Abstract

Plasmacytoid dendritic cells (pDC) represent innate immune cells capable to detect viruses in their endosomal environment via Toll-like receptors (TLRs). Viral nuclear acid recognition leads to the massive production of type I interferon (IFN I) and induction of the antiviral state in uninfected cells. Crosslinking of the surface regulatory receptors, such as BDCA-2, with monoclonal antibodies or with some viruses leads to the activation of MEK1/2-ERK signaling pathway and inhibition of IFN I production in pDC. In this study, the role of MEK1/2 kinase has been highlighted. Its inhibition reversed the inhibitory effect of BDCA-2 crosslinking and its direct activation with PMA led to the inhibition of IFN-α production. Yet an unclear role of pDC in sensing of BK polyomavirus virus (BKV) responsible for kidney transplant rejection was investigated as a major topic of this thesis. Experiments with the pDC cell line Gen2.2 and HRPTEC primary cell line showed that pDCs were not able to detect BKV particles, however, exposure of activated Gen2.2 cells to BKV inoculum dramatically upregulated production of IFN-α. Most importantly, coculture of Gen2.2 cells with BKV-infected HRPTEC cells resulted in IFN-α and TNF-α production, which was prevented by Bafilomycin. These results suggest that BKV-infected HRPTEC cells are detected by cell-cell contact with Gen2.2 cells resulting in TLR7/9-mediated IFN-I and proinflammatory cytokine production.

Key words: plasmacytoid dendritic cells, Toll-like receptors, BK polyomavirus, IFN-α, TNF-α, innate immunity, cell-cell contact