the main contributor to disease activity. The most effective treatment, corticosteroids, has a high adverse effect burden so there is a need to define more specific therapeutic agents with less side effects. In addition, for some patients with progressive active disease, corticosteroids are often unhelpful; therefore better understanding of the mechanisms of disease is needed for development new drugs. This study examines the potential immune processes involved in disease activity in sarcoidosis using gene expression profiling of peripheral blood mononuclear cells (PBMCs) (n=29) and bronchoalveolar lavage cells (BALCs) (n=12). Patients with well-defined pulmonary sarcoidosis and secure tissue-supported diagnosis were recruited from the Oxford Sarcoidosis Service during a defined 2 year period. Patients were not on treatment at the point of sampling. A CTAS[1] -validated chest radiograph-blood disease activity score comprising lymphocyte, ACE and IgG levels (SCAS, scores from 0 to 12 reflecting low to high activity) was used to measure activity at the point of sampling. Gene expression profiles were derived from PBMC and BALCs using the Illumina HT-12 v4 expression chip. All RNA had a RIN≥8. We found a significant positive correlation between the 'immune response' gene set and SCAS for BALCs, by GSEA and Metacore functional analyses. Within this gene set, a transcriptional signature related to monocyte activity and function was shown to be the most significant gene network with an unexpected downregulation of TGFb receptor signalling pathway in low activity BALCs. In PBMCs and BALCs, the two IFN-g-inducible, monocyte-produced genes CXCL-9 and CXCL-10 were the soluble factors that most correlated with increasing activity (r≥0.5 by Spearman Correlation). In an independent cohort, SCAS levels were examined against $CD14^{hi}$ classical monocyte levels (n=40, same inclusion criteria). This showed a marked correlation between monocyte frequency and level of activity as measured by SCAS (r=0.67; p<0.001; Spearman Rank correlation). These Results implicate monocytes as a major contributor to disease activity in sarcoidosis and propose monocyte pathways as potential specific targets for new therapeutics in sarcoidosis.

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S78 INCREASED CD16BRICD62LDIMCD11B+SUBSET OF NEUTROPHILS IN BRONCHOALVEOLAR LAVAGE FROM PATIENTS WITH INTERSTITIAL LUNG DISEASE

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Introduction The Interstitial Lung Diseases (ILD) are a heterogeneous group of inflammatory and fibrotic diseases of the interstitium, with worst cases resulting in pulmonary fibrosis (PF). Increased neutrophils are found within the lung or bronchoalveolar lavage (BAL) in ILD and predict a poor prognosis. Neutrophil adhesion molecules, e.g., CD18/b2 integrins (LFA-1; CD11a, Mac-1; CD11b and CR3; CD11c) and L-Selectin (CD62L) regulate cellular recruitment and fibrosis in animal models of bleomycin-induced PF. Expression of the Fc receptor (CD16) is upregulated during neutrophil activation, whilst ICAM-1 (CD54) is a marker for neutrophil reverse-transmigration back across the endothelium.

Study Aim Investigate adhesion molecule expression profile of neutrophils in ILD patients compared to controls.

Methods BAL samples were collected from ILD and non-ILD patients undergoing bronchoscopy with informed consent. Adhesion molecule expression was studied via flow cytometry by staining cells with CD16, CD62L, CD11b, CD11c, CD11a, CD18 and CD54 antibodies.

Results Flow cytometric analysis of BAL showed significantly more neutrophils in ILD lavage express CD11b and CD18 compared to non-ILD controls (p=0.0016 and p=0.0211 respectively). No significant differences were found in CD11c or CD11a expression. Further analysis revealed ILD lavage contained a higher percentage of $CD16^{bri}CD62L^{dim}$ neutrophil subset expressing CD11b than non-ILD lavage controls (p<0.0001); a subset previously associated with a suppressive phenotype.[1] In addition, ICAM-1 expression was significantly down-regulated in ILD lavage neutrophils (p=0.0397) and this was also reflected in the $CD16^{bri}CD62L^{dim}$ neutrophil population (p=0.0445).

Conclusions From our preliminary study, we have observed an increased percentage of $CD16^{bri}CD62L^{dim}CD11b^{+}$ subset of neutrophils in ILD lavage compared to controls. ILD lavage neutrophils express significantly less ICAM-1. This suggests that more neutrophils are entering and being retained within the lung in ILD. Further experiments will dissect whether ILD neutrophils have altered functions (such as NETosis, ROS production, adhesion or migration) to contribute to disease progression.

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S79 LOCALISED HYPOXIA ENHANCES NEUTROPHIL EXTRAVASATION AND ACTIVATION IN INTERSTITIAL LUNG DISEASE

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Background Neutrophilic inflammation is common in various diseases and may contribute to the pathophysiology of interstitial lung disease (ILD), however the underlying mechanism are not fully understood. Localised tissue hypoxia is often accompanied with inflammation, which may alter cellular responses to drive immunopathology.

Hypothesis We propose that hypoxia modulates neutrophil functions including integrin activation, neutrophil extravasation and neutrophil extracellular trap (NET) release that may contribute to pulmonary damage in ILD

Methods Pulmonary hypoxia was assessed using both fluoromisonidazole (FMISO)-PET scanning of ILD patients and immunohistochemical HIF-1a staining in ILD and control lung sections. To examine the effects of hypoxia, isolated neutrophils were cultured under hypoxia (1% oxygen) or normoxia (21% oxygen) prior to experimentation. Neutrophil integrin expression was evaluated using flow cytometry. Neutrophil