Title:	Salmonella Typhimurium Adhesin OmpV Activates Host Immunity To Confer Protection against Systemic and Gastrointestinal Infection in Mice
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Abstract:	Salmonella enterica Typhimurium is a rod-shaped Gram-negative bacterium that mostly enters the human body through contaminated food. It causes a gastrointestinal disorder called salmonellosis in humans and typhoid-like systemic disease in mice. OmpV, an outer membrane protein of S. Typhimurium, helps in adhesion and invasion of bacteria to intestinal epithelial cells and thus plays a vital role in the pathogenesis of S. Typhimurium. In this study, we have shown that intraperitoneal immunization with OmpV is able to induce high IgG production and protection against systemic disease. Further, oral immunization with OmpV-incorporated proteoliposome (OmpV-proteoliposome [PL]) induces production of high IgA antibody levels and protection against gastrointestinal infection. Furthermore, we have shown that OmpV induces Th1 bias in systemic immunization with purified OmpV, but both Th1 and Th2 polarization in oral immunization with OmpV-proteoliposome (PL). Additionally, we have shown that OmpV activates innate immune cells, such as monocytes, macrophages, and intestinal epithelial cells, in a Toll-like receptor 2 (TLR2)-dependent manner. Interestingly, OmpV is recognized by the TLR1/2 heterodimer in monocytes, but by both TLR1/2 and TLR2/6 heterodimers in macrophages and intestinal epithelial cells. Further, downstream signaling involves MyD88, interleukin-1 receptor-associated kinase (IRAK)-1, mitogen-activated protein kinase (MAPK) (both p38 and Jun N-terminal protein kinase (JNK)), and transcription factors NF-κB and AP-1. Due to its ability to efficiently activate both the innate and adaptive immune systems and protective efficacy, OmpV can be a potential vaccine candidate against S. Typhimurium infection. Further, the fact that OmpV can be recognized by both TLR1/2 and TLR2/6 heterodimers increases its potential to act as good adjuvant in other vaccine formulations.
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