The Centre for Blood Research Seminar Series

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LSC 3 - Life Sciences Centre
2350 Health Sciences Mall
12-1pm

"Structure and proteolytic processing of a critical secreted Mycobacterium tuberculosis virulence factor and insights into its export mechanism"

Mycobacterium tuberculosis use a special secretion system to export virulence proteins across its unique lipid-rich cell wall, acting to permeabilize the macrophage phagosomal membrane within the human host. This helps the bacterium escape the compartment and permits subsequent cell-to-cell spread. Important to ESX-1 function are a set of specialized secreted proteins that somehow mediate this process. Here, I describe the X-ray and EM structures of one of these secreted proteins, EspB, showing it oligomerizes with apparent heptameric symmetry. This generates a barrel-shaped structure with a central pore that I suggest contributes to EspB's transport and/or macrophage killing functions. We also describe how EspB is post-translationally processed by a protease called MycP1 during the export process - another even that is critical to infection. Finally, we gain new insight into ATPase-mediated export of EspB by recognition of a conserved signal sequence. Together, the data advance our understanding of molecular details related the human/TB interaction.