## A79 ROLE OF ET-1 AND GM-CSF ON THE DIFFERENTIATION POTENTIAL OF MONOCYTES IN SYSTEMIC SCLEROSIS

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**Background and objectives** Systemic sclerosis (SSc) is a rare but potentially life threatening connective tissue disease characterised by vasculopathy, inflammation, the production of autoantibodies and excessive fibrosis of skin and internal organs. Fibrosis is defined by an excess production of extracellular matrix (ECM) molecules predominantly of type I collagen. The main producers of collagen are myofibroblasts. These cells are characterised by the expression of α-SMA.
Monocytes are one of the first cells that infiltrate inflamed or damaged tissue and they bear a high differentiation potential. Furthermore, in SSc it is suggested that monocytes are activated and play an important role in disease onset and progression. We postulate that monocytes can differentiate into myofibroblasts-like cells under the influence of soluble factors such as endothelin-1, IL-4 and GM-CSF which are elevated in SSc serum.
**Materials and methods** To study the effect of ET-1 as well as GM-CSF and IL-4, we isolated monocytes from whole blood of healthy controls or SSc patients by ficoll and positive selection with CD14 beads. Monocytes were cultured in the presence of the above soluble factors over 14 days. Expression of α-SMA and type I collagen was then determined by Western blotting, qPCR and immunofluorescence.
**Results** Monocytes from healthy individuals and SSc patients responded different to certain stimuli. In particular, we found that differentiation of healthy monocytes into α-SMA expressing cells is strictly dependent on GM-CSF. However, in patient monocytes ET-1 and IL-4 are also able to promote α-SMA expression but to a lesser extend than GM-CSF. Furthermore, we observed that type I collagen expression requires GM-GSF treatment but can be enhanced with costimulation of ET-1.
**Conclusions** These data suggest that monocytes can differentiate into a myofibroblast-like phenotype and that SSc patient monocytes require a less complex stimulation to do so. Understanding the role of monocytes in fibrosis may contribute to the development of novel therapies for systemic sclerosis.