Generating iPSC derived alveolar macrophages as a novel model for respiratory research

Alveolar macrophages play a key role in respiratory disease and inflammation, thus the study of these cells is essential for the development of novel therapies. Slow progress in this field is in part due to the limitations of models available including animal models and primary cells. Novel models are required to aid the study of diseases such as Chronic Obstructive Pulmonary Disease and Cystic fibrosis. iPSC-derived cells provide a reproducible and physiologically relevant alternative and allow for large scale production necessary for drug discovery.

This study aimed to produce iPSC-derived alveolar macrophages (iAM) using an established protocol for the production of iPSC derived macrophage progenitors. Briefly, progenitor cells were matured in conditioned media obtained from normal human lung fibroblasts (NHLF), BEAS-2-B or small airway epithelial cells (SAEC). Macrophage phenotype is plastic and known to be dependent on environmental signals, thus the use of conditioned media from lung cells is hypothesised to induce differentiation to iAM. These cells were characterised and compared to iPSC-derived microglia (iMGL) which are extensively characterised in the literature and routinely used in our company. This was done by flow cytometry, ELISA, ICC, phagocytosis and chemotaxis assays.

iAM showed significantly lower expression of CD33 compared to iMGL (20±5% reduction) while other markers, CD14, CD16, CD11b and MARCO remained the same (n=3). In addition, iAM showed greater uptake of pHrodo-*S. aureus* (5-30% more), with the biggest difference observed in cells cultured in NHLF conditioned media.

Here, we show the initial characterisation of iAM as a novel model for respiratory research. iAMs show different functional characteristics to iMGL and could be an invaluable tool for drug discovery in this field.