OC15 - **Modulation of macrophage polarisation by novel monosaccharide-based Toll-like receptor 4 antagonists: implications in treatment of CVD**

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Macrophages plasticity plays an important role in homeostasis and diseases. Macrophages can change their phenotype (M1- proinflammatory and M2- anti-inflammatory) in response to environmental factors. Toll like receptor 4 (TLR4) has been shown to be implicated in M1 polarisation and development of cardiovascular diseases (CVD), suggesting that the modulation of TLR4 signalling can reflect on M1/M2 balance which will be beneficial for treatment of CVD. The main goal of this study was to determine the potential of novel synthetic glycolipids (FP7 and FP12) active as a TLR4 antagonists, to modulate M1 polarisation in human THP-1 and PBCM derived macrophages. Bacterial LPS and two forms of oxidised LDL were utilised as triggers of M1 polarisation in macrophages. Results demonstrated that both FP7 and FP12 inhibited the activation of MyD88-dependent (p38 MAPK and NF-kB) and MyD88-independent (STAT1 and IRF3) second messengers which was associated with downregulation of the production of M1-linked proinflammatory molecules such as IL1-beta, IL6, TNF-alpha, IL8 or INF-beta. Furthermore, FP7 and FP12 decreased the expression of M1-linked CD80/CD86 receptors and iNOS-induced nitric oxide release in M1 macrophages. Finally, both TLR4 antagonists affected M1/M2 balance by increasing the expression of M2-associated proteins such as: CD206, Arginase-1 and SOCS1. These results demonstrate the ability of FP7 and FP12 to negatively regulate M1/M2 macrophage polarisation balance, suggesting their potential therapeutic use for pharmacological intervention of CVD.