serological variables and reflected the uptake of opsonized SNEC by neutrophils in the blood.

Conclusion: SNEC ELISA allows for the sensitive detection of pathologically relevant autoantibodies in the serum of patients with SLE. The clearance of nuclear remnants by neutrophils enhances inflammatory responses supporting the role of clearance deficiency in the etiopathogenesis of SLE.

REFERENCE:

- [1] Biermann MHC, Boeltz S, Pieterse E, Knopf J, Rech J, Bilyy R, van der Vlag J, Tincani A, Distler JHW, Krönke G, Schett GA, Herrmann M and Muñoz LE (2018) Autoantibodies Recognizing Secondary Necrotic Cells Promote Neutrophilic Phagocytosis and Identify Patients With Systemic Lupus Erythematosus. *Front. Immunol.* 9:989. doi: 10.3389/fimmu.2018.00989

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SP0175 POST-TRANSLATIONAL MODIFICATIONS OF ANTIBODIES: WHERE THERE'S SMOKE THERE'S FIRE

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Rheumatoid arthritis (RA) is a prototype autoimmune disease, with the hallmark signs of synovial inflammation and the presence of autoantibodies. One of the most prominent examples of such autoantibodies are anti-citrullinated protein antibodies (ACPA), which are directed against a wide-array of citrullinated proteins. The immune response to citrullinated antigens is a dynamic response that expands before the onset of disease and generates antibodies that are extensively glycosylated in the variable domain. This feature of ACPAs is remarkable and might be involved in the breach of tolerance to citrullinated proteins as well as function as an additional biomarker to predict disease onset in subjects at risk.

Next to ACPA, it has become clear that the autoantibody response in RA extends towards several other modified proteins, such as proteins modified by carbamylation or acetylation. Carbamylation leads to the formation of homocitrulline. Structurally, homocitrulline greatly resembles citrulline but is one methylene group longer. In contrast, acetylation is mediated by intracellular acetyltransferases and is structurally less related to citrulline or homo-citrulline. Although the presence of autoantibodies against these post-translationally modified proteins (Anti-Modified Protein Antibodies; AMPA) hallmark RA, at present, there is no conceptual framework explaining the concordant presence of different AMPA-responses in RA. In the context of this presentation, the latest insights into the development of humoral response against citrullinated-, carbamylated and acetylated proteins in relation to their role as biomarkers to predict the development of RA will be discussed.

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SP0176 PATHOGENIC ANTIBODIES IN PHOSPHOLIPID SYNDROM

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Antiphospholipid syndrome (APS) is prothrombotic systemic autoimmune disorder characterized with multisystem manifestation, most commonly venous and arterial thromboembolism and/or recurrent pregnancy loss. The varying clinical phenotype is associated with heterogeneity in the pathogenic antiphospholipid antibodies (aPL) that are central to the diagnosis of APS. According to the international consensus statement on classification criteria, APS is classified when persistently elevated levels of specific aPL, such as lupus anticoagulant (LA), anticardiolipin (aCL) and anti-β2 glycoprotein I (anti-β2GPI) antibodies, are confirmed in addition to clinical manifestations (1, 2). The exact pathogenesis of APS is unknown, but aPL have been described to activate monocytes, neutrophils, dendritic cells and placental tissue (3). Despite the fact that many different proteins have been identified as being involved in the pathogenesis of APS, accumulating evidence from in vitro experiments as well as animal studies has revealed that β2GPI is the main target for aPL. It was also shown that triple aPL positivity, defined by detection LA, high titres of aCL and anti-β2GPI antibodies, correlates better with both thrombosis and pregnancy morbidity than any other aPL profile (4).

