

**P069** Investigation of SIGIRR function in human dendritic cells  
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SIGIRR (single immunoglobulin IL-1 related receptor) is a member of the TIR domain containing receptor family, which also includes TLRs. In mouse, SIGIRR functions as an inhibitor of IL-1 and TLR signalling and expression of SIGIRR is cell type specific, being expressed on murine dendritic cells (DCs) but not macrophages. Since TLR signalling induces maturation of DCs we hypothesised that SIGIRR is involved in the regulation of DC maturation and set out to test this hypothesis in human monocyte derived DCs.

The expression pattern of SIGIRR was examined in human monocytes and monocyte derived DCs using RT-PCR, qPCR and FACS analysis. These showed that SIGIRR is expressed on human monocytes and monocyte derived DCs as observed in mouse. To examine SIGIRR function, an adenovirus encoding human wild type SIGIRR was used for over-expression studies and its effect on TLR signalling was investigated. Over-expression of wild type SIGIRR inhibited IL-1 as well as TLR2, -3, -4, -5 and TLR7/8 signalling in DCs. Furthermore, adenovirus-expressed SIGIRR co-localises with MyD88 through TIR domain interaction in human myeloid cells.

Thus, the inhibitory role of SIGIRR in TLR signalling was demonstrated in a primary human cell system for the first time.