pro-fibrotic mediator TGF- β 1, plays a critical role in the pathogenesis of Idiopathic Pulmonary Fibrosis (IPF). Both galectin-1 and galectin-3 potentiate this TGF- β 1 signaling pathway to promote fibrogenesis, although the exact mechanism is unclear. Integrins are glycoproteins thus their activity can be facilitated by glycan-mediated interactions with N-linked glycosylation the most well studied.¹

Objective To investigate whether galectin-1 and galectin-3 interact directly with α v β 1, α v β 5 and α v β 6 integrins using biophysical methods.

Methods Integrin-galectin interactions were determined by surface plasmon resonance (SPR) in the presence of divalent cations and the effect of extensive integrin deglycosylation or removal of N-linked oligosaccharides alone explored. SPR was used to assess integrin-galectin interactions in the presence of small molecule galectin inhibitors, GB1107 (galectin-3 selective inhibitor) or GB1490 (galectin-1 selective inhibitor). Binding of both galectins to N-Acetyl-D-glucosamine was assessed by isothermal titration calorimetry (ITC).

Results SPR data showed that both galectin-1 and galectin-3 bind to recombinant human α v β 1, α v β 5 and α v β 6 in a glycosylation-dependent manner. Minimal integrin-galectin binding was observed following integrin protein deglycosylation or in the presence of small molecule galectin inhibitors which act via the galectin carbohydrate binding domain (CBD). However, the removal of integrin N-linked oligosaccharides alone resulted in only a partial decrease in integrin-galectin binding. Additionally, ITC demonstrated that both galectin-1 and galectin-3 were unable to bind N-Acetyl-D-glucosamine; the α 5 β 1 terminal sugar required for α 5 β 1-fibronectin binding.

Conclusion Galectins are able to bind to integrins via their post-translational glycosylation sites. Collectively, these data suggest that the presence of both N-linked and O-linked glycan residues are essential for integrin-galectin binding, and that this binding may occur at the galectin galactoside-binding pocket. Understanding the precise role of galectins in integrin-mediated TGF- β 1 activation and IPF pathogenesis may be critical for the continued development of more effective and selective treatments for IPF patients.

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Please refer to page A190 for declarations of interest related to this abstract.

S98 DISSECTING HUMAN PLEURA AT SINGLE-CELL RESOLUTION

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The mesothelium is a serous membrane lining of the coelomic cavities, which comprise the pleura, pericardium, peritoneum, tunica vaginalis testis and tunica serosa uteri. It is a dynamic

Abstract S98 Figure 1 Human parietal pleura scRNAseq of freshly prepared cells. T-distributed stochastic neighbour embedding (tSNE) of jointly analysed single-cell transcriptomes from 12,162 cells from 2 pneumothorax patients. Vasc_Endo, vascular endothelial cells; SMC_Per, smooth muscle cells; T_ILC, T cells, innate lymphoid cells; B_pDCs, B cells, plasmacytoid dendritic cells; Lymph_Endo, lymphatic endothelial cells

structure important for tissue homeostasis by regulating inflammation and wound healing. Defects of the pleura are involved in the pathogenesis of pleural fibrosis and adhesions, and in malignant mesothelioma, an aggressive cancer associated with previous exposure to asbestos.

Currently, there is an inadequate understanding of pleural biology in health, which impedes the development of treatments for these pleural pathologies. To address this, we aimed to establish a reproducible protocol for the isolation and culture of mesothelial cells from human pleural tissue. Moreover, using single-cell RNA profiling, we explored the cellular heterogeneity of human pleura in 8 patients treated for pneumothorax (figure 1). This resulted in the generation of a comprehensive atlas composed of mesothelial, stromal and immune cells, providing a valuable resource for further pleural research.

S99 FLUORESCENCE-LIFETIME IMAGING: A NOVEL DIAGNOSTIC TOOL FOR SUSPECTED LUNG CANCER

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Introduction and Objectives Lung cancer is the commonest cause of cancer-related deaths. Early detection improves outcomes, however, the diagnostic yield of existing sampling techniques is suboptimal. Fluorescence-lifetime imaging microscopy (FLIM), an autofluorescence-based technique which measures endogenous fluorophore decay rates, may aid identification of optimal biopsy sites in suspected lung cancer. We describe the