Several autoantibodies outside those included in APS classification criteria could be also relevant to APS pathogenesis (5) and therefore, antibodies against other antigen targets have been investigated. Current evidence shows that some of these antibodies, particularly antibodies against domain I of β2GPI (anti-DI-β2GPI) and phosphatidylserine dependent anti-prothrombin antibodies (aPS/PT)

might be relevant in the better recognition of APS patients. These antibodies are commonly referred as non-criteria aPL (6) because they have not been yet accepted as laboratory criterion for the diagnosis of APS. The DI of β2GPI has been identified as the most relevant antigenic target involved in β2GPI/anti-β2GPI antibody binding. Anti-DI-β2GPI antibodies were found to be strongly related to thrombosis and pregnancy complication and are more frequently detected in patients with APS than in asymptomatic aPL carriers (7). High titres of anti-DI-β2GPI are also frequently present in triple aPL positive patients. Nevertheless, it is far too soon to recommend replacement of anti-β2GPI testing with an anti-DI-β2GPI antibody assay because it was shown that about 30% of patients with anti-β2GPI antibodies are negative for anti-DI-β2GPI antibodies (8). The clinical significance of autoantibodies reacting with epitopes other than DI was also investigated in multicenter study (9). The results showed a diverse clinical association with reactivity to different epitopes on β2GPI, suggesting all domains were relevant. Therefore, more detailed profiling of domain specificity and avidity of anti-β2GPI antibodies may be useful as risk stratification for clinical events.

aPS/PT antibodies also represent strong risk factor for thrombosis. Results of multicenter study demonstrated that IgG aPS/PT detection might contribute to a better and more reliable identification of APS patients (10).

Due to the heterogeneity of aPL (criteria and non-criteria) the interpretation of aPL results is huge challenge in daily routine practice and should always be related to clinical symptoms and therefore, interaction between the laboratory and clinician is essential.

REFERENCES:

- [1] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006;4(2):295-306.
- [2] Wilson WA, Gharavi AE, Koike T, Lockshin MD, Branch DW, Piette JC, et al. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome: report of an international workshop. *Arthritis Rheum.* 1999;42(7):1309-11.
- [3] Yin D, de Laat B, Devreese KM, Kelchtermans. The clinical value of assays detecting antibodies against domain I of β2-glycoprotein I in the antiphospholipid syndrome. *Autoimmunity Reviews* 2018;17:1210-1218.
- [4] Pengo V, Ruffatti A, Legnani C, Gesele P, Barcellona D, Erba N, Testa S, Marongiu F, Bison E, Denas G, Banzato A, Padayattil JS, Iliceto S. Clinical course of high-riskpatients diagnosed with antiphospholipid syndrome. *J Thromb Haemost* 2010;8:237-242.
- [5] Sciascia S, Amigo MC, Roccatello D, Khamashta M. Diagnosing antiphospholipid syndrome: 'extra-criteria' manifestations and technical advances. *Natural reviews* 2017;13:548-560.
- [6] Amengual O, Atsumi T. Antiphospholipid syndrome: "the best prophet of the future". *Modern Rheumatology* 2018; 409-416.
- [7] Chighizola CB, Gerosa M, Meroni PL. New Tests to Detect Antiphospholipid Antibodies: Anti-Domain I Beta-2-Glycoprotein-I Antibodies. *Curr Rheumatol Rep* 2014;16:402-410.
- [8] Pengo V, Ruffatti A, Tonello M, Cuffaro S, Banzato A, Bison E, Denas G, Padayattil JS. Antiphospholipid syndrome: antibodies to Domain 1 of beta2-glycoprotein 1 correctly classify patients at risk. *J Thromb Haemost* 2015;13:782-787.
- [9] . Artenjak A, Locatelli I, Brelih H, Simoncic DM, Ulcova-Gallova Z, Swadzba J, et al. Immunoreactivity and avidity of IgG anti-beta2-glycoprotein I antibodies from patients with autoimmune diseases to different peptide clusters of beta2-glycoprotein I. *Immunologic Research* 2015;61:35-44.
- [10] Amengual O, Forastiero R, Sugiura-Ogasawara M, Otomo K, Oku K, Favas C, et al. Evaluation of phosphatidylserine-dependent antiprothrombin antibody testing for the diagnosis of antiphospholipid syndrome: results of an international multicentre study. *Lupus* 2017;26:266-76.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Lessons learned from checkpoint inhibitors

SP0177 IMPACT OF CHECKPOINT INHIBITORS ON B CELLS

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Immune checkpoint inhibitors (ICI) are a new class of biological agents that has revolutionized the treatment of cancer. Unlike conventional cytotoxic agents that