ABSTRACT

Bacteria while infecting a host brings a group of arsenals with it in terms of antigens/ligands to pathogenize the host. Host immune cells on the other hand induce innate immune (pro- inflammatory) responses and adaptive immune responses against them to win the battle and clear out infections. In the thesis work, we have studied two of these bacterial ligands namely, Vibrio parahaemolyticus OmpU (VpOmpU) and SteA of Salmonella enterica Typhimurium for their role in modulation of host innate immune responses. V. parahaemolyticus is a non-invasive, marine bacterium, which causes severe gastroenteritis in humans upon consumption of raw or undercooked sea food. The role of VpOmpU in pathogenesis of V. parahaemolyticus was not explored till date. In our attempt to characterize VpOmpU for modulation of host's innate immune responses, we have observed that it induces pro-inflammatory responses in macrophages and monocytes via TLR2-MyD88-IRAK-1-MAPkinases-AP-1 and NF- κB pathway. TLR2 forms hetero-dimer either with TLR1 or TLR6 to recognize different ligands. We have shown that VpOmpU is recognized by both TLR1/2 and TLR2/6 hetero-dimer in macrophages. This is the first report of a natural ligand recognized by both TLR1/2 and TLR2/6 hetero-dimers. Salmonella enterica Typhimurium is an invasive Gram negative bacterium which has been known to cause gastroenteritis in humans known as salmonellosis and typhoid-like disease in mice. It is equipped with a specialized machinery called the type-3 secretion system through which it translocate various effector proteins directly into the host cytoplasm. These effectors then modulate various host-responses and help the bacteria to survive in the host. We are showing that, SteA, an effector protein of S. Typhimurium suppresses host-immune responses by interfering with NF-κB activation. We have further elucidated the mechanism that SteA employs to suppress this pathway. So far, the two enteric bacterial ligands that we have studied in the thesis work have differential effect on host's immune responses, such as, VpOmpU activates, whereas, SteA suppresses host's immune system.These observations suggest the complexity inflicted by the antigens/ligands in the bacterial pathogenesis and, this underscores the need to study in great detail, the role of bacterial ligands in host modulation, to be able to design effective therapy or vaccine.