

Poster Presentation

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Functional analysis of the zinc efflux protein CzcD

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The bacteria *Streptococcus pneumoniae* is the primary cause of the disease pneumonia making it the world's foremost bacterial pathogen. Every years *S. pneumoniae* causes more deaths than AIDS, malaria and tuberculosis combined, accounting for more than one million deaths annually, primarily in children under the age of 5.

Zinc is essential for the survival of *S. pneumoniae*, however, this requirement is offset by the potential of zinc for toxicity when in excess. During infection the innate immune system utilises zinc as an antimicrobial agent. The integral membrane protein CzcD facilitates zinc efflux in *S. pneumoniae* allowing for survival during periods of zinc stress. Previous work has established that *S. pneumoniae* CzcD knock-out strains resulted in a phenotype in which intracellular zinc accumulates to lethal concentrations, therefore, CzcD is implicated to play a crucial role in maintaining correct levels of zinc to prevent toxic accumulation.

To understand how zinc homeostasis is maintained in *S. pneumoniae* my work aims to structurally and functionally characterise the CzcD protein. This includes the determination of the structure of CzcD via X-ray crystallography to elucidate the molecular mechanisms by which zinc homeostasis occurs and the characterisation of the affinity of CzcD for zinc (and other transition metals) by isothermal titration calorimetry (ITC). Fulfilment of these aims would improve the understanding of how the vital process of metal homeostasis is maintained in *S. pneumoniae*.

This poster will outline the progress made towards the characterisation of CzcD by X-ray crystallography, including the development of a protocol for the overexpression, purification and crystallisation of CzcD as well as findings on the characterisation of the affinity and specificity of CzcD for various metals via ITC.

[1] O'Brien. K. et al (2009) *The Lancet*. 374, 893-902.

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