Serum Amyloid A is a candidate mediator for altered macrophage polarisation in cigarette smoke-related disease

E.X. Lim, D.A. Anthony, H.J. Seow, G.P. Anderson and S. Bozinovski, Department of Pharmacology University of Melbourne, Parkville, VIC 3010, Australia. (Introduced by Ross Vlahos)

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a debilitating inflammatory lung disease caused by cigarette smoking and worsened by frequent respiratory infections. Activated macrophages and neutrophils accumulate in the airways, cause extensive host tissue damage and fail to clear infection and cellular debris. This suggests that there is a defect in pro-resolution pathways that normally clear inflammation. Polarization of recruited monocytes into M2 repair-like macrophages is critical to the resolution of inflammation, however very little is known about this process in COPD. Our laboratory has recently identified a protein termed Serum Amyloid A (SAA) that is abundant in COPD lungs. We hypothesize that SAA promotes a protective M2 macrophage phenotype that contributes to resolution of inflammation, which is impaired by cigarette smoke exposure.

Aims: To investigate the effect of cigarette smoke extract (CSE) exposure on macrophage polarization and how SAA affects macrophage polarization *in vitro*.

Methods: The human THP-1 monocytic cell line was differentiated into macrophages *in vitro* with GM-CSF and M-CSF in the absence and presence of increasing SAA concentrations (0, 0.1, 1 μg/mL) for 6 days. Differentiation was performed in the presence of CSE generated through bubbling of cigarette smoke in the differentiation media. At the completion of differentiation, Q-PCR was performed and macrophage phagocytosis was measured using FITC-labeled beads followed by FACS analysis.

Results: SAA mRNA levels were increased upon CSE exposure. M2 related scavenger genes (CD163, CD36, MER Tyrosine Kinase, Stabilin-1) and negative regulators (Interleukin-10, FcγRIIB) expressions were increased in both SAA-differentiated macrophages and macrophages exposed to CSE. Macrophage phagocytic function also significantly increased in both populations.

Discussion: CSE induces SAA expression, identifying it as a candidate for M2 polarization. Furthermore, *in vitro* differentiation with SAA alone drives an M2 polarization pattern that is similar to what is observed in COPD macrophages.