S119 MICRORNA-200B REPRESSES TGF- β1 INDUCED EMT IN BEAS-2B AND PRIMARY BRONCHIAL EPITHELIAL CELLS

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Introduction MicroRNAs (miRNAs) are small non-coding RNAs that function as endogenous gene regulators. They may initiate a process called epithelial-mesenchymal transition (EMT) that leads to aberrant extracellular matrix remodelling and is implicated in a number of airway diseases. Dysregulation of miRNAs has been indicated in chronic lung disorders, the third most common cause of mortality in adults.

Materials and methods NanoString was used to assay the differential expression of miRNAs at 1, 4 and 24 hrs following TGF-β1 treatment of BEAS-2B cells (immortalised primary bronchial epithelial cells) and control. QRT-PCR validated the expression profile of miR-200b. BEAS-2B and PBECs (primary bronchial epithelial cells) were transfected with miR-200b mimics to study expression of EMT markers at mRNA and protein level. MiRNA targets were identified and validated using multiple computational tools and qRT-PCR respectively.

Results nCounter assay allowed identification of novel miRNAs including miR-200 family. MiR-200b mimic transfection (24 hrs) followed by TGF-β1 treatment (48 hrs) demonstrated a significant increase in E-Cadherin ($p \leq 0.05$, $p \leq 0.001$) and a significant decrease in Fibronectin ($p \leq 0.001$, $p \leq 0.01$) in BEAS-2B cells and PBECs. Protein studies suggested a similar trend in both the cells. The most prominent targets of miR-200b identified were RHOA, SMURF2, ZNF532 and ZEB2. A significant decrease was observed in ZNF532 ($p \leq 0.01$) and ZEB2 ($p \leq 0.001$) in miR-200b transfected and TGF-β1 treated BEAS-2B cells ($n = 3$). Differential expression of mRNA targets was observed in two sets of patient derived PBECs.

Conclusion miR-200b suppressed TGF-β1 induced EMT by maintaining the epithelial framework of BEAS-2B cells and PBECs. Results provide new insights into miR-200b regulation in fibrosis and basis for therapeutic application in lung injury.

S120 SERUM MICRORNA PROFILES IN IPF PATIENTS – BIOMARKERS OR POTENTIAL THERAPEUTIC TARGETS?

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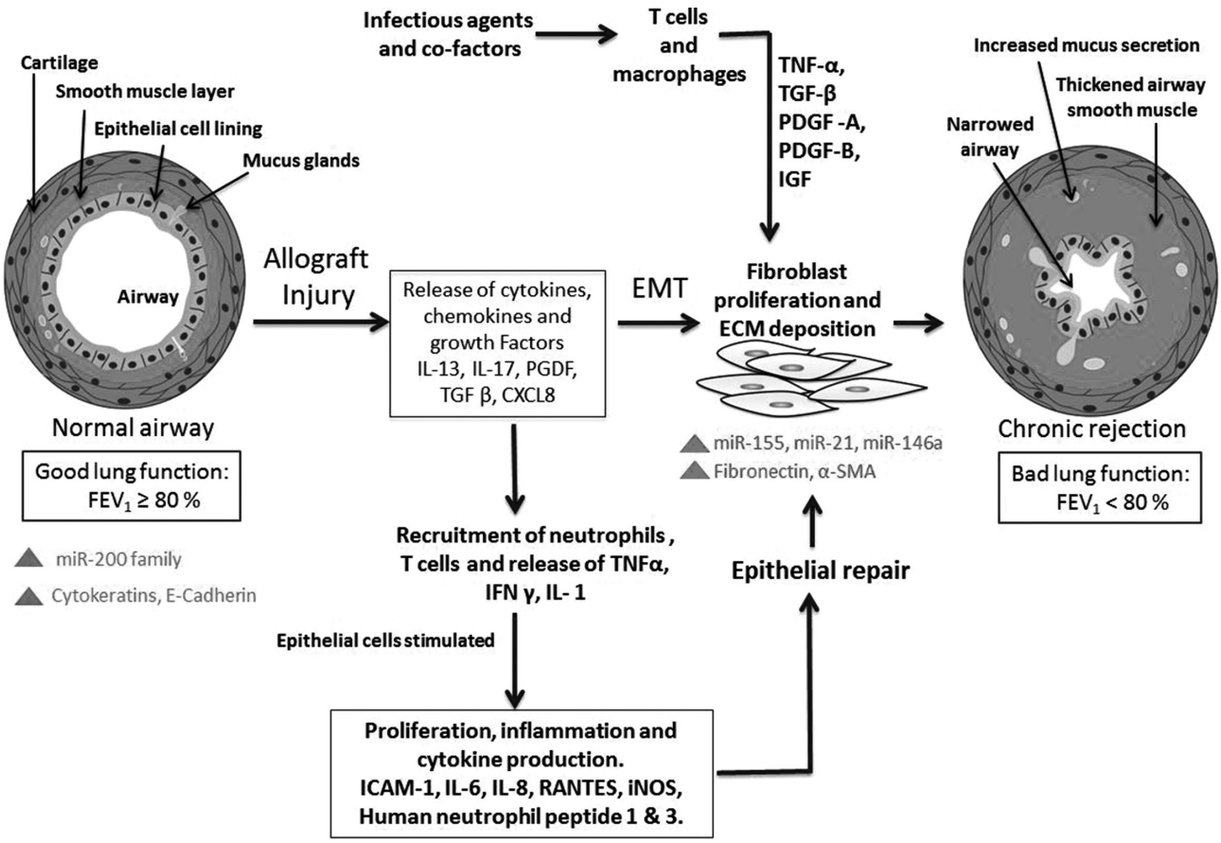
Introduction and objectives Idiopathic Pulmonary Fibrosis (IPF) has limited therapeutic options and predicting the natural history in individual cases is difficult. Exosomes are extracellular microvesicles that are involved in cell-cell signalling. MicroRNA isolated from exosomes has been implicated in several fibrotic models.[1] At present the role of miRNAs in development of lung fibrosis is unclear. We aim to characterise miRNAs isolated from IPF patients and relate these to measures of disease severity.

Methods We assessed exosomes isolated from the serum of IPF patients ($n = 8$) and aged matched healthy controls ($n = 6$). Exosomes were characterised by western blot and Nanosight



Abstract S119 Figure 1