P045 Involvement of TRAF2, 3 and 6 in Herpes Simplex Virus (HSV) activated signal transduction and cytokine expression in macrophages

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Macrophages play important roles in the innate immune response against infections, including the initial recognition of pathogens by specific pattern recognition receptors (PRR), which recognize pathogen-associated molecular patterns (PAMP)s. PAMP dependent PRR activation initiates specific intracellular signalling pathways, which activate transcription factors and regulate gene expression leading to early host defence. To mount an appropriate immune response to an infection, intimate regulation of these events is needed. The TRAF-family of proteins have been shown to contribute to diversification of TLR-signalling as well as being involved in RIG-I/MDA-5 signalling through interactions of TRAF 2, 3 and 6 with the common adaptor IPS-1/MAVS/VISA/Cardif. The aim of the present study is to characterize the roles of TRAF2, 3 and 6 in HSV-activated signal transduction and expression of cytokines (IL-6, type I IFN, TNF-α, and RANTES) in a murine macrophage cell line (RAW264.7). The results obtained show that TRAF6 is required for induction of all cytokines, TRAF3 participates in virus-induced expression of IL-6, type I IFN, and TNF-α, while TRAF2 is involved only in production of IL-6 and TNF-α. We are currently evaluating the role of the 3 TRAF family members in HSV-activated signalling through the NF-κB, MAPK, and IRF-3 pathways, and will present the data at the meeting.