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Title: Mast cells influence the physiological functions of fibroblasts

Ms. Mariam 16258 Bagher Mariam.Bagher@med.lu.se [1,2], Dr. Oskar 17396 Hallgren Oskar@Hallgren@med.lu.se [1,2], Prof. Gunilla 17397 Westergren-Thorsson Gunilla.Westergren-Thorsson@med.lu.se [1] and Prof. Leif 17398 Bjermer Leif.Bjermer@med.lu.se MD [2]. [1] Medical Faculty, Lund University, Experimental Medical Sciences, Lund, Sweden and [2] Dep. of Respiratory Medicine and Allergology, Experimental Medical Sciences, Lund, Sweden .

Body: Rationale: Mast cells (MC) play a role in allergic disease and anaphylaxis, by releasing their granules containing pro-inflammatory and pro-fibrotic mediators. Recent studies, suggest that mast cells may have a role in non-allergic chronic lung diseases. Since tissue remodelling and fibrosis is a key feature in these diseases our hypothesis is that the mast cell-fibroblast interplay is altered. Methods: MC isolated from human peripheral blood and fibroblasts (HFL-1 fibroblasts and primary fibroblasts from lungs) were used in the experiments. The effects of the MC proteases; chymase and tryptase on fibroblasts were analyzed with western blot and q-PCR. To investigate the impact of cell-cell interaction, co-cultures between MC and fibroblasts was established and differentiation and production of extracellular matrix proteins were investigated. Results: Mast cell tryptase significantly increased HFL-1 cell migration while chymase had no effect. This effect was not due to increased cell proliferation as neither tryptase nor chymase influenced the cell number. Tryptase triggered increased expression of alpha-smooth muscle actin, a marker for myofibroblasts. This was accompanied by a change in the production of collagens and proteoglycans. MC adhered directly to HFL-1 and primary fibroblasts when using co-cultures. The cell-cell contact caused alterations in the fibroblast phenotype and in the extra cellular matrix production. Conclusions: These data indicate that MC and their mediators influence fibroblast phenotype and the production of extra cellular matrix proteins. Our results suggest that mast cells may play an important role in tissue remodelling and fibrosis by modulating the physiological function of fibroblasts.