Contribution ID: 62

Structural insight into the synergistic activities of NADase and SLO in the pathogenesis of Group A Streptococcus infection

Group A Streptococcus (GAS) is a strict human pathogen renowned for its highly aggressive destruction of host tissues that can lead to life-threatening diseases including streptococcal toxic shock syndrome and necrotizing fasciitis. GAS possesses a unique pathogenic trait to enhance its virulence by utilizing the synergism of two secreted toxins, Streptolysin O (SLO) and NAD+-glycohydrolase (NADase). How NADase and SLO assemble into a complex to synergistically promote intracellular survival and resistance to innate immunity within human cells is a long-standing question. By combining X-ray crystallography and small-angle X-ray scattering (SAXS), we decipher the first structure of NADase/SLO complex and reveal the dynamic nature of the complex in solution. The functionally-relevant conformations of the NADase/SLO complex revealed by SAXS suggest the dynamic interplay between SLO and NADase is fundamental to the functioning of the complex. Moreover, the introduction of a complex-disruptive mutation in GAS genome results in decreased resistance to phagocytic killing in vitro. Furthermore, mice infected with GAS mutant harboring the disrup-tive mutation displayed reduced skin lesions. This work delivers the structure-functional relationship of the NADase/SLO complex and pinpoints the key interacting residues that are central to the coordinated actions of NADase and SLO in the pathogenesis of GAS infection.

Primary author: Prof. WANG, Shu-Ying (Department of Microbiology and Immunology, College of Medicine, National Cheng Kung University, Tainan, Taiwan)

Co-authors: Mrs TSAI, Wei-Jiunn (Institute of Basic Medical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan); Dr HAMMEL, Michal (Molecular Biophysics and Integrated Bioimaging, Lawrence Berkeley National Laboratory, Berkeley, CA, USA); Dr JENG, U-Ser (National Synchrotron Radiation Research Center, Hsinchu Science Park, Hsinchu, Taiwan)

Presenter: Prof. WANG, Shu-Ying (Department of Microbiology and Immunology, College of Medicine, National Cheng Kung University, Tainan, Taiwan)