Title:	Differential Recognition of Vibrio parahaemolyticus OmpU by Toll-Like Receptors in Monocytes and Macrophages for the Induction of Proinflammatory Responses
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Keywords:	OmpU TLR Vibrio parahaemolyticus Innate immunity Proinflammatory responses
Issue Date:	2019
Publisher:	American Society for Microbiology
Citation:	Infection and Immunity, 87(5).
Abstract:	Vibrio parahaemolyticus is a human pathogen, and it is a major cause of severe gastroenteritis in coastal areas. OmpU is one of the major outer membrane porins of V. parahaemolyticus. Host-immunomodulatory effects of V. parahaemolyticus OmpU (VpOmpU) have not been elucidated yet. In this study, in an effort towards characterizing the effect of VpOmpU on innate immune responses of the host, we observed that VpOmpU is recognized by the Toll-like receptor 1/2 (TLR1/2) heterodimer in THP-1 monocytes but by both TLR1/2 and TLR2/6 heterodimers in RAW 264.7 macrophages. To the best of our knowledge, this is the first report of a natural pathogen-associated molecular pattern (PAMP) recognized by both TLR1/2 and TLR2/6 heterodimers; so far, mainly the synthetic ligand Pam2CSK4 has been known to be recognized by both the TLR1/2 and TLR2/6 heterodimers. We also have shown that VpOmpU can activate monocytes and macrophages, leading to the generation of proinflammatory responses as indicated by tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and NO production in macrophages and TNF-α and IL-6 production in monocytes. VpOmpU-mediated proinflammatory responses involve MyD88-IRAK-1 leading to the activation of mitogen-activated protein (MAP) kinases (p38 and Jun N-terminal protein kinase [JNK]) and transcription factors NF-κB and AP-1. Further, we have shown that for the activation of macrophages leading to the proinflammatory responses, the TLR2/6 heterodimer is preferred over the TLR1/2 heterodimer. We have also shown that MAP kinase activation is TLR2 mediated.
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