2.19 Interactions between Immunomodulatory Fibroblasts and T Cells regulate lung damage responses in viral and fibrotic lung injury

Dr Kerrie Hargrave[1], Dr George Finney[1], Dr Chris Hansell[1], Dr John Cole[1], Dr Jagtar Singh Nijjar[2], Dr Mark Jackson[3], Dr Karin Williams[4], Dr Charles McSharry[1], Dr Anthony Chalmers[4], Dr Megan MacLeod[1], Dr Julie Worrell[5]

[1]School of Infection and Immunity, University of Glasgow, Glasgow, United Kingdom. [2]Weatherden Ltd, London, United Kingdom. [3]School of Cancer Sciences, University of Glasgow, Glasgow, United Kingdom. [4]CRUK, RadNet Glasgow, University of Glasgow, Glasgow, United Kingdom. [5]UCD Conway Insititute, School of Medicine, University College Dublin, Dublin, Ireland

Background: Pulmonary fibroblasts respond to environmental signals triggered by injury or infections, shaping subsequent lung responses. Fibroblasts contribute to tissue repair or inflammation and fibrosis. We hypothesise that dysregulated response to viral infection renders the lung more susceptible to fibrosis. **Methods:** We performed RNA-sequencing on sorted lung fibroblasts isolated from naïve and influenza virus (IAV) infected mice (primary/re-challenge). To examine chronicity of damage responses, IAV induced transcriptional alterations were compared to bleomycin induced lung injury (fibrosis/resolution). Phenotype/location of injury altered fibroblasts and immune cells was determined using flow cytometry and immunohistochemistry. Translational relevance of key genes was assessed using human idiopathic pulmonary fibrosis (IPF) fibroblasts. **Results:** Damageresponsive fibroblasts were elevated in both models, while bleomycin injury upregulated MHCII+ fibroblasts. Additionally, the immunomodulatory molecule, podoplanin, was localised near lung immune cell infiltrates (T/B cells). Following IAV re-infection, genes involved in T cell communication were upregulated in lung fibroblasts. Interestingly, these genes remained elevated during the remodelling phase of bleomycin injury, suggesting ongoing communication between fibroblasts and T cells. Strikingly, CD274+ IPF fibroblasts had reduced levels of interferon response genes, indicating blunted ant-viral responses. **Conclusions:** Previous viral infection alters subsequent fibroblast responses influencing fibrosis development and may contribute to IPF pathogenesis. **Conflicts of Interest:** The authors declare that they have no conflicts of interest.