muscle cells undergo continuous cycles of death and regeneration as a consequence of the pressure of the immune response targeting antigens preferentially expressed within regenerating fibers (1, 2).

Objectives: I will review recent evidence on the relative role of unconventional cellular and molecular pathways activated in the tissues of subjects with IMM and in relevant experimental models of skeletal muscle regeneration and autoimmunity, focusing on the action of antigen-specific and regulatory T cells and immune cells populations of innate cells.

Methods: Review of available published data and of data recently generated on the topic.

Results: Muscle necrosis and the ensuing inflammation was consistently associated in mice with up-regulated expression of bona fide autoantigens targeted in patients with IIM, in particular of histidyl-transfer RNA synthetase (HisRS). Phagocytosis of HisRS-expressing apoptotic myoblasts and appropriate inflammatory costimuli are necessary to elicit the production of anti-HisRS autoantibodies and to jeopardize muscle regeneration. Soluble pattern recognition receptors, and in particular the prototypic long pentraxin PTX3 play a critical role in preventing the accumulation of cell debris in the inflamed skeletal muscle, restricting the immunogenic potential of dying and regenerating myofibers.

Conversely the local expression of type I IFN is necessary for the prolonged autoantibody response and for the maintenance and spreading of the immune-mediated muscle damage, as demonstrated using IFN α / β R-null mice (3-5). A specialized population of regulatory T (Treg) cells, has been recently characterized in the inflamed and regenerating muscle, which influence both the immune response, by promoting the M1-to-M2 switch, and the activation of precursor/stem muscle cells. Treg cells control the efficacy of muscle repair and might be involved in preventing the systemic effects of the autoimmune response generated as a consequence of the disruption of the immunologically protected environment of the skeletal muscle (6, 7).

Conclusion: Identification of the pathways that are physiologically involved in restricting the onset and accelerating the termination of autoimmune responses targeting the skeletal muscle might be valuable for the identification of novel targets for molecular intervention in patients with IIM.

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SP0104 THE JANUS-FACED GLADIATOR: NEUTROPHILS IN STERILE INFLAMMATION AND AUTOIMMUNITY

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Background: Neutrophils, and particularly neutrophil extracellular traps (NETs), have been connected with inflammatory and autoimmune diseases, such as RA, SLE, gout and many others. However, the outcome of a deficiency of NET-formation can be observed in chronic granulomatous disease and Papillon-Lefèvre

syndrome and is characterized by non-resolving inflammation and frequent autoimmunity.

Objectives: I will give an overview over pro- and anti-inflammatory effects of neutrophils and NETs, respectively, focusing on our results in gout and SLE.

Methods: We investigated the impact of NET-deficiency and/or neutrophil-depletion on animal models of SLE (pristane-induced lupus) and gout (MSU crystal-induced arthritis). Mechanistic studies were performed with isolated neutrophils from mice and humans.

Results: In experimental lupus and gouty arthritis neutrophil depletion or neutropenia worsens disease. Also mice strains with normal neutrophil numbers but defects in NET formation (NOX2 or PAD4-deficient mice) have exacerbated and unresolving inflammation.

Release of inflammatory mediators by stimulated neutrophils was highest at intermediate cell densities ($20-40 \times 10^6$ cells/cm³). Above such densities, mediator release by normal neutrophils was outweighed by proteolytic degradation via proteases expressed on aggregated NETs. Additionally, binding to aggregated NETs conferred protection of the serine protease neutrophil elastase (NE) against inactivation by α 1-antitrypsin (A1AT).

Conclusion: Although neutrophils are often regarded as archetypical pro-inflammatory cells, evidence is increasing that they can also exert anti-inflammatory and immunoregulatory function. Formation and aggregation of NETs and degradation of inflammatory mediators by serine proteases are important neutrophil tools to resolve gouty arthritis and other forms of localized inflammatory conditions. On the downside, NETs come at the price of collateral tissue damage and may cause occlusion of ductal structures.

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SP0105 REGULATION OF AUTOANTIBODY ACTIVITY BY T CELL SUBSETS

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Our recent data show that the IL-23–T_H17 axis controls the intrinsic inflammatory activity of autoantibodies and thereby triggers the clinical onset of autoimmune arthritis in mice and humans suffering from rheumatoid arthritis. TH17 cells regulate expression of sialyltransferases in newly differentiating antibody-producing cells and determine the glycosylation profile and activity of immunoglobulin G (IgG) that is produced by the consecutively emerging plasma cells.

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FRIDAY, 14 JUNE 2019

08:15:00 – 09:45:00

Seeing is believing: Nanotechnologies in tissue imaging

SP0106 LOOKING THROUGH MY BACK BONE

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Background: Because bone marrow is the source of all immune cells, knowing the blood supply of bones is essential to understand diverse mechanisms such as arthritic bone inflammation, anti-infectious immune defense or sterile inflammation.

Objectives: We wanted to clarify, how immune cells are able to function inside of the bone and also leave bones for peripheral functions.

Methods: Using an array of different imaging approaches and innovative animal models as well as insights from clinical studies in humans we have made the bone open to ways of studying, that have not previously possible.

Results: Using these methods we have defined an entirely new concept of how a closed circulatory loop is established in long bones. Thereby we show the mechanistic role of osteoclasts and define, how T cells and neutrophils use the system to fight against viral infection or invade ischemic tissue. This allows an integrated