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The 'rules of engagement' for the *nan*Repressor- the regulator for sialic acid catabolism in pathogens

Christopher Horne¹ and Renwick Dobson^{1,2}

¹University of Canterbury, New Zealand

²University of Melbourne, Australia

Eukaryotic cell surfaces are decorated with complex glycoconjugates such as glycoproteins found at the terminal non-reducing positions of these glycoconjugates are negatively charged sialic acids, which mediate a diverse array of cellular interactions, recognition and adhesion processes (Schauer, 2000). Sialic acids comprise a large family of over 50 distinct nine-carbon sugars; the most common member is known as N-acetylneuraminic acid (Almagro-Moreno & Boyd, 2009). In human mucous-rich environments, such as the respiratory or gastrointestinal tracts, sialic acid-coated glycoconjugates are highly abundant (Vimr 2013). *Escherichia coli*, a gram-negative human mucosal pathogen and a common inhabitant of the upper respiratory tract, scavenge and utilizes host-derived sialic acids as an alternative nutrient source using a suite of enzymes. This suite includes a lyase, kinase, epimerase, deacetylase, and a deaminase (Vimr et al., 2000; 2004). The utilization of sialic acid is transcriptionally regulated in bacteria by the *nan*Repressor, however detailed structural and mechanistic evidence explaining this process is lacking. The *nan*Repressor from *E. coli* has been shown to regulate the *nan*CMS and *yjh*BC operons, in addition to the degradation pathway, by binding to two/ three tandem base pair repeats of the sequence GGTATA (Kalivoda et al. 2013). While the biological role of the *nan*CMS operon is known, the function of the *yjh*BC operon has yet to be determined. To characterize the interaction between the *nan*Repressor and DNA we have applied analytical ultracentrifugation, providing stoichiometric information and binding constants of the complex. Small-angle X-ray scattering was employed to determine the solution structure of the *nan*Repressor, with and without DNA. Excitingly, I have solved the first crystal structure of Yjhc and have recently collected 2.1 Å data for the *nan*Repressor. Our overarching goal is to develop the first detailed 'picture' of how the *nan*Repressor regulates gene expression and elucidate the biological role of the *yjh*BC operon.

Biography

Christopher Horne is in his third year of his PhD research under Associate Professor Renwick Dobson at the University of Canterbury, New Zealand. He is working in the field of biochemistry, his PhD project is aimed at unravelling the molecular details of sialic acid regulation in bacterial pathogens. The primary focus is to elucidate the first detailed 'picture' of the interaction between the transcriptional regulator and DNA. To address this question, he has developed expertise in a combination of structural and biophysical techniques, including analytical ultracentrifugation, electrophoretic mobility shift assays, X-ray crystallography, and small angle X-ray scattering. Thanks to a prestigious University of Canterbury Doctoral scholarship, he was able to work in the labs of University of Canterbury's Biomolecular Interaction Centre (BIC) which fosters partnerships between academic research and industry.

christopher.horne@pg.canterbury.ac.nz

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