination, we conclude that BLEIA was developed high sensitively and specifically measurement for OXT. But it might not be able to measure of OXT in plasma of ASD patients, which is estimated to very low level. Finally, we will propose to the modification of secondary antibody immobilized magnetic particles preparation, assay protocol and labeled antigen or re-selection of anti-OXT antibody, to contribute as clinical laboratory test for psychiatric disorder, ASD.

Biography

Yoshihiro Sano has completed his Ph.D at the age of 28 years from Showa University. His work is development of high sensitive analytical method for peptide hormone etc, now.

AUTHOR INDEX

Abdel Halim	26	Gopal C. Kundu	45	Rong Shao	56
Abdel Halim	94	Hakima Amri	90	Rosa María Viguera	116
Akbar Esmaeili	86	Hitoshi Sohma	88	Shao Shujuan	50
Alan Prem Kumar	43	Irina Smolina	83	Sherifa A. Hamed	44
Alexander Baras	69	Jagat R Kanwar	64	Sherifa A. Hamed	73
Anita Kamra Verma	106	Jan W Eriksson	36	Shohreh Jalaie	103
Anka N. Veleva	101	Jean Gabert	28	Sima T. Tarzami	71
Balakrishnan Aristatile	104	Jean Gabert	82	Stanley P. L. Leong	57
Brisa S. Fernandes	53	Jeremy Warren	102	Sule AKIN	74
Caifu Chen	85	Jeremy Warren	27	Supriya Singh	117
Crispin R. Dass	29	Kalyani Jambunathan	100	Tao Chen	89
Crispin R. Dass	96	Kyu Oh Kim	114	Tatjana Abaffy	48
Da-Yong Lu	77	Lin Guo	115	Valentina Donzella	62
Da-Yong Lu	65	Longo-Mbenza B	42	Vandana Panwar	118
Devindra Sehra	79	Longo-Mbenza B	72	Victor V. Levenson	80
Dhiman Sarkar	97	Manisha Vaish	52	Xi Yang	107
Elkin Galeano	98	Marina A. Guvakova	39	Xiang Zhang	76
Eva M. Molina-Trinidad	112	Mark Gerstein	92	Yanggu Shi	59
Fahad Aziz	35	Michael Holinstat	95	Yasuhiro Nihon-Yanagi	70
Fahad Aziz	78	Mitsuaki Shirahata	84	Yi-Hsien Lin	109
Fei Ye	58	Moonsoo M. Jin	91	Yoshihiro Sano	119
Forka Ac	113	Nan Dai	75	Yung-Kai Huang	34
Francesco Crea	40	Naoko Sueoka-Aragane	49	Yurij Ionov	51
Gargi D Basu	60	Orest Hurko	108	Zahra Mojtahedi	63
Geetika Chakravarty	41	Renaud Seigneuric	61		
Georg F. Weber	38	Robert A. Warner	33		

Previous Conferences

2011



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
Proteomics & Bioinformatics 6-8 June 2011
HICC, Hyderabad, India



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



International Conference & Exhibition on
Pharmaceutical Biotechnology 6-8 June
2011 HICC, Hyderabad, India



International Conference and Exhibition on Virology
5-7 September 2011 Baltimore, USA



2nd World Congress on Bioavailability &
Bioequivalence: Pharmaceutical R & D
Summit 6-8 June 2011 Las Vegas, USA



International Conference on Pharmaceutical
Regulatory Affairs 6-7 September 2011 Baltimore,
USA



International Conference on Pharmaceutics
& Novel Drug Delivery Systems 7-8 June
Las Vegas, USA



2nd World Congress on Biomarkers & Clinical
Research 12-14 September 2011 Baltimore, USA

2008-2010



International Conference
on **Diabetes and
Metabolism** 13-14

December 2010 Santa Clara, USA



International Conference
& Exhibition on
**Bioequivalence
& Bioavailability,**

Pharmaceutical R & D Summit, March
01-03, 2010



2nd Annual World Summit
Antivirals

July 18-20, 2009



International Conference
on **Biomarkers &
Clinical Research** 22-23

November 2010 Santa Clara, USA



**Integrating Glycomics
with other Omics in
Cancer Detection and
Diagnosis** January 19-20,

2010, Stanford University School of
Medicine, USA



1st **CCSB-2009**

February 16-17, 2009



International Conference
and Exhibition on
Analytical and Bioanalytical

**Techniques: Pharmaceutical R & D
Summit**, 01-03 November 2010

Hyderabad, India



3rd World Congress of
Gene-2009 December 1-7,
2009



2nd **PRICPS-4th AOHUPO**

June 22-26, 2008



7th Annual World Congress
of **International Drug
Discovery Science &
Technology** October 22-25



95th **ISCA**

January 5-8, 2008

Upcoming Conferences



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



2nd World Congress on **Biotechnology** 29 Nov-1 Dec 2011 Philadelphia, USA



2nd World Congress on **Diabetes & Metabolism** 6-8 December 2011 Philadelphia, USA



World Congress on **Paediatrics & Gynaecology** 6-8 December 2011 Philadelphia, USA



2nd world Congress on **Analytical and Bioanalytical Techniques** 16-17 December 2011 San Francisco, USA



International Conference on **Metabolomics & Systems Biology** 20-22 February 2012 San Francisco, USA



2nd World Congress on **Pharmaceutics & Novel Drug Delivery Systems** 20-22 February 2012 San Francisco, USA



2nd World Congress on **Clinical Research** 5-7 March 2012 Omaha, USA



International Conference and Exhibition on **Biometrics & Biostatistics** 5-7 March 2012 Omaha, USA



World Congress on **Gastroenterology & Urology** 12-14 March 2012 Omaha, USA



International Conference and Exhibition on **Nanotechnology & Nanomedicine** 12-14 March 2012, Omaha, USA



3rd World Congress on **Bioavailability & Bioequivalence: Pharmaceutical R & D Summit** 26-28 March 2012 Hyderabad, India



International Conference and Exhibition on **Neurology & Therapeutics** 14-16 May 2012 Las Vegas, USA



International Conference and Exhibition on **Biosensors and Bioelectronics** 14-16 May 2012 Las Vegas, USA



2nd World Congress on **Proteomics & Bioinformatics** 2-4 July 2012 Las Vegas, USA



3rd World Congress on **Biomarkers & Clinical Research** 2-4 July 2012 Las Vegas, USA



2nd World Congress on **Virology** 20-22 August 2012 Las Vegas, USA



International Conference on **Addiction Research and Therapy** 20-22 August 2012 Las Vegas, USA



3rd World Congress **Biotechnology** 24-26 September 2012 Hyderabad, India



International Conference and Exhibition on **Food Processing & Technology** 24-26 September 2012 Hyderabad, India



2nd World Congress **Pharmaceutical Regulatory Affairs** 22-24 November 2012 Hyderabad, India

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

3rd World Congress on Biomarkers & Clinical Research

2-4 July 2012 Las Vegas, 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

26 Joseph 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