Objectives: To verify the hypothesis about the role of SAA1 rs12218 T/C gene polymorphism in the aptitude to various clinical JIA phenotypes.

Methods: The study included 132 children, of whom 66 were diagnosed with JIA and 66 were healthy unrelated volunteers (the college students) as a control group, comparable by gender and age. The group of patients with JIA consisted of 44 girls and 22 boys, with an average age of 11.7 ± 4.2 years and an average disease duration of 4.8 ± 3.8 years. The diagnosis and classification of JIA was established according to ILAR-2004 criteria. The JIA group included 30 (45%) patients with oligoarthritis (uJIA), of which 20 patients (67%) were negative for the HLA-B27 antigen (JIA-B27−) and 10 (33%) patients with anterior uveitis (uJIA); 20 (30%) patients were assigned to the group with the polyarticular variant (pJIA), while all of them were seronegative for the rheumatoid factor; 16 (24%) patients were diagnosed with JIA with a systemic onset (sJIA). The frequencies of the T/C polymorphism of the SAA1 gene were assessed using an allele-specific polymerase chain reaction in a real-time mode (RT-PCR).

Results: In the group of patients diagnosed with uJIA and (JIA-B27−), the frequency of the C allele was significantly higher compared to the control (53.3% and 57.5% versus 37.1%, p = 0.035 and 0.022, respectively). No significant differences were detected in the frequencies of the mutant C allele between sJIA and pJIA and the control group. The logistic analysis of the frequency distribution of the alleles of the SAA1 gene demonstrated an increased risk of the C allele in formation of an aptitude to the uJIA variant (OR 1.94, 95% CI 1.00-3.76, p = 0.048). In the sJIA group, the risk of the C allele aptitude was also increased compared to the control (OR 2.29, 95% CI 1.05-5.04, p = 0.022).

Conclusion: The data obtained confirm for the first time the involvement of the rs12218 polymorphism of the SAA1 gene in an aptitude to the oligoarthritis JIA clinical phenotype. The presented results require further replication researches using an enlarged number of patients from different population groups.

Disclosure of Interests: None declared

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AB0020

CORRELATION BETWEEN SERUM AND SYNOVIAL EXPRESSION OF IL-17A AND MIRNA IN PATIENTS WITH RHEUMATOID ARTHRITIS PATIENTS

R. Shumnaileva1, D. Kachakova2, T. Velikova3, R. Kaneva2, Z. Kolarov2, S. Monov1. 1Medical University – Sofia, Bulgaria; 2Department of Internal Medicine, Clinic of Rheumatology, Sofia, Bulgaria; 3Medical University – Sofia, Department of Medical Chemistry and Biochemistry, Molecular Medicine Center, Sofia, Bulgaria; 4Clinical Immunology, University Hospital Lozenetz, Sofia, Bulgaria

Background: Interleukin 17 (IL-17) is a proinflammatory cytokine, which overproduction promotes the autoimmune reaction in rheumatoid arthritis (RA). Posttranscriptional regulation of IL-17 by specific microRNAs (miRNAs) is of great interest in the recent years. 146a was associated with IL-17 expression in IL-17 producing T-cells in the synovium when miR-155 enhanced Treg and Th17 cells differentiation and IL-17A production by directly targeting the suppressor of cytokine signaling 1 (SOCS) 1. It has been shown that IL-17 production in lymphocytes or T-cells in the synovium when miR-155 enhanced Treg and Th17 cells differentiation and IL-17A production by directly targeting the suppressor of cytokine signaling 1 (SOCS) 1. It has been shown that IL-17 production in lymphocytes or T-cells in the synovium when miR-155 enhanced Treg and Th17 cells differentiation and IL-17A production by directly targeting the suppressor of cytokine signaling 1 (SOCS) 1. It has been shown that IL-17 production in lymphocytes or T-cells in the synovium when miR-155 enhanced Treg and Th17 cells differentiation and IL-17A production by directly targeting the suppressor of cytokine signaling 1 (SOCS) 1.

Objective: To examine a possible correlation between systemic and local concentrations of IL-17A and systemic and local mir-146a, mir-155 and mir-223 expression in RA patients.

Methods: Expression levels of three miRNAs were determined in matched serum and SF samples of RA patients by quantitative real-time polymerase chain reaction method. RT-PCR was used. Determination of IL-17A were compared between matched serum and SF samples from 20 RA patients by Human IL-17A ELISA kit (Gene probe, Diacilone, France). Healthy donors were used as controls.

Results: mir-146a, mir-155 and mir-223 showed overexpression in RA SF when compared to HC SF (in 70.83%, p=0.007; in 79.17%, p=1.6x10^-4 and in 79.17%, p=1.6x10^-5, respectively). The ROC curve analysis showed diagnostic accuracy for mir-146a in SF with AUC=0.769, p=0.006. AUC for SF mir-155 was 0.858, p=2.3x10^-7 and AUC for SF mir-223 was 0.841 p=4.8x10^-5. SF levels of mir-146a and mir-155 were overexpressed in 52.17% and in 76.09% of the RA patients compared to its systemic levels, SF mir-223 was underexpressed in 58.7% of the patients compared to its systemic levels. Levels of IL-17A were higher in RA SF compared to serum (8.645 pg/ml versus 0.315 pg/ml, p=0.012). ROC curve analysis for SF IL-17A showed area under the curve (AUC) = 0.885, p<0.0001.

Conclusion: The difference between the systemic and local concentration of IL-17A and miRNAs expression shows that the inflammatory disease process leads to their altered expression with a possible role of these molecules in the disease pathogenesis. The higher local levels of mir-155, mir-146 and IL-17A confirm the data about the possible role of these miRNAs in regulating IL-17A production. The opposite changes of IL-17A and miR-223 systemic and local levels confirm the data about the possible role of miR-223 in regulating IL-17 function. Further analysis with larger sets is needed to confirm these results.

References:

Acknowledgments: The study was supported by Grant 14-D-2012, Grant 60/2013 and Grant 61/2011 from Medical University-Sofia, Bulgaria.
An increase in the factor load indices for IgA to CD74 (R=0.925) was established, provided that the IL-17F genotype is homozygous for the his/arg allele (R=0.544). The genotypes IL-17F his/his showed an inverse interrelation with the increase in serum IgA to CD74 level (R=0.421).

Conclusion: Serum concentration of IgA to CD74 exceeded normal reference level in axSpA patients in 70.1% of cases that was associated with ASDAS and BASDAI levels. Presence of heterozygote IL-17F polymorphism in his/arg allele was associated with increasing serum concentration of IgA to CD74 and with increased disease activity (ASDAS and BASDAI). Decreasing of serum IgA to CD74 concentration, less axSpA activity (ASDAS and BASDAI) were found in patients with presence of heterozygote IL-17F polymorphism in his/arg allele.

Disclosure of Interests: Elizaveta Vasilienko: None declared, Maxim Korolev: None declared, Sergey Lapin: None declared, Irina Kholopova: None declared, Anna Dadalova: None declared, V Mazurov: None declared, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau. Pfizer, Novartis, AbbVie, JSC BIOCAD, Celgene, MSD, Sanofi

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AB0023

ASSOCIATION OF NCF2, NCF4 AND CYBA GENES POLYMORPHISMS WITH RHEUMATOID ARTHRITIS IN A CHINESE POPULATION

T. P. Zhang1, Q. Huang2, H. F. Pan3, D. Q. Ye4, X. Li5 on behalf of the. 1The First Affiliated Hospital of University of Science and Technology of China, Hefei, China; 2Anhui Medical University, Hefei, China; 3The First Affiliated Hospital of University of Science and Technology of China, Hefei, China

Background: Recent studies have focused on the special roles of NADPH-oxidase, which is composed of gp91phox, p22phox, p47phox, p67phox, p40phox encoded by CYBB, CYBA, NCF1, NCF2, NCF4 genes, in multiple autoimmune diseases. Nevertheless, the association of genetic variation in NADPH-oxidase genes with rheumatoid arthritis (RA) was not extensively studied in Chinese population.

Objectives: We performed this study to examine the association of NCF2, NCF4, CYBA genes polymorphisms with RA susceptibility in a Chinese population.

Methods: Six single nucleotide polymorphisms (SNPs) (NCF2 rs10911363, NCF4 rs1883131, rs4821544, rs729749, CYBA rs3794624, rs4673) were genotyped in a cohort composed of 593 RA patients and 596 normal controls. All patients were consecutively enrolled from the Department of Rheumatology at the First Affiliated Hospital of University of Science and Technology of China and the First Affiliated Hospital of Anhui Medical University, and the normal controls was enrolled from the same region. Improved multiple ligase detection reaction (iMLD R) was used for genotyping. Chi-square (χ2) test was used to analyze the association of the genotype and allele frequencies of above SNPs and RA. Odds ratios (OR) and 95% confidence interval (CI) were also evaluated using Logistic regression analyses, and haplotype analysis was assessed using SHEsis software.

Results: There were 101 males and 492 females in RA group with a mean age of 51.59±6.68 years, and the normal control group included 97 males and 499 females with an average age of 52.32±12.63 years. We observed that NCF4 rs4821544 CT genotype, C allele frequencies in RA patients were significantly decreased when compared to controls (CT vs. TT: P = 0.043; CC vs. CT: P = 0.031), and rs4821544 polymorphism was significantly associated with an increased RA risk under the dominant model (TT vs. CT+CC: P = 0.031). Moreover, our results also indicated that rs729749 CT genotype frequency was significantly lower in RA patients than that in controls (CT vs. CC: P = 0.033). No significant association between NCF2, CYBA genes polymorphisms and RA susceptibility was observed. There were no significant differences in allele, genotype frequencies of above SNPs between RA patients with RF-positive and with RF-negative, as well as anti-CCP-positive RA patients and anti-CCP-negative RA patients.

Conclusion: In summary, NCF4 rs4821544, rs729749 polymorphisms might contribute to RA susceptibility, while NCF2, CYBA genes polymorphisms were not associated with RA susceptibility.

References:

AB0022

INTERRELATIONS OF INCREASED AXIAL SPONDYLOARTHRITIS ACTIVITY AND THE SERUM CONCENTRATION OF IMMUNOGLOBULIN A TO CD74 WITH GENETIC POLYMORPHISMS OF INTERLEUKIN 17 ALLELES

E. Vasilienko1,2, M. Korolev1, S. Lapin1, I. Kholopova1, A. Dadalova1, V. Mazurov1, I. Gaydukova1,2. 1North-Western State Medical University named after I.I. Mechnikov, Department of Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E. Ewaldch, St. Petersburg, Russian Federation; 2St Petersburg Clinical Rheumatology Hospital No.25, St. Petersburg, Russian Federation; 3The Federal Research Center Institute of Cytology and Genetics, Novosibirsk, Russian Federation; 4The First Pavlov State Medical University of St. Petersburg, Laboratory for Diagnostics of Autoimmune Diseases, St. Petersburg, Russian Federation

Background: Genetic predisposition takes one of the main parts at pathogenesis of axial spondyloarthritis (axSpA). Currently, HLA-B27 is a single genetic marker that used in classification criteria of axSpA. However, the presence of HLA-B27 does not affect the activity of the disease. An alternative biomarker of axSpA activity could be an immunoglobulin (Ig) A antibody to an invariant chain peptide associated with class II human leukocyte antigen (HLA) (anti-CD74).

Objectives: The goal is to determine genetic polymorphisms of IL17 alleles prevalence in patients (pts) with axSpA and their interrelations with the disease activity and concentration of IgA to CD74.

Methods: In 48 patients with a reliable diagnosis of axSpA, aged 18 to 69 years ASDAS, BASDAI, BASFI were calculated. The polymorphisms of alleles of interleukin (IL)-17A-197 a/g, IL-17F7 his/his, IL-17F -11139 c/g, IL-17B -27 his/his were evaluated. Serum concentration of IgA to CD74 was measured (the normal reference interval according to the instructions for the laboratory kit for serum IgA to CD74 is 0.2-10.0 U/L).

Results: The mean age of pts was 45.1±14.2 years, male 72.9%, BASDAI 4.7±2.6, BASFI 3.0±2.5, BASFI was enrolled from the same region. Improved multiple ligase detection reaction (iMLD R) was used for genotyping. Chi-square (χ2) test was used to establish the relation between interleukin-17 alleles' polymorphisms in patients with axial spondyloarthritis, n=48.

Disclosure of Interests: Rafał Czajkowski: None declared, Ewa Robak: None declared, Mariusz Gawrylowicz: None declared, Anna Dadalova: None declared, V Mazurov: None declared, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau. Pfizer, Novartis, AbbVie, JSC BIOCAD, Celgene, MSD, Sanofi

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Table 1. Interleukin-17 alleles’ polymorphisms in patients with axial spondyloarthritis, n=48

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Pts with presence of polymorphism, n</th>
<th>Pts with presence of polymorphism, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-17A-197 AA</td>
<td>14</td>
<td>IL-17F7 his/his</td>
</tr>
<tr>
<td>IL-17A-197 GG</td>
<td>18</td>
<td>IL-17F7 his/his</td>
</tr>
<tr>
<td>IL-17A-197 GG</td>
<td>16</td>
<td>IL-17F7 arg/arg</td>
</tr>
<tr>
<td>IL-17F7-11139 CC</td>
<td>26</td>
<td>IL-17F7-11139 CC</td>
</tr>
</tbody>
</table>

Exceeded levels of IgA to CD74 were identified at 96 pts (70.1%). The factor analysis showed a relationship between ASDAS (R=0.857), BASDAI (R=0.842), BASFI (R=0.857) and level of IgA to CD74 (R=0.667), (table 2).

Table 2. Interrelations between serum concentration of IgA to CD74, the activity indices and genetic polymorphisms of interleukin-17 alleles in axSpA patients (factor loads), n=48

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Factor loading (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
<td>Factor 1</td>
</tr>
<tr>
<td>IgA anti-CD74</td>
<td>0.525</td>
</tr>
<tr>
<td>BASDAI</td>
<td>0.734</td>
</tr>
<tr>
<td>ASDAS</td>
<td>0.657</td>
</tr>
<tr>
<td>BASFI</td>
<td>0.545</td>
</tr>
<tr>
<td>IL-17 F7 His/His</td>
<td>-0.421</td>
</tr>
<tr>
<td>IL-17F7 His/Arg</td>
<td>0.631</td>
</tr>
</tbody>
</table>