

Optimisation of phorbol myristate acetate (PMA) mediated differentiation of U937 human lung monocytes to alveolar like macrophages

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SUMMARY

Respiratory disease remains an increasing global health burden, however few new medicines for asthma and chronic obstructive pulmonary disease (COPD) have reached the market in the past decade. Whilst there has been a considerable amount of research investment into the development of new inhaled medicines, many fail due to safety or efficacy. One of the main reasons for this is the observation of a foamy alveolar macrophage responses in rats in pre-clinical studies which limits the dose of these compounds in subsequent studies despite not knowing if these observations are toxic in humans. The ultimate aim of this work is to develop an accurate, immune responsive, human alveolar macrophage based co-culture model for the assessment of inhaled medicines. Accordingly, U937, a human lung-derived monocyte cell line, was differentiated to a macrophage phenotype in the presence of phorbol myristate acetate (PMA). The activation, differentiation and functionality characteristics of native and treated cells were assessed using a combination of cell viability and morphological analyses, microarray technology, flow cytometry and phagocytic ability. The concentration of PMA was found to have a more significant impact than incubation time on the expression of macrophage cell surface markers, morphology and viability.
