Title:	Regulatory role of MAPK p38 in VvOmpU- mediated inflammatory responses
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Abstract:	The innate immune response is orchestrated by intricate signalling pathways, particularly in macrophages, crucial players in the immune defence against pathogens. This study delves into the differential response of Vibrio vulnificus outer membrane protein OmpU (VvOmpU), a known immunomodulator, in RAW264.7 macrophages and bone marrow-derived macrophages (BMDMs). Through a comprehensive analysis integrating flow cytometry, ELISA assays, and gene expression profiling, we elucidated the involvement of MAPK-p38 signalling in the pro-inflammatory responses induced by VvOmpU. While MAPK JNK was not found to contribute significantly to reactive oxygen species (ROS) generation or IL-6 production, p38 is involved in both IL-6 and TNF-α in RAW264.7 macrophages. Interestingly, it was observed in the laboratory that, in VvOmpU induces an anti-inflammatory response marked by IL-10 production alongside pro-inflammatory cytokines, and notably in BMDM but not in RAW 264.7 macrphages p38 facilitates this IL-10 induction. Previous investigation in the literature implicates the role of dual-specificity phosphatase 1 (DUSP1), as a negative regulator of p38 in macrophages (Zhao et al., 2005). Towards understanding whether DUSP1 is involved in this dual role of p38 in cell line vs primary cells we have made shRNA for knockdown experiments targeting DUSP1 in RAW264.7 cells. Further, towards understanding the pro- and anti-inflammatory role of VvOmpUour findings highlight a potential link between macrophage polarization states, with BMDMs favouring an M2 phenotype associated with anti-inflammatory properties following VvOmpU treatment. Conversely, RAW264.7 macrophages exhibit a distinct macrophage polarization, suggesting a differential polarization induced by VvOmpU. This study underscores the intricate interplay between MAPK signalling, macrophage polarization, and immune modulation by VvOmpU, providing insights into the complex host- pathogen interactions in the context of Vibrio vulnificus.
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