B AND T CELL ENGAGEMENT DURING SYSTEMIC LUPUS ERYTHEMATOSUS DEVELOPMENT

Nikolina Mihaylova[1], Silviya Bradyanova[1], Kalina Nikolova-Ganeva[1], Nikola Kerekov[1], Petroslav Chipinski[1], Ekaterina Ivanova-Todorova[2], Dobroslav Kyurkchiev[2], Melinda Herbáth[3], József Prechl[3], Andrey Tchorbanov[1,4]

[1] *Laboratory of Experimental Immunology, Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria*

[2] *Laboratory of Clinical Immunology, University Hospital "St. Ivan Rilski", Department of Clinical immunology, MF, Medical university of Sofia, Sofia, Bulgaria*

[3] *Immunology Research Group, Hungarian Academy of Sciences, Budapest, Hungary*

[4] *National Institute of Immunology, Sofia, Bulgaria*

Background and aims: Self-specific B and T cells play a main role in pathogenesis of Systemic lupus erythematosus (SLE) and are a logical target for selective therapy. The complement receptor type 1 (CR1) on human B-lymphocytes has suppressive activity and engagement of this receptor inhibits B cell activation. The protein Annexin A1 (Anx A1), is a modulator of the immune system and abnormal expression was found on activated B and T cells during human autoimmunity.

We hypothesize that it may be possible to down-modulate the activity of autoreactive T and B cells from SLE patients in humanized NOD/SCID model by treating them with a neutralizing antibody against Anx A1 or by protein engineered molecules, which co-crosslink the BCR and CR1.

Materials and methods: Protein chimeric molecules construction, Immunodeficient NOD/SCID mice transfer with human PBMC from SLE patients, ELISA for dsDNA antibodies and cytokines, flow cytometry for apoptosis and activation markers, ELISpot and MTT assays, protein array.

Results: Reconstituted NOD/SCID mice showed presence of several auto-antibodies, proteinuria, as well as immunoglobulin deposition in the renal glomeruli. Treatment of the transferred NOD/SCID mice either with DNA-like chimera and anti-Anx A1 antibody prevented appearance of anti-DNA antibodies and proteinuria, while the PBS-injected animals had high levels after the transfer. The treatment reduced the levels of disease-associated cytokines also.

Conclusions: It is possible to down-regulate the activity of pathogenic human T and B cells in humanized NOD/SCID mouse model of SLE by targeting Anx A1 or CR1 with a specific monoclonal antibody or chimeric molecule.