2.12 Aberrant lipid metabolism drives pulmonary fibrosis

Marissa O'Callaghan[1,2], Elizabeth J Tarling[3], Harshavardhana Ediga[4], Evelyn Lynn[1,2], Aurelie Fabre[1,2], Elizabeth F Redente[5], James P Bridges[5], Satish Madala[4], Michael Keane[1,2], Cormac McCarthyc[1,2]

[1]St Vincent's University Hospital, Dublin, Ireland. [2]University College Dublin, Dublin, Ireland. [3]University of California LA, Los Angeles, USA. [4]University of Cincinnati Medical Center, Ohio, USA. [5]National Jewish Health Denver, Colorado, USA

Background: Lipid homeostasis is important in the lung as 90% of surfactant is lipid. We hypothesise that aberrant lipid metabolism contributes to the fibrotic niche in IPF. **Methods:** We performed lipidomic analysis on lung tissue from human IPF,bleomycin,silica and *Abcg1*-/- mice. We exposed IPF fibroblasts to oxidised and unoxidised PC and CE lipids, measuring expression of fibrotic markers. **Results:** There was increased lipid content in IPF ($p=0.03$), bleomycin ($p=0.06$), silica ($P=0.02$) and *Abcg1*-/- mice ($p<0.001$) lung tissue. Specific increases were noted in 16:0 and 20:4 containing lipids; these lipids were chosen for IPF fibroblast exposure. ACTA2 and Col1a1 expression were upregulated in IPF fibroblasts following exposure to saturated PC 16:0 ($p<0.001$) and CE 16:0 ($p<0.01$) and there was no change after unsaturated PC 20:4 (p=ns) and CE 20:4 (p=ns). When PC 20:4 and CE 20:4 are oxidised they upregulate ACTA2 and Col1a1 expression ($p<0.01$). This effect is reduced, but not neutralised, by co-treatment with CD36 receptor blocker. **Conclusion:** We have shown that total lipid increases in IPF and hypothesise that unsaturated lipid becomes oxidized and this in turn drives production of pro-fibrotic cytokines. This may be a crucial hit in driving uncheckered fibrosis seen in IPF. **Conflict of Interest:** The authors declare no conflict of interest.