SAT0188 **SKELETAL MUSCLE FIBERS IN MYOSITIS ACTIVELY UPREGULATE IMMUNOPROTEASOME SUBUNITS**

S. Bhattarai[1], K. Ghannam[1], S. Krause[2], L. Martinez-Gamboa[1], A. Marg[3], S. Spuler[3], O. Benveniste[4], W. Stenzel[5], E. Feist[1]. *[1]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin, Berlin; [2]Friedrich Baur Institute, Ludwig Maximilians University, Munich; [3]Muscle Research Unit, Experimental and Clinical Research Center, Charité – Universitätsmedizin Berlin, Berlin, Germany; [4]La Pitié-Salpêtrière Hospital, Internal Medicine Department, AP-HP, INSERM U974, UPMC, Paris, France; [5]Department of Neuropathology, Charité – Universitätsmedizin Berlin, Berlin, Germany*

Background: Idiopathic inflammatory myopathies (IIMs) are characterized by enhanced sarcolemmal expression of MHC class I molecules and infiltration of immune cells including $CD8^+$ T cells into skeletal muscle tissue. Immunoproteasome is a proteolytic complex that can efficiently produce peptides for antigen presentation via major histocompatability complex class I (MHC class I) molecules and is highly expressed in immune cells. Previously, we described upregulated expression of immunoproteasome subunits (β1i and β5i) within myositis muscle biopsies at the mRNA level suggesting its possible involvement in diseases pathogenesis [1].

Objectives: The aim of this study was to clarify, whether immunoproteasomes are expressed within the muscle fibers of patients with IIMs and therefore, could be associated with the increased MHC class I surface expression.

Methods: Cryosections of muscle biopsies from sporadic Inclusion body myositis (sIBM), Immune-mediate necrotizing myopathy (IMNM), Dermatomyositis (DM) patients and healthy controls were examined for expression of proteasome subunits and cellular infiltrates by western blot and double-immunofluorescence. Proteasome activity was measured and compared between the different groups using a proteolytic assay *in vitro*.

Results: Western blot analyses of muscle biopsies from IBM (n=9), IMNM (n=9), DM (n=9) patients showed a strong upregulation of β1i and β5i subunits. Of note, double immunofluorescence provided clear evidence for an expression of immunosubunits β1i and β5i especially in the infiltrated muscle fibers in all studied disease conditions, whereas healthy muscle (n=4) fibers showed no staining for β1i and β5i. Interestingly, expression of proteasome immunosubunits was accompanied by increased MHC class I expression on the same muscle fibers. Both $CD68^+$ and $CD14^+$ macrophages showed strong staining of β1i and β5i in all disease group. In IBM, among the infiltrating cells about 50% of CD8+ T cells stained positive for β1i and β5i. In agreement with these results, significant increase in proteasomal chymotrypsin-like (CTL) activity was observed.

Conclusions: These results suggest direct involvement of immunoproteasome subunits β1i and β5i in the pathogenesis of myositis through enhanced upregulation of MHC class I.

References:

[1] Ghannam K, Martinez-Gamboa L, Spengler L, Krause S, Smiljanovic B, Bonin M, et al. (2014) Upregulation of Immunoproteasome Subunits in Myositis Indicates Active Inflammation with Involvement of Antigen Presenting Cells, CD8 T-Cells and IFNγ. PLoS ONE 9(8): e104048. doi:10.1371/journal.pone.0104048

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2016-eular.2858