was significantly higher in the GPA-AAV group (%7.14 vs. %0.26 p<0.01, OR=30, %95 CI: 3.8–237). No significant difference was detected between the MPO-AAV and control groups.

Conclusion: HLA analysis of this small series of Turkish AA patients revealed a negative correlation between PR3-ANCA positivity and HLA-DRB1*04:01 and HLA-DPB1*02:01 alleles in opposition to the results reported from different European AAV cohorts (1:3). On the other hand, a significant increase in both GPA and PR3-AAV subgroups for a previously unpublished HLA-DRB1*16:01 allele may suggest that HLA association may show ethnic or regional differences, and further analyses in larger series of AA patients may reveal the molecular basis of this observation.

REFERENCES

Disclosure of Interests: None declared


AB0007

IL12B POLYMORPHISMS ARE ASSOCIATED WITH ELEVATED SERUM LEVELS OF IL-12P40, IL-23 AND GENETIC PREDISPOSITION TO RHEUMATOID ARTHRITIS

Mariana Ivanova Goycheva1, Irena Manolova1, Georgi Vasilev2, Lyuba Miteva3, Rumen Stolirov4, Spaska Stanilova5, 1Medical Faculty, Medical University, University Hospital "St. Ivan Rilski"; Clinic of Rheumatology, Sofia, Bulgaria; 2Medical Faculty, Trakia University, Department of Molecular Biology, Immunology and Medical Genetics, Stara Zagora, Bulgaria; 3Medical Faculty, Medical University, University Hospital "St. Ivan Rilski"; Laboratory of Clinical immunology, Sofia, Bulgaria; 4Medical Faculty, Medical University, University Hospital "St. Ivan Rilski"; Clinic of Rheumatology, Sofia, Bulgaria

Background: Rheumatoid arthritis (RA) is the most common type of autoimmune arthritis in which genetic predisposition in close interaction with environmental triggers seems to be the major factor in the disease pathogenesis. Genetic analyses suggest a polygenic inheritance, as the largest genetic contribution to RA susceptibility remains the HLA–DRB1 gene, residing within the HLA gene complex. Since immune dysregulation plays a key role in immune-mediated inflammatory disorders, genetic variations within cytokine loci may contribute to variability in the immune response determining susceptibility or resistance to a certain autoimmune disease.

Objectives: We aimed to investigate whether IL12B polymorphisms are involved in causation of RA and in variations of circulating IL-23 and IL-12p40 levels in our Bulgarian population.

Methods: A total of 125 RA patients aged from 18 to 79 years in comparison to 124 age- and sex-matched healthy controls (HC) were genotyped for rs17860508 and rs3212227. Both IL12B polymorphisms were investigated by polymerase chain reaction (PCR) - based methods. Serum IL-12p40 and IL-23 concentrations measurement was done using ELISA test in 67 RA patients and 55 age-matched HC.

Results: An association between the rs17860508 polymorphism and RA development was established under the allelic model (allele 2 vs allele 1; OR = 1.68, 95%CI = 0.91–3.14; p = 0.017), the recessive model (allele 2 vs allele 1 + allele 3; OR = 2.00, 95%CI = 1.10–3.41; p = 0.017), and the dominant model (1 + 2 vs 1; OR = 2.11, 95%CI = 1.15–3.90, p = 0.014), and the recessive model (1 + 2 vs 1; OR = 2.00, 95%CI = 1.10–3.62, p = 0.022). These results suggest that the homozgyous 2 genotype could be predisposing, while 1.1 genotype might be protective factor to RA susceptibility. No association between the rs3212227 and RA risk was revealed under the same genetic model.

Methods: The study included 59 patients with rheumatoid arthritis (RA) and 59 age sex-matched healthy controls (HC). The age range for patients was from 18 to 79 years. The mean age of RA patients was 52.8 years with 54% females and 46% males. The mean age of HC was 48.4 years with 56% females and 44% males. In all patients, serum levels of IL-12p40 and IL-23 were measured using ELISA test. All patients were divided into three groups: 1) early disease onset (<5 years) n=22; 2) disease duration of 5-10 years n=30; 3) disease duration of >10 years n=7. The differences in circulating IL-12p40 and IL-23 levels between the groups were analyzed by using two-tailed unpaired Student’s t-test. A p-value < 0.05 was considered statistically significant.

Results: The mean IL-12p40 levels were significantly higher in the early disease onset group compared to the other groups (p=0.037). No significant difference was observed in the IL-23 levels between the groups. The highest circulating IL-23 levels were observed in carriers of the rs3212227 AA genotype and rs17860508 2.2 genotype compared to the remaining genotypes.

Conclusion: IL12Bpro (rs17860508) and 3’ UTR (rs17860508) polymorphisms does confer susceptibility to RA either as an individual or combinatorial effect and might influence the RA occurrence through regulating the expression of IL-12/IL-23 family proteins.

Disclosure of Interests: Mariana Ivanova Goycheva Speakers Bureau: Abbvie, Pfizer, UCB, Novartis, Irena Manolova: None declared, Georgi Vasilev: None declared, Lyuba Miteva: None declared, Rumen Stolirov Speakers Bureau: Abbvie, Pfizer, Amgen, UCB, Novartis, Spaska Stanilova: None declared


AB0008

CLINICAL AND GENETIC FEATURES OF NON-BACTERIAL OSTEOYELITIS IN RUSSIAN FEDERATION

Mikhail Kostik1, Maria Makhova1, Evgeniy Suspitin1,2, Anna Sokolenko1,2, Vyacheslav Zorin3, Eugenia Isipova3, Shamil Magomedov4,5, Inna Kostik6, Hiroshi Takayanagi7, Alexander Mushkin7, Evgeny Irmantov1,2, 1Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russian Federation; 2N.N. Petrov Institute of Oncology, Saint-Petersburg, Russian Federation; 3Science research Institute of Phthisiopulmonology, Saint-Petersburg, Russian Federation; 4Republican Children's Clinical Hospital, Makuhakha, Russian Federation; 5Dagestan State Medical Academy, Makhaakha, Russian Federation; 6Children's Rehabilitation Center "Detyske Dury", Saint-Petersburg, Russian Federation; 7The University of Tokyo, Tokyo, Japan

Background: Chronic non-bacterial osteomyelitis (CNO) is Data about incidence, prevalence and clinical and genetic features of chronic non-bacterial osteomyelitis (CNO) in Russia is scarce.

Objectives: The aim of our study was to evaluate clinical and genetic peculiarities of CNO in Russia.

Methods: The diagnosis of CNO was made with criteria, proposed by Jansson [1, 2], after the exclusion of other causes of bone disease. Our cohort consists of three main subtypes: i) early-onset (<5 years) CNO (n=22); ii) CNO, associated (n=20) and iii) not associated (n=59) with rheumatic diseases (RD). Targeted next generation sