OMICS Group
Accelerating Scientific Discovery

International Conference on
Clinical Microbiology & Microbial Genomics

November 12-14, 2012 Hilton San Antonio Airport, USA

A systems and genomics approach to *Pseudomonas* derived protein: RahU in host-parasite interactions, pleotropic regulation of biofilm in *Pseudomonsas*, and innate immunity in macrophages

Ashok R. Amin
Virginia Tech and Rheumatrix Consulting, USA

Abstract

Two *P.aeruginosa* strains (non-mucoid and mucoid) were isolated from the same cystic fibrosis patient. Differential proteomics and gene expression arrays showed increase in RahU gene (PA0I122) and protein expression in non mucoid isolate. This gene belonged to the aegerolysin family of proteins of unknown function but binds with high affinity to "inflammatory" oxidized (Ox) phospholipids. Functional genomics analysis showed (a) LysoPC increased (but by PAPC, Ox-PAPC and arachidonic acid inhibited) rahU promoter activity/and protein expression in $rahU^+$. (b) There was an increase in biofilm formation in $rahU^-$ cells as compared to $rahU^+$ cells; and (c) Phospholipids which modulated rahU promoter activity also regulated biofilm formation in Pseudomonas. These results show that phospholipids that can bind to rahU protein-regulates *r*ahU gene and protein expression, which in turn modulates biofilm formation. Recombinant endotoxin free rahU (DeTox-RahU) had no significant effect on cell apoptosis? or cell viability in human cells. Gene expression array of murine macrophage cells (RAW 264.7) stimulated with LPS showed inhibition of 55 common transcripts by DeTox -RahU and an anti-inflammatory drug: Prednisone. One of the common transcripts was iNOS mRNA showing decreased levels of nitric oxide (NO) in the presence of LPS. The IC_{50} of DeTox-RahU (0.6µM) was distinct from the known inhibitors of NO production: prednisone (50µM) and L-NMMA (100µM). DeTox-RahU at physiological concentrations also significantly inhibited chemotactic activity of human monocytes toward CCL2 or chemotactic supernatants from apoptotic T-cells.

These reports show previously unknown pleiotropic and opportunistic properties of *P. aeruginosa* - derived: RahU at the molecular level in modulating both microbial physiology, morphology and host innate immunity using inflammatory phospholipids as common docking and signaling molecules.

Biography

Dr. Amin graduated in Microbiology and completed his NIH sponsored postdoctoral fellowship in Immunology before serving as Associate Professor of Medicine and Director of Rheumatology Research at NYU. He was Head and Professor of Genetics at VCOM. He later functioned as Vice President of Research and Development at Carilion Clinic and at Advaxis Inc. He has published more than 100 papers in genomics, immunology and translational research in areas of complex inflammatory/infectious diseases and cancer in reputed journals and procured 22 patents. Two of the patents were used to develop the FDA-approved drug ORACEA™ for the treatment of Rosacea which is earning royalties for NYU and the inventors. He is the Founder of Rheumatrix Consulting Inc.