AB0009 PADI4 GENE POLYMORPHISM AS A PREDICTOR OF RESPONSE TO METHOTREXATE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Methotrexate (MTX) is the most widely used disease-modifying anti-rheumatic drug in the treatment of juvenile idiopathic arthritis (JIA); however, there is a variation in the clinical response to MTX among the patients [1]. Previous studies have shown conflicting results regarding predictors of the response to MTX. No unequivocal predictive SNP has been found yet, because many were assessed in only one study, or were predictive in one study and showed no effect in others [2].
Objectives: The aim of the study was to assess whether the *PADI4* rs2240336 gene polymorphism is a predictor of the disease severity and the response to MTX in patients with JIA from Bashkortostan, Russia.
Methods: 283 patients with JIA were genotyped for the *PADI4* rs2240336 gene polymorphism using real-time PCR. The statistical analysis was performed using two-tailed Fisher's exact test, odds ratio, 95% confidence interval and logistic regression in Microsoft Excel, WinPepi v.11.44, R v.3.2.0, SNPStats programs. The disease course was assessed as more severe if the MTX therapy was required. The response to MTX was considered as good if clinical remission on medication (Wallace) was achieved, otherwise – as insufficient. An addition of a biological agent to the MTX therapy was also assessed as a marker of an insufficient response.
Results: The requirement of the MTX treatment and its absence was noted at 261 (92.3%) and 22 (7.8%) children with JIA respectively, and the distribution of the genotypes and alleles of the *PADI4* rs2240336 gene polymorphism were similar in both groups (p=0.982). At the same time the frequency of the genotype AG was significantly higher (59.8% vs. 35.5%, p=0.0029, OR=2.71, 95% CI 1.41–4.94), and the frequency of the genotype GG was significantly lower (23.8% vs. 45.2%, p=0.0041, OR=0.38, 95% CI 0.20–0.73) in patients, who received MTX and not achieved clinical remission on medication (n=122) than in those who achieved (n=62). The best model of inheritance was overdominant, where the genotype AG marked an insufficient response to MTX (AG vs. GG + AA, p=0.0017, OR=2.71, 95% CI 1.44–5.11). The association with an insufficient response to MTX was also observed under the dominant (AG + AA vs. GG, p=0.0034, OR=2.64, 95% CI 1.38–5.06) and codominant (AG vs. GG, p=0.0041, OR=3.20, 95% CI 1.58–6.48) models of inheritance. Moreover, the genotype AG frequency was significantly elevated in patients who required an addition of a biological agent to the MTX therapy (n=73) (p=0.012, OR=2.097, 95% CI 1.20–3.66) and the overdominant model of inheritance also proved the best (p=0.0088, OR=2.10, 95% CI 1.20–3.68).
Conclusions: Thus, in this study we revealed that the genotype AG of the *PADI4* rs2240336 gene polymorphism was a marker of increased risk of an insufficient response to MTX in children with JIA from Bashkortostan, Russia. If this finding will be confirmed in other studies, it can be potentially used for the early prediction of the response to MTX in patients with JIA.
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AB0010 ASSOCIATION OF GENE POLYMORPHISMS IN ETS-1 WITH RANKL IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a complicated autoimmune disease characterized by progressive destruction of cartilage and bone. Recently, receptor activator of nuclear factor κB ligand (RANKL) have been found to be involved in the differentiation of osteoclasts [1]. Also, the association between the RANKL expression and the pathogenesis of bone-destructive rheumatoid arthritis (RA) has been described in several joints [2]. It indicated that RANKL play a crucial rule in RA. Meanwhile, E26 transformation specific sequence 1 (ETS-1), belonging to the ETS family of transcription factors that regulate the expression of various immune-related genes, was reported to confer susceptibility and development to RA [3]. Moreover, ETS-1 was found to be overexpressed in RA synovial membrane and to be involved in the destructive pathway of RA [4], but it was not clearly defined.
Objectives: We aimed to identify how RANKL changes in RA and whether polymorphisms in ETS-1 play a role in that changes by describing in Chinese Han population.
Methods: 170 RA patients and 136 healthy controls were included for this analysis. Clinical information was gathered and disease activity was determined according to the disease activity score for 28 painful/swollen joints (DAS28). The serum level of RANKL were detected by magnetic luminex assays. Four single nucleotide polymorphisms (SNPs) in ETS-1 were genotyped by high resolution melting (HRM) curve method.
Results: Compared with healthy controls, Level of RANKL in serum of patients was elevated (28.69 (17.24–44.90) versus 14.24 (17.00–20.00), $P<0.01$). The RA patients with rs73013527 TT genotype had higher RANKL levels (P=0.019 in a dominant model). Furthermore, we found that T allele of rs73013527 was overrepresented in RA group as well (25.7% versus 42.6%, $P<0.001$). Besides, an association was found between rs73013527 TT genotype and DAS28 (P=0.001). No statistically significant difference was observed in the distribution of other three SNPs (rs10893872, rs4937333 and rs11221332) alleles or genotypes in this study (all $P>0.05$).
Conclusions: This study suggests that RANKL increased in RA and the polymorphisms in the ETS-1 region may be associated with the changes of RANKL in RA. The patients with rs73013527 TT genotype may be not prone to RA but have higher RANKL which could lead a sever condiction. However, larger studies, most likely through multicenter collaboration will be needed to fully validate the significance of these findings.
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AB0011 HLA-DP POLYMORPHISMS PLAY PROTECTIVE ROLE IN SYSTEMIC LUPUS ERYTHEMATOSUS IN CHINESE HAN POPULATION

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Background: With the application of Genome-Wide Association studies (GWAS), the SLE risk gene loci in HLA-DR and HLA-DQ are gradually revealed [1]. However, the association of HLA-DP polymorphisms with SLE is pretty few reported. Considering the variants in rs3077 and rs9277535 in HLA-DP region were estimated influenced the immune response by affecting antigen presentation of HLA class II molecules to CD4+ T cells [2], it is worthy to explore the role of HLA-DP polymorphisms in SLE.
Objectives: Exploring the effects of presently hot HLA-DP SNPs, rs3077 and rs9277525 on SLE.
Methods: 335 SLE patients and 635 healthy controls were recruited in present study. Genotyping was performed with polymerase chain reaction-high resolution melting (PCR-HRM) assay and the data was analyzed using SPSS19.0.
Results: A significantly positive correlation was observed between the SNP rs3077 and rs9277535 of HLA-DP and SLE susceptibility (rs3077, OR=0.74, 95%CI=0.60–0.91, P=0.004; rs9277535, OR=0.72, 95%CI=0.60–0.91, P=0.001). Moreover, in cytokines, there was significant positive association between rs3077 and IL-17 and INF-γ(P=0.037 and P=0.020 respectively; recessive model, P=0.011 and P=0.008, respectively) and the AA genotype predisposed to lower IL-17 and INF-γcompared with other two genotypes. However, none positive connection was found between rs3077 and IL-1 alpha, IL-4, IL-6, IL-10, and IL-23 (P=0.739, 0.624, 0.685, 0.887, and 0.937 correspondingly). None significant positive correlation could be observed between rs9277535 and any cytokines.
Conclusions: HLA-DP polymorphisms (rs3077 and rs9277535) play a protective role in SLE susceptibility. And rs3077 play the role by affecting antigen presentation of HLA class II molecules for CD4+T cells and down-regulating the Th17 signal pathway.
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