Contribution ID : **285** Type : **Oral**

UNRAVELLING THE STRUCTURAL AND MECHANISTIC DIVERSITY OF BACTERIAL AUTOTRANSPORTER VIRULENCE FACTORS

Friday, 25 November 2016 14:00 (15)

Autotransporter proteins are the largest group of outer membrane and secreted virulence factors from important bacterial pathogens such as Salmonella enterica, Shigella flexneri, Neisseria meningitidis and pathogenic E. coli strains. They are important contributors to bacterial pathogenesis, functioning as toxins, adhesins and facilitators of biofilm formation. Their importance to human health has generated great interest. However, we are still struggling to understand their mechanisms of action. There are currently only 12 structures of autotransporters in the protein data bank.

Our research centres on the AIDA-I-type autotransporters which are the largest family of autotransporters. We were the first to determine the structure and mechanism of action for one of these family members Antigen 43a from uropathogenic E. coli (UPEC)1. Our work showed how Antigen 43 causes aggregation and biofilm formation, which are important for UPEC colonisation and persistence within the urinary tract. Since this time we have been using the MX beamlines at the Australian Synchrotron to determine the crystal structures of two new autotransporters. Our findings have revealed a surprising structural diversity amongst the autotransporters, which has allowed us to elucidate their distinct mechanisms of action and roles in bacterial pathogenesis. Interestingly, the structures have also revealed how bacteria use post-translational modifications to change the virulence functions of their proteins.

This research is also helping us to understand how we can target these autotransporters for therapeutic intervention. To this end we are again using X-ray crystallography to help aid us in the development of specific inhibitors of key autotransporters.

Keywords or phrases (comma separated)

Are you a student?

No

Do you wish to take part in</br>the Student Poster Slam?

No

Are you an ECR? (<5 yrs</br>since PhD/Masters)

No

What is your gender?

Male

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Session Classification : Concurrent Session 4: Structural Biology II - Sponosred by DECTRIS

Track Classification : Structural Biology