NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

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Hosted by Assoc. Prof Liou Yih-Cherng

Combating pathogenic bacteria by blocking their adhesins

By **Peter L. Davies**

Department of Biomedical and Molecular Sciences, Queen's University, Canada

Bacteria use a variety of adhesion proteins (adhesins) for attachment to their hosts. One type common in Gram-negative bacteria is the RTX adhesin. This long, single polypeptide chain is exported C-terminal end first through the Type I Secretion System, but is retained in the outer membrane by its N-terminal domain, which is too large to pass through the secretion pore. Bioinformatic searches show this RTX adhesin type is present in both environmental bacteria and animal pathogens. Each RTX adhesin has one or more different ligand-binding domains at their distal end, many of which have yet to be characterized. We hypothesize that these domains determine the surfaces and hosts (niche) to which the bacteria will bind. Moreover, we suggest that ligand competitors and antibodies can potentially block adhesion of the bacterium before it can become established as a biofilm or an infection. *Vibrio cholerae*, the causative agent of cholera, has a 0.23-MDa RTX adhesin called FrhA in which we have located two distal ligand-binding domains. One is a sugar-binding domain with affinity for the terminal fucose moieties of cell surface glycans that include blood group antigens. This domain of the FrhA adhesin causes both agglutination and hemolysis of human red blood cells. *V. cholerae* that have FrhA deleted lack the ability to bind and agglutinate red blood cells. The same result can be achieved with wild-type *V. cholerae* by adding fucose to block the sugar-binding domain. The other ligand-binding domain in FrhA has affinity for the C-terminal tripeptide of various proteins. This also contributes to hemagglutination. However, it does not bind directly to red blood cells or to the bacteria but to the biofilm that *V. cholerae* produces when binding its target surfaces. Here the optimal peptide antagonist, Tyr-Thr-Asp, can be used in combination with fucose to prevent *V. cholerae* from infecting its host. These adhesin-blocking strategies may help fight bacterial infections as antibiotic resistance becomes widespread.

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About the Speaker

Peter L. Davies is a Professor and Canada Research Chair in Protein Engineering at the Queen's University. His main research concerns Antifreeze protein, Ice binding, Biochemistry, Crystallography and Biophysics. His biological study spans a wide range of topics, including Threonine, Hydrogen bond and Protein folding. Peter L. Davies is the 2021 recipient of the Canadian Science Publishing Senior Investigator Award. A lifetime achievement awarded annually by the Canadian Society for Molecular Biosciences (CSMB), this award recognizes a Canadian scientist with a record of outstanding research achievement in the fields of biochemistry, molecular or cellular biology.