Abstract Group: 1.5. Diffuse Parenchymal Lung Disease

Title: LSC 2012 abstract – Phenotypic profiling of invading lung fibroblasts in 3D cell culture models

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Body: Rationale: Fibroblasts exhibit an extraordinary capacity to undergo phenotypic changes during development and disease, both in vitro and in vivo. These changes include altered motility, migration or activation. Enhanced migratory capacity of primary lung fibroblasts (lfs) in IPF patients was found in vitro, but the underlying mechanisms remain elusive. The aim of this study was to decipher morphological, molecular and functional differences between invading (i) and non-invading (n-i) lfs in 3D cell culture models. Methods/Results: We established a high-content 3D invasion model, enabling the separation of i from n-i lfs that allows the comparative analysis of parameters like morphology, invasion depth and protein/mRNA expression levels. Analysis revealed two significantly distinct subtypes. 7.62 % of untreated lfs invaded the collagen matrix. Invasion was augmented by TGFβ1 and EGF treatment. Gene expression analysis of i vs n-i lfs demonstrated significantly different expression profiles. Several markers, previously reported to be associated with IPF (MMP13 (ex. ratio=4.47), MMP3 (3.97), Osteopontin (1.45), Pten (0.34)) and genes of unknown function, were found deregulated in i lfs. Conclusion: Lfs show two distinct subtypes in a 3D cell culture model. Gene expression profiling of i lfs revealed features highly similar to the (myo)fibroblast phenotype found in IPF. Our 3D invasion model constitutes a highly useful tool for high-content pharmacological screenings.