QJM: An International Journal of Medicine, 2016, S5–S6

doi: 10.1093/qjmed/hcw122
Sunday September 24th 2016
***QJM* Abstract**

Plenary Scientific Session 3

Invited Faculty Speaker

Prof. Hal Collard, University of California, San Francisco, USA

'Possible IPF: Howe we got in this mess and how we got out'

The natural history of asbestosis and idiopathic pulmonary fibrosis according to HRCT phenotype

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Mr. Abhinav Mathur (University of Edinburgh)
Ms. Phoebe Wright (University of Edinburgh)
Dr. Lisa Nicol (University of Edinburgh)
Mrs. Pauline McFarlane (University of Edinburgh)
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Asbestosis and idiopathic pulmonary fibrosis (IPF) share clinical and radiological features. When the parenchymal HRCT features are compatible with usual interstitial pneumonia (UIP), the distinction is based entirely on the exposure history.

We aimed to compare the natural history of IPF with asbestosis in patients in whom the parenchymal HRCT features were deemed compatible with definite or probable UIP. We hypothesised that there would be no difference in survival in these patients.

Methods: Data from a cohort of consecutively presenting patients with IPF (n = 370) or lung fibrosis in the setting of significant past asbestosis exposure (asbestosis) (n = 96) were analysed. Both groups were stratified into definite and probable UIP based on consensus ATS/ERS HRCT criteria. Patients with a history of asbestos exposure and parenchymal or pleural features strongly suggestive of asbestos exposure e.g. curvilinear bands, rounded atelectasis or pleural plaques were excluded if they did not have additional HRCT features of definite or probable UIP. Survival rates were estimated using the Kaplan-Meier method; hazard ratios were estimated using Cox-proportional models with relevant adjustments.

Results: There was no significant difference in the survival of IPF and asbestosis patients with definite UIP HRCT (median 3.1 vs. 3.9 yr; adjusted HR = 1.34 [95% CI 0.69-2.61], p = 0.393) or probable UIP HRCT (mean 5.5 vs. 7.9 yr; adjusted HR = 1.40 [95% CI 0.82-2.38], p = 0.217).

Conclusions: Patients with IPF and asbestosis when stratified according to HRCT appearance have similar survival. This may have important implications for patient management and clinical trials of anti-fibrotic therapy.

Heterogeneity of lung mesenchymal lineages and its impact on tissue regeneration.

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Dr. Anna Selvaggio (Cedars-Sinai Medical Center)
Ms. Takako Mizuno (Cedars-Sinai Medical Center)
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Dr. Barry Stripp (Cedars-Sinai Medical Center)
Dr. Jonathan McQualter (Cedars-Sinai Medical Center)

The wound repair process of the lung epithelium is governed by highly coordinated interactions between epithelial stem cells and mesenchymal niche cells. However, surprisingly little is known about the cellular identity of the mesenchymal niche compartment in lung. This study sought to identify the heterogeneity of this compartment and determine the cellular relationships that guide cell fate and regulate the wound-repair process. We undertook a high throughput flow cytometry screen to identify mesenchymal cell markers in mouse and human lungs and then applied a multi-parameter Spanning tree Progression of Density normalized Events (SPADE) analysis to reveal substantial heterogeneity in this compartment. To establish whether distinct subsets exhibited functional differences we assessed proliferation and mesenchymal differentiation, which were found to be broad ranging. We also assessed the epithelial-supportive capacity of different subsets and discovered that this function is not characteristic of all mesenchymal cells but rather restricted to cells with greater progenitor cell activity. Specifically, a subset of highly proliferative cells with multi-lineage differentiation potential support the proliferation of epithelial stem cells, while more differentiated myofibroblasts do not. We are currently performing these analyses on human explant tissue from patients with interstitial lung disease to identify how the cellular composition of the mesenchymal niche compartment changes in the fibrotic lung. This supports the concept that lung regeneration is tightly controlled by dynamic changes in the mesenchymal niche compartment and provides important insight into how changes in the cellular composition of this compartment in interstitial lung diseases impedes normal epithelial homeostasis.

Expression of RXFP1 is Decreased in Idiopathic Pulmonary Fibrosis: Implications for Relaxin-Based Therapies

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Introduction: Relaxin is a hormone that has been considered as a potential therapy in fibrotic diseases. To gauge the potential