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Title: LSC 2012 abstract – Activation of Wnt/β-catenin signaling promotes lung epithelial repair in emphysema

J. 600056 Callegari [1], K. 600057 Mutze kathrin.mutze@helmholtz-muenchen.de [1] and M. 600058 Königshoff [1]. [1] HMGU, Comprehensive Pneumology Center, Munich, Germany .

Body: Emphysema is characterized by airspace enlargement, tissue destruction and reduced Wnt signaling. Wnt/β-catenin activation attenuated experimental emphysema. Here, we aim to elucidate the mechanism of Wnt/β-catenin induced alveolar epithelial cell repair in vitro and in vivo. Alveolar epithelial type II cells were isolated from untreated (ATIIc) or elastase treated (ATIIe) C57BL/6 mice at day 3, 7 and 14 with similar purity (>94%) and viability (>92%). ATIIe cells depicted increased cell numbers (i.e. 6,07±1,62x106 ATIIe and 3,39±0,86x106 ATIIc, day14), and significantly reduced expression of the Wnt target genes Axin2, LEF1 and LRP6 (i.e. LRP6 0,29±1,42 ATIIe vs. 2,38±0,56 ATIIc, day7) as determined by qRT-PCR. Freshly isolated ATIIe cells exhibited increased apoptosis susceptibility (Annexin V/PI staining). Live cell imaging of cultured ATII cells revealed altered ATIIe cell morphology and migratory behavior. Wnt activation of ATII cells by rWnt3a led to increased expression of Wnt target genes (i.e. Axin2 -2,15±0,12 rWnt3a for 24h vs. -5,18±0,29 control), epithelial markers SPC, TJP1, and Occludin, and increased proliferative capacity (BrdU). Primary ATIIe cells exhibited reduced Wnt/β-catenin activity and altered functional capacity. Wnt/β-catenin activation led to increased epithelial marker expression and stabilized ATII cell monolayers. Thus, activation of Wnt/β-catenin is a suitable tool to increase alveolar epithelial cell repair capacity in pulmonary emphysema.