NUS National University of Singapore

Department of Biological Sciences
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Bacterial TIR proteins and evasion of the immune response

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The innate immune response acts as the first line of defence against invading pathogens. Key components are the Toll-like receptors (TLRs), integral membrane proteins. The TLRs recognize specific molecular patterns and initiate a signaling pathway, culminating in the production of pro-inflammatory cytokines and an immune response. Central to the generation and propagation of the TLR signaling pathway are heterotypic interactions between Toll-like-Interleukin-1 receptor (TIR) domains found in both the TLRs and a range of adaptor proteins. TIR domains have been identified in a number of pathogenic bacteria. These have been shown to have roles in virulence and function in a number of ways to inhibit the TLR signaling pathway. Research in my laboratory has focused on the TIR protein from the highly pathogenic, plague-causing bacterium, Yersinia pestis (YpTdp). Plague was responsible for the widespread pandemics which wiped out a large proportion of the Middle Eastern and European populations in the Middle Ages. Although Y. pestis infections are now rare and usually treatable, plague still represents a significant bioterrorism threat. We have expressed the TIR domain (YpTIR, S130-A285) of the Y. pestis TIR protein and investigated both its interaction profile as well as its biophysical state in solution. Mammalian cell based assays revealed that expression of the full length YpTdp, downregulated IL-1β- and LPS- dependent signalling to NFκB although the YpTIR had no effect. I will further discuss the work we have down on this protein and highlight how this has led to studies on other negative regulators of the innate immune system.

Artwork by Ann Nee, DBS, NUS