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Genomics, genetic basis of disease and functional genomics

AB0001

INTERFERON SIGNATURE IN CHILDREN WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS AND IT'S DYNAMIC AFTER BISPHOSPHONATES TREATMENT

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Background: Chronic non-bacterial osteomyelitis (CNO) is an immune-mediated chronic inflammatory bone disease which predominantly affects children and adolescents. The pathogenesis of CNO related to imbalance between pro-inflammatory and anti-inflammatory cytokines. Interferon-I mediated pathway is associated with pathogenesis of different pediatric rheumatic diseases, such as juvenile systemic lupus erythematosus (jSLE), juvenile dermatomyositis (JDM), systemic onset of juvenile idiopathic arthritis (soJIA), and, most of all, with macrophage activation syndrome. The data on interferon-I regulated pathway in CNO is absent. NSAIDs, non-biologic and biologic anti-inflammatory drugs and bisphosphonates (BF) are treatment options for patients with CNO. The main adverse event of BF is a flu-like syndrome probably caused by the excessive cytokine release stimulated by BF.

Objectives: The aim of our study was to evaluate activity of Interferon-I mediated pathway in CNO patients and it's dynamics after BF treatment.

Methods: This prospective study included children with CNO requiring BF treatment (n=9), patients with soJIA (n=8), JDM (n=11) and jSLE (n=40) and healthy controls (HC, n=21). The activity of Interferon-I mediated pathway was assessed using interferon I score (IFN1 score). The score represented the median expression of 5 IFN1-regulated genes (IFI44L, IFI44, IFIT3, LY6E, MX1) measured by quantitative real-time PCR. Patients with CNO were treated with standard 3-day regimen (1 mg/kg/day). We measured interferon score before pamidronate (Day 0, n=9) and after (Day 3, n=7).

Results: Median interferon score was 1.09 (0.96; 1.67) in CNO patients, 1.95 (1.3; 5.75) in soJIA, 7.6 (1.78; 29.0) in JDM and 16.9 (2.55; 40.3) in jSLE and 0.95 (0.82; 1.17) in HC (p=0.00001). Where were no difference in the IFN1 score between CNO and HC (p=0.222). In 6/7 CNO patients interferon score increased after pamidronate (p=0.015). The median interferon score after pamidronate increased and became 3.06 (0.87; 4.9, p=0.043); this may possibly explain the development of BF-related flu-like symptoms (cytokine release syndrome).

Conclusion: While interferon I-regulated pathway is not directly associated with CNO pathogenesis, BF likely activates interferon-I-regulated pathway and thus could be a possible cause of flu-like syndrome.

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AB0002

ASSOCIATION OF C1Q GENETIC POLYMORPHISMS WITH SUSCEPTIBILITY TO RHEUMATOID ARTHRITIS IN BULGARIAN COHORT

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Background: Complement is strongly implicated in the pathogenesis of autoimmune diseases like systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Its component C1q plays a dualistic role, triggering the inflammatory cascade on one hand and directing the clearance of immune complexes on the other. Homozygous genetic deficiency of C1q is strongly associated with SLE and SLE-like phenotype as almost 90% of C1q deficient individuals develop SLE or similar disease. Nevertheless, there are few and inconsistent studies exploring the single nucleotide polymorphisms (SNPs) of the C1q gene cluster in relation to the pathogenesis of SLE and RA.

Objectives: The aim of the study was to evaluate the possible association of five SNPs – rs292001, rs172378, rs294179, rs665691 and rs682658 in complement C1q gene cluster with susceptibility to SLE and RA in Bulgarian cohort.

Methods: Fifty patients with SLE, sixty-one patients with RA and sixty-seven healthy controls were genotyped for the five SNPs by TaqMan allelic discrimination assay.

Results: Frequency of genotypes and alleles of rs294179, rs665691 and rs682658 SNPs was similar between patients with SLE, RA and healthy controls. For rs172378 SNP, the minor G allele (OR = 2.73; 95% CI, 1.59-4.67, p=0.0003) and GG genotype (OR = 5.12; 95% CI, 1.60-16.49, p=0.006) were associated

with susceptibility to RA. In our cohort in accordance with others, AA rs292001 SNP genotype was associated with increased risk for RA (OR = 3.32; 95% CI, 1.19-9.20, p=0.021). For SLE patients, AA rs292001 SNP genotype was low presented and did not associate with disease.

Conclusion: GG genotype of rs172378 SNP in C1q gene cluster could be considered as a new risk factor for RA.

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AB0003

HLA-ALLELES IN SUSCEPTIBILITY TO SYSTEMIC AND OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS IN THE BELARUSIAN POPULATION

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Background: Juvenile idiopathic arthritis (JIA) is a complex trait, the most common rheumatic disease in children. Considering clinical heterogeneity of the disease, the genetic background of particular JIA subtypes may also vary significantly.

Objectives: This work was aimed to reveal characteristic patterns of HLA associations within 11 loci for two clinically different forms of JIA in the Belarusian population.

Methods: 24 patients diagnosed with systemic JIA, 24 patients with oligoarticular JIA and 24 healthy controls were included into the study. The JIA patients were divided into subgroups according to IAR classification criteria. High-throughput HLA typing was performed using TruSight HLA v2 Sequencing Panel (Illumina) on MiSeq system. Sample analysis was performed using Assign TruSight HLA v2.0 software.

Results: *DQA1**05:01:01 and *DQB1**02:01:01 alleles showed protective effect against both systemic (p = 0.007; OR=0.08; 95% CI=[0.009-0.65] and p = 0.01; OR=0.09; 95% CI=[0.01-0.83]) and oligoarticular JIA