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 microbeads, 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 patients with sarcoidosis, and identified a population of intercellulin 10 producing monocytes in patients and controls after LPS stimulation. Monocytes from sarcoidosis patients have reduced capacity to produce IL-10 after LPS stimulation compared to control (6.57% vs 11.71% of total monocytes, p<0.001, Abstract S109 figure 1A); but addition of NKT cells improved this capacity (6.57% to 9.13%, 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 IL-10-producing, T cell suppressor subset. NKTcell were able to interact with monocytes in vitro and increased IL-10 production by monocytes. These previously unrecognised findings, both in monocyte-NKT cell 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.

---

**Abstract S109 Figure 1**

**Figure S111 THE ROLE OF TNF-RELATED APOPTOSIS INDUCING LIGAND (TRAIL) IN PULMONARY FIBROSIS**

doi:10.1136/thoraxjnl-2011-201054b.111

1E McGrath, 1A Lawrie, 1H Marriott, 2F Mercer, 1S Cross, 2R Chambers, 1D H Dockrell, 1M K B Whyte. 1University of Sheffield, Sheffield, UK; 2University College London, London, UK

**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 samples were 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...