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Title: Evidence of increased pluripotent cells in adult human lung tissue derived from fibrotic lungs compared to non-fibrotic control lungs

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Body: Introduction: Tissue-specific multipotent stem cells have been identified in the human lung. However, their role in lung homeostasis or lung disease is not clear. Methods: Primary human lung cells were cultured from fibrotic adult lung parenchyma (n=14) and from non-fibrotic control lungs (n=17). The characterization of different cell types was performed by immunofluorescence stainings. Results: Undifferentiated primary cells grew from adult human lung parenchyma, showing neither a clear epithelial nor mesenchymal morphology/immunofluorescence typing (=intermediate cells). When cultured in the respective appropriate media, intermediate cells transformed into mesenchymal cells (positive for fibronectin and α -smooth muscle actin) or into alveolar epithelial type II cells (positive for E-cadherin and surfactant protein-A). Pluripotency of intermediate cells was proven by positive stainings for Oct3/4 and NANOG. Successful induction of adipogenic, osteogenic, myogenic, and chondrogenic differentiation was performed in intermediate cells. Finally, significantly more pluripotent cells were generated from fibrotic lung tissue (n=14) than from non-fibrotic controls lungs (n=17). Conclusions: Our data demonstrate that adult human lung contains pluripotent cells which are able to differentiate towards an epithelial as well as a mesenchymal cell type solely by changing their microenvironment. These pluripotent cells might have a pivotal function in lung homeostasis and tissue repair. The observed increased incidence of these cells in fibrotic lung tissue suggests a role in fibrogenesis.