ABSTRACT

OmpU is an outer membrane protein of Vibrio cholerae. It is porin in nature and helps the bacterium for well survival in the human gut during pathogenesis. Towards characterising the host-immunomodulatory responses, we have previously shown that OmpU has the ability to activate innate immune cells, such as, monocytes and macrophages for the production of pro- inflammatory cytokines such as, TNF alpha and IL-6. Monocytes are the precursors of macrophages. For the induction of pro-inflammatory cytokine production OmpU hetero- dimerizes TLR1/2, recruits MyD88 to the receptor complex and activates NF-κB transcription factor in both the cell types. In the thesis work, we are showing that in both monocytes and macrophages, OmpU-induced pro-inflammatory responses also involve activation of MAPKinases (p38 and JNK) and AP-1 transcription factor. Interestingly, we observed that in OmpU-treated macrophages, TLR2 activation leads to only p38 activation but not JNK. JNK activation in OmpU-treated macrophages happens through another pathway involving CD36- dependent ROS generation by NADPH oxidase complex. For the first time, we are showing that a gram-negative bacterial protein can activate scavenger receptor CD36 as pattern recognition receptor. Additionally, we found that in OmpU-treated monocytes both JNK and P38 activation is linked to the TLR2 activation only. Therefore, the ability of macrophages to employ multiple receptors such as, TLR2 and CD36 to recognize a single ligand, in this case OmpU, probably explains the very basic nature of macrophages being more pro-inflammatory than monocytes.