that NKT cell deficiency in sarcoidosis results in abnormal monocyte activity.

**Methods** Twenty-five steroid-naive non-smoking patients with histological confirmation of sarcoidosis were recruited from the Sarcoidosis-ILD service. Circulating monocyte numbers and phenotype were first characterised using multi-colour flow cytometry. We then isolated monocytes from blood using magnetic beads, examined cytokine production after LPS stimulation with intracellular cytokine FACS staining and ELISA; and using monocyte-NKT cell co-culture assays, questioned whether NKT cells affected these monocyte functions.

**Results** We found an increase in circulating CD14CD16 in affected these monocytic functions. We then questioned the role of IL10-producing monocytes and show (with mixed lymphocyte reaction and CFSE assays) that these cells suppress T cell proliferation (p<0.001, Abstract S109 figure 1A); but addition of NKT cells improved this capacity (6.57% to 9.15%, p<0.001, Abstract S109 figure 1B). We then questioned the role of IL10-producing monocytes and show (with mixed lymphocyte reaction and CFSE assays) that these cells suppress T cell proliferation (p<0.001, Abstract S109 figure 1C).

**Conclusions** Our data show that sarcoidosis patients have increased inflammatory monocytes but a reduced IL10-producing, T cell suppressing subset. NKT cells were able to interact with monocytes in vitro and increased IL10 production by monocytes. These previously unrecognised findings, both in monocyte-NKT cross talk and in sarcoidosis immunobiology, suggest that one consequence of NKT deficiency in sarcoidosis is abnormal monocyte function with resultant loss in control of T cell proliferation. This reveals a potential new pathway of pathogenesis in sarcoidosis.

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**Abstract S109 Figure 1**

**S110**

**TARGETED DELETION OF GαQ/Gα11 IN SURFACTANT PROTEIN C-POSITIVE EPITHELIAL CELLS REDUCES TGFB ACTIVATION AND RESULTS IN INFLAMMATION AND ALVEOLAR AIRSPACE ENLARGEMENT**

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Activation of latent TGFβ by the epitheliob-depressed αvβ6 integrin is central in the pathogenesis of lung injury and fibrosis, and disruption of this pathway promotes emphysema development. We have previously shown that Cαq and RhoA signalling pathways are central to αvβ6 integrin induced TGFβ activation in vitro. To assess the role of the Gq/11 signalling pathway in the lungs, we generated mice with deletion of the Gq and G11 α-subunits in Surfactant protein C (SftpC)-positive epithelial cells (Gq/C11DKO). SftpC-Cre mice were crossed with constitutive Cα11-deficient animals (Cαat−/−; G11KO) carrying floxed alleles of the Gαq gene (Cαatfl/fl). and then backcrossed onto appropriate null mice. Lungs were perfused, inflated and fixed prior to processing for histological and immunohistochemical analysis at 2, 4, 6 and 8 weeks. Bronchoalveolar lavage (BAL) cells were collected at 6 weeks for mRNA, nuclear protein extraction or histological analysis. Focal inflammatory infiltrates were visible in the Gq/C11DKO lungs as early as 2 weeks, but became larger and more widespread at later timepoints. Gq/C11DKO mice also exhibited significant age-related airspace enlargement compared with G11KO mice from 4 weeks onwards. From 6 weeks, inflammation was closely associated with localised disruption of the alveolar architecture and the appearance of enlarged and vacuolated macrophages within the airspaces. BAL fluid from Gq/C11DKO mice contained significantly higher cells numbers (12.5±2.5×10⁵/mcL) than G11KO mice (9.6±2.0×10⁵/mcL) with increases in the percentage of neutrophils, lymphocytes and enlarged and vacuolated alveolar macrophages. mRNA analysis of Gq/C11DKO BAL cells showed significantly increased MMP12, RELMα and Arginase 1 suggesting an increase in the number of alternatively activated macrophages. To assess levels of active TGFβ in the lungs, phosphorylated SMAD2 (pSMAD2), a component of the TGFβ signalling pathway, was measured by ELISA of nuclear extracts from BAL cells. Gq/C11DKO BAL cells contained significantly lower levels of pSMAD2 than those from G11KO mice, suggesting decreased levels of active TGFβ in the lungs of Gq/C11DKO mice. These data suggest that the Cαq/11 signalling pathway in SftpC-positive epithelial cells regulates TGFβ activation in the lungs and that deficiency in this pathway results in pulmonary inflammation and disruption of the alveolar architecture of the lung.

**S111**

**THE ROLE OF TNF-RELATED APOPTOSIS INDUCING LIGAND (TRAIL) IN PULMONARY FIBROSIS**

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**Introduction** The concept of driving cellular apoptosis as a potential therapy for diseases characterised by inappropriate cellular persistence or proliferation is of widespread interest. We previously showed a death receptor ligand, TRAIL, accelerates neutrophil apoptosis without associated cell activation (J Immunol 170:1027–33) and other work revealed TRAIL-induced apoptosis of human lung fibroblasts. The aims of this project were to study the role of TRAIL in a bleomycin lung injury model in wild-type and TRAIL−/− mice and in patients with idiopathic pulmonary fibrosis (IPF).

**Methods** Mice received intratracheal bleomycin or saline control. Bronchoalveolar lavage (BAL) at 5, 7, 16 and 25 days was analysed by cytospin morphology and haemocytometer count for % neutrophils, % neutrophil apoptosis, total number of neutrophils and total number of apoptotic cells. Flow cytometry was also used to analyse apoptosis. Collagen deposition in whole lung samples was analysed using a hydroxyproline assay. TRAIL expression and TUNEL positive events were also analysed. Serum and lung tissue from IPF patients/controls were examined for TRAIL expression and concentration. Lung function and survival data were retrieved from patient charts.

**Results** BAL analysis revealed statistically significant differences between TRAIL−/− and wild-type mice, with TRAIL−/− mice showing increased neutrophil numbers and reduced neutrophil apoptosis as absolute count or as % total cell count. Collagen deposition was statistically greater in TRAIL−/− mice at 16 days. At day 25, TRAIL−/− mice had decreased TUNEL positive events compared to wild-type mice. Histological analysis of murine lung sections revealed specific TRAIL expression in bronchus associated...