

P063 CD200-CD200R, novel inhibitory regulators
of TLR function

**Subhankar Mukhopadhyay, Dawn ME Bowdish,
Neil Barclay and Siamon Gordon**

*Sir William Dunn School of Pathology, South Parks Road,
OX1 3RE, Oxford, UK*

We compared innate and classical cytokine activation of elicited M ϕ by using *Neisseria meningitidis* (NM)-a gram-negative bacterium and/or IFN- γ , respectively, to identify specific markers for innate activation. Innate activation was further defined by the use of SR-A^{-/-} and TLR-4^{-/-} M ϕ , since SR-A and TLR-4 independently recognise selected *Neisserial* surface proteins and LPS and are responsible for NM uptake and secretion of cytokines, respectively. Similarly, IFN- γ ^{-/-} and IFN- γ R^{-/-} M ϕ defined classical cytokine activation. Analysis showed that the inhibitory ligand receptor molecules CD200 and CD200R of immunoglobulin superfamily are respectively induced and down modulated by NM. Further studies indicated that NM mediated differential regulation of CD200 and CD200R is independent of SR-A, but does depend on LPS, TLR-4, the MyD88 signalling pathway and the NF- κ B family member c-Rel. Similar to NM, other selective TLR agonists also differentially regulated CD200 and CD200R. In response to NM/other purified TLR agonists CD200^{-/-} M ϕ induced significantly high levels of proinflammatory cytokines both *ex vivo* and *in vivo*, as well as increased nuclear translocation of NF- κ B and enhanced phosphorylation of p38 MAPK. Our results suggest that the inhibitory CD200-CD200R pair is differentially regulated during TLR mediated inflammation and in turn negatively regulates TLR signalling to limit inflammation.