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Identification and characterization of RahU: A novel virulent factor induced by *Pseudomonas* during host-bacterial interactions. Regulation of biofilm, PAMPS, inflammation, nitric oxide and chemotaxis

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Differential expression of proteins was performed from two *P.aeruginosa* strains (non-mucoid and mucoid) isolated from the lung of an individual with cystic fibrosis. An orphan protein with characteristic of aegerolysins was identified. This gene (PA0I122) was named as RahU [seizer] due to its pleotropic activity in controlling bacteria genes and eukaryotic immune cells. Functional genomics analysis showed that RahU binds with high affinity to "inflammatory" oxidized (Ox) phospholipids. Furthermore, (a) LysoPC increased (but by PAPC, Ox-PAPC and arachidonic acid inhibited) rahU promoter activity (b) Phospholipids which modulated rahU promoter activity also regulated biofilm formation in *Pseudomonas*. 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 similar to the 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 IC50 of DeTox-RahU (0.6 μM) was distinct from the known inhibitors of NO production: prednisone (50 μM) and L-NMMA (100 μM). DeTox-RahU at physiological concentrations also significantly inhibited chemotactic activity of human monocytes toward CCL2 or chemotactic supernatants from apoptotic T-cells. In summary, RahU is a virulent protein which not only protects the *Pseudomonas* by regulating biofilm formation, but blocks the activity of innate immune response to PAMPS. These reports show previously unknown pleiotropic and opportunistic properties of *P. aeruginosa*.

Biography

Ashok R. Amin graduated in Microbiology and completed postdoctoral fellowship in Immunology at NYU before serving there as associate Professor of Medicine and director of Rheumatology Research. He was head and Professor of Genetics at VCOM and later functioned as vice president of research at Carilion Clinic and at Advaxis Inc. He has published papers in genomics, immunology and translational research in areas of complex inflammatory/infectious diseases and cancer and procured patents leading to the royalty earning FDA-approved drug: ORACEA for the treatment of Rosacea. He is the founder of Rheumatrix Inc.

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