

P004 Phagocytic receptor (Fc γ R) mediated NF κ B activation – a proinflammatory response suppressed by *Leishmania* amastigotes.

Claire J. Escaron, Rachel Pullan, Charlotte Odendall and Emmanuelle Caron

Centre for Molecular Microbiology and Infection, Division of Cell and Molecular Biology, Imperial College London, Flowers Building, Armstrong Road, London, SW7 2AZ

Phagocytosis involves particle recognition, receptor ligation, cytoskeletal rearrangement and particle internalisation. Binding of phagocytic ligands also initiates, e.g. through NF κ B activation, transcription of genes that contribute to the ensuing immune response. Two main mechanisms of phagocytosis have been defined in mammalian macrophages, with distinct early signalling and cytokines produced. They are typified respectively by Fc γ Receptor (Fc γ R) and Complement Receptor 3 (CR3) that internalise IgG- and C3bi-opsonised particles. These are the main opsonin receptors for phagocytosis involved during innate (CR3) and adaptive (Fc γ R) immunity. We show that ligation of Fc γ R is sufficient to induce NF κ B activation in mouse macrophages. When J774.A1 cells were challenged with IgG-opsonised red blood cells, Fc γ R ligation mediated NF κ B activation as seen by p65 nuclear translocation and I κ B degradation. Interestingly, pre-treatment of macrophages with Cytochalasin D did not block phagocytic receptor induced NF κ B activation, suggesting that remodelling of actin cytoskeleton and transcriptional activation are two independent Fc γ R-induced responses. *Leishmania* parasites are known to interfere with T Helper 1 cell response in infected mammals. We show here that IgG-opsonised amastigotes do not activate NF κ B, a strong indication that they inhibit Fc γ R signalling. By elucidating activation of NF κ B downstream of phagocytic receptor ligation we may reveal targets potentially exploited by pathogens that colonise macrophages.