**Methods:** To this end, we compared the phenotype, TLR-mediated responses and CD8$^+$T-cell activation by moDCs and CXCL4 exposed moDCs.
**Results:** Already prior to TLR stimulation, CXCL4-moDCs displayed a more matured phenotype. We found that CXCL4 exposure can sensitize moDCs for TLR-ligand responsiveness, as illustrated by a dramatic upregulation of CD83, CD86 and MHC class I, and markedly increased secretion of IL-12 and TNF-$\alpha$ in response to TLR3 and TLR7/8-agonists. Next, we analyzed the effect of CXCL4 in modulating DC-mediated CD8$^+$ T-cell activation. CXCL4-moDCs strongly potentiated proliferation of polyclonal CD8$^+$ T-cells and production of interferon (IFN)-$\gamma$ and IL-4, in an antigen-independent manner. While the internalization of antigen was comparable to moDCs, antigen processing by CXCL4-moDCs was impaired. Yet, these cells were more potent at stimulating antigen-specific CD8$^+$ T-cell responses.
**Conclusions:** Together our data supports that increased levels of circulating CXCL4 may contribute to immune dysregulation through the modulation of innate and adaptive responses by dendritic cells.
**References:**
[1] Van Bon, L & Affandi, A J; et al. 2014. Proteome-wide analysis and CXCL4 as a biomarker in systemic sclerosis. N. Engl. J. Med. 370: 433–43.
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**Disclosure of Interest:** None declared
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## AB0055 IL-1 BETA AND CASPASE-1 P45 EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH ADULT-ONSET STILL'S DISEASE

S. Bindoli, F. Fabris, L. Punzi, P. Galozzi, P. Sfriso. *Rheumatology Unit-Department of Medicine, University of Padova, Padova, Italy*

**Background:** Adult-onset Still's disease (AOSD) is a systemic inflammatory condition characterized by episodes of spiking fever, evanescent rash, arthralgia, leukocytosis and hyperferritinemia. The inflammatory status of AOSD could result from a deregulation of the NLRP3 inflammasome as Interleukin-1 (IL-1) is pivotal in the pathogenesis of AOSD.
**Objectives:** To evaluate IL-1 beta and caspase-1 p45 expression in AOSD patients.
**Methods:** 11 AOSD patients with systemic chronic disease (mean age: 44.5±15.6 years; mean disease duration: 3.0±1.7 years) and 5 healthy donors (mean age: 41.8±7.5) were enrolled. Anakinra (in 6 patients) and DMARDs (in 5 patients) adequately controlled the disease. PBMCs (peripheral blood mononuclear cells) obtained by Ficoll centrifugation were stimulated with lipopolysaccharide (LPS) [10 ng/ml] and ATP [1 mM] for 0.5, 1, 6 and 24 hours. IL-1$\beta$ level was measured in the supernatant by ELISA and the expression of caspase-1 p45 at protein level was detected by Western Blotting.
**Results:** In unstimulated PBMCs minimal IL-1$\beta$ production was found both in AOSD patients and controls. After 6 hours stimulation, IL-1$\beta$ level was increased whereas we observed a reduced processing of caspase-1 p45 particularly in AOSD patients treated with Anakinra.

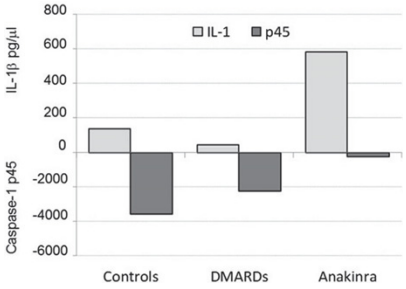


Figure 1. IL-1$\beta$ secretion and caspase-1 p45 intracellular expression: differences between stimulated and unstimulated PMBCs in anakinra and DMARDs treated AOSD patients and in healthy controls.

**Conclusions:** Patients with refractory AOSD, who therefore need Anakinra, seem to have an increased production of IL-1$\beta$ compared to healthy controls and to AOSD patients who respond to standard therapies. Altered processing of caspase-1 p45 in AOSD patients support the involvement of the NLRP3 inflammasome pathway in the pathogenesis of the disease.
**Disclosure of Interest:** None declared
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## AB0056 EMERGING ROLE OF IL-33/ST2 AXIS IN ENDOTHELIAL CELL INJURY OF LUPUS NEPHRITIS

S. Yu, Y. Tao. *Rheumatology, The Second Affiliated Hospital of Guangzhou Medical, Guangzhou, China*

**Background:** "Alarmins" are prototypic endogenous pro-inflammatory factors as they are released from necotic cells and provoke local damage or systemic inflammation. Evidences are accumulating to support the inclusion of "Alarmins" as targets of autoreactivity as well as inducers in the pathogenesis of Systemic Lupus Erythematosus (SLE). Interleukin (IL)-33 is a novel member of the family of "Alarmins" because of its characteristics and functions in mediating host immune responses. On this background, we sought to determine the role of IL-33/ST2 axis in lupus pathogenesis. The role of IL-33/ST2 axis has not previously been described in lupus nephritis.
**Objectives:** This project will study the followings: (1) To determine whether IL-33 was present in renal glomerular endothelial cells; (2) To assess the functional and intracellular signal transuction mechanisms regulating the link between IL-33/ST2-mediated innate immunity and inflammation in CD4$^+$ T cells-endothelial cells co-culture system of lupus patients.
**Results:** Immunofluorescence (IF) for IL-33 in the kidney were performed in both MRL$^{lpr}$ lupus mice and C57BL/6J mice. On double staining for IL-33 and lectin, IL-33 was clearly seen in glomeruli and also in peritubular areas. To determine whether the IL-33 staining in glomeruli and peritubular areas was in endothelium, double IF staining for IL-33 and von Willebrand factor (vWF) was performed. IL-33 co-localized with vWF in glomeruli and in peritubular areas. The increased levels of IL-33 mRNA transcripts were detected in kidney of MRL$^{lpr}$ lupus mice compared with C57BL/6J mice. Expression of cell-surface ST2 was increased on the CD4$^+$ T cells of lupus patients when compared with healthy controls. Serum sST2 level was significantly higher in SLE patients with *flare* than those without *flare* ($p<0.05$).
**Conclusions:** As a result of external stimuli or infection, renal glomerular endothelial cells undergo cellular death and release the "Alarmin", IL-33, to alert the lupus immune system. Released IL-33 interact with their target cells, CD4$^+$ T cells via their specific receptor ST2 to subsequently induce innate and adaptive responses, activate inflammatory pathways in the pathogenesis of lupus nephritis.
**Disclosure of Interest:** None declared
**DOI:** 10.1136/annrheumdis-2017-eular.1700

## AB0057 THE ROLE OF GROWTH DIFFERENTIATION FACTOR (GDF)-15 AND TRANSFORMING GROWTH FACTOR (TGF)-β IN THE DEVELOPMENT OF PULMONARY FIBROSIS

V. Yazisiz, S. Oygen, M. Çavuşoğlu, M. Kahraman, E.G. Gök, S. Karahan, I. Uçar, M.E. Terzioğlu. *Rheumatology, Akdeniz University, Antalya, Turkey*

**Background:** The pathogenesis of pulmonary fibrosis is not fully understood and it is thought to develop secondary to inflammation. The main cause of pulmonary fibrosis is considered to be interstitial lung disease (ILD), which can be associted with connective tissue disorders (CTD).
**Objectives:** The aim of this study was to investigate serum GDF-15 and TGF-$\beta$ levels in patients with diagnosis of CTD associated with ILD.
**Methods:** A total of 103 adult patients (19 rheumatoid arthritis, 18 Sjögren's syndrome, 32 systemic sclerosis, 3 systemic lupus erythematosus and 31 healthy controls) were included in the study. Pregnant, acute coronary syndrome, previous myocardial infarction and/or stroke history, heart failure and malignancy were excluded. Serum GDF-15 and TGF-$\beta$ levels were studied by ELISA method in peripheral blood samples.
**Results:** There were 44 patients with CTD-ILD, 28 patients without ILD and 31 healthy controls. The age and gender distributions of participants in all three groups were not different. Serum TGF-$\beta$ and GDF-15 levels in patients with CTD-ILD and CTD without ILD were significantly higher than healthy controls (respectively, 3.05±0.26, 3.05±0.22, 1.39±0.33 pg/ml, $p<0.001$ for TGF-$\beta$ and 1.17±0.17, 1.12±0.05, 0.95±0.21 pg/ml, $p<0.001$ for GDF-15). There were no statistically different from patients with ILD and without ILD for both TGF-$\beta$ (p:0.864) and GDF-15 levels (p:0.146) in CTD. Also, GDF-15 and TGF-$\beta$ levels of patients with systemic sclerosis were not different from other CTD's.

Table 1. Comparison of analysis results of patient and control groups

| | Connective tissue disorders | | Healty Controls (n: 31) | p |
|---|---|---|---|---|
| | ILD (+) (n: 44) | ILD (–) (n: 28) | | |
| Gender (Female) (n, %) | 35 (79.5%) | 22 (78.5%) | 23 (74.2%) | 0.831 |
| Age (years) (Mean±SD) | 53.95±11.9 | 53.61±9.2 | 51.68±12.8 | 0.641 |
| TGF-β(pg/ml) (Mean±SD) | 3.05±0.26 | 3.05±0.22† | 1.39±0.33 | <0.001 |
| GDF-15 (pg/ml) (Mean±SD) | 1.17±0.17 | 1.12±0.05‡ | 0.95±0.21 | <0.001 |

†ILD vs non-ILD p=0.864. ‡ILD vs non-ILD p=0.146.

**Conclusions:** Our findings indicate that TGF-$\beta$ and GDF-15 are increased in CTD patients but, they are not a specific markers for CTD-ILD
**Disclosure of Interest:** None declared
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