cells from RA synovial biopsy cell suspensions (n=4) showed surface expression of CD28.

Conclusions: We have generated a unique dataset from different phases of RA progression. Our results provide guidance for the selection of co-signaling molecules as therapeutic targets as well as for preventing the progression to RA. In particular, *CD28* expression was elevated in synovial tissue biopsies before the development of RA and it was also expressed on the majority of synovial tissue infiltrating CD4+ and CD8+ T cells from RA patients. These observations provide rationale to target CD28 for both RA treatment and disease interception.

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THU0012 | **HLA-DBR1 ALLELES PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS: RELATION TO DISEASE SUSCEPTIBILITY AND SEVERITY**

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Background: Rheumatoid arthritis (RA) is a complex, chronic autoimmune disease (AID) that affects approximately 0.5%–1% of the population worldwide. RA is considered to be complex diseases of unknown etiology, where the environmental, immunological and genetic factors contributed to susceptibility and severity of the disease. Since the first evidence suggesting the involvement of human leukocyte antigens (HLAs) in RA was reported in 1969, the HLA region have been at the center of genetic studies of RA.

Objectives: We undertook this study to elucidate the association between HLA-DRB1 alleles profile and susceptibility to and severity of RA in a Polish population.

Methods: We analyzed the data on a total of 472 RA patients in whom HLA-DRB1 allele genotyping had been performed. DNA sequences for exon 2 of the DRB1 locus were typed using polymerase chain reaction-sequence-based typing (PCR-SBT).

Results: Identification of the variants potentially associated with risk and protection was carried out by comparison to the DKMS Polish Bone Marrow Donor Registry (41306 alleles). A significant increase in the frequency of the HLA-DRB1*15:01 (p=0.001), DRB1*04 (p<0.0001), DRB1*01:01 (p<0.0001), DRB1*10:01 (p=0.003) and *09:01 (p<0.0001) were identified in patients with RA and showed strong association with the disease susceptibility. Furthermore, the HLA-DRB1*07:01 allele was found to be protective (p<0.0001) in our RA patients. In the RA patients with HLA-DRB1*52:01 allele the mean value of PLT (p=0.03) and organ symptoms (p=0.02) were more frequent than in RA patients without this allele. In RA patients with DRB1*01:01, DRB*04 as well as DRB1*15:01 alleles the number of tender joints (p=0.03), diabetes (p=0.03) and renal failure) p=0.03) were observed less frequently compared with RA patients without these alleles. We also observed that in RA patients with DRB1*10:01 the VAS score was higher than in RA patients without this allele.

No association was detect between the HLA-DRB1*07:01 and DRB1*09:01 and disease activity and laboratory parameters among RA patients.

Conclusions: Current finding indicated that HLA-DRB1*15:01 DRB1*04, DRB1*01:01 and DRB1*10:01 alleles may be associated with susceptibility to as well as severity of RA.

Disclosure of Interest: None declared

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THU0013 | **TOWARDS THE DEFINITION OF A RISK MODEL PROFILE OF PERICARDITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A GENETIC STUDY**

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Background: We have recently demonstrated that polymorphisms (SNPs) in TRAF3IP2 gene are associated with susceptibility for systemic lupus erythematosus (SLE) and can predispose to the development of pericarditis (1). Moreover, we found that other genes previously associated with susceptibility to SLE (MIR1279, STAT4, PTPN2) seem to be involved in the development of pericarditis (2). At this

purpose, we built a genetic risk model for the development of pericarditis in SLE (3).

Objectives: We aimed to expand the knowledge on the genetic risk of pericarditis in SLE by studying the role of rs2205960 (TNFSF4) and rs2233945 (ATG16L1) SNPs, previously associated with SLE susceptibility, improving our genetic risk model.

Methods: We recruited SLE patients (diagnosed according to 1997 revised ACR criteria) and healthy subjects served as controls. Study protocol included complete physical examination and blood drawing. The clinical and laboratory data were collected in a standardized, computerized, electronically-filled form (3). Clinical and laboratory features were assessed with a dichotomous score (present=1; absent=0). SNPs genotyping was performed by allelic discrimination assay. A case/control association study and a genotype/phenotype correlation analysis were performed and a risk profile model for pericarditis in SLE was built.

Results: Three-hundred fifteen SLE patients [285 F (90.5%), 30 M (9.5%), mean age 43.11±11.28 years, mean age at onset 32.19±11.84 years] and 278 healthy controls were enrolled. Pericarditis was present in 56 (17.8%) SLE patients. Deviations from Hardy–Weinberg equilibrium for the studied SNPs were not observed. The variant alleles of the rs2205960 (TNFSF4, P=0.013, OR=2.14) and of the rs2233945 (ATG16L1 P=0.009, OR=2.32) were significantly associated with susceptibility to pericarditis. A risk profile model for pericarditis considering the risk alleles of TRAF3IP2, MIR1279, STAT4, PTPN2, TNFSF4 and ATG16L1 showed that patients with more than 5 risk alleles have a significantly higher risk to develop pericarditis (P<0.001, OR=8.01). Anti-Sm antibodies were the only laboratory parameter associated with the development of pericarditis. Thus, a multivariate analysis by binary regression analysis, considering as dependent variable the presence or absence of pericarditis and as independent variables all the studied SNPs associated with pericarditis, was performed. In a stepwise approach including anti-Sm, TRAF3IP2, MIR1279, STAT4, PTPN2, TNFSF4 and ATG16L1 SNPs, the model explains about 25% (R^2 Cox &Snell) of the variability involved in the susceptibility to pericarditis.

Conclusions: We describe for the first time the contribution of TNFSF4 and ATG16L1 SNPs in pericarditis development in SLE patients. We improved our genetic risk profile model to better and earlier identify SLE patients more susceptible to develop this complication.

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THU0014 | **NO ASSOCIATION OF SNP RS3761847 WITH THE EXPRESSION OF THE TRAF1-C5 LOCUS AND INVASION OF RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS**

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Background: Polymorphisms in the *TRAF1-C5* locus have been associated with susceptibility to rheumatoid arthritis (RA). A single nucleotide polymorphism (SNP) rs3761847, located in the first intron of the *TRAF1* gene, has been identified as an RA risk locus in a genome-wide association study (GWAS); the relationship of rs3761847 with joint damage are unclear. One of the key mechanisms of joint destruction is the degradation of and invasion of cartilage by RA synovial fibroblasts (RASF).

Objectives: To determine whether the expression of *TRAF1-C5* genes and the invasion of RASF are associated with the genotype at rs3761847.

Methods: The genotype at rs3761847 was determined via TaqMan Allelic Discrimination Assay. Invasion assays were performed using Matrigel-coated invasion chambers. Peripheral blood mononuclear cells (PBMC) were obtained by density gradient centrifugation. Neutrophils were isolated from the red blood cell layer by erythrocyte lysis; CD14+ cells were separated using magnetic cell sorting. Macrophages were differentiated from plastic-adhered monocytes in M-CSF (50ng/ml) for 8 days. Cells were stimulated with lipopolysaccharide (LPS, 100ng/ml) plus interferon γ (IFNγ, 20ng/ml), interleukin 4 (IL-4, 20ng/ml) or tumour necrosis factor α (TNF-α, 10ng/ml). Gene expression was measured by SYBR Green real-time PCR using HPRT1 as a housekeeping gene.

Results: rs3761847 was in Harvey-Weinberg equilibrium in RASF (n=54, p=0.98) with genotype frequencies of 0.42 AA, 0.45 AG and 0.13 GG. When grouped by genotype, the expression of TRAF1 (total), TRAF1 transcript variant 2 and complement C5 mRNA showed no significant difference (p=0.929, p=0.583, p=0.980 respectively). This was also the case for invasion of RASF (n=43, p=0.548; mean cell count 10.4 AA, 8.3 AG and 11.1 GG). There was no correlation of genotype with common RA disease markers (CRP p=0.718, ESR p=0.179, RF titre p=0.466, ACPA titre p=0.712). In contrast, analyzing TRAF1 expression in different types of blood cells, significantly higher levels of TRAF1 mRNA were detected in monocytes carrying the AA genotype compared with the GG genotype at rs3761847, both in unstimulated (2.26-fold) as well as LPS+IFNγ-activated cells (2.04-fold; p<0.05, n=3 each). No significant association of TRAF1 expression or transcript variant utilization with rs3761847 was observed in the other blood-derived cell types studied, i.e. PBMC, macrophages and neutrophils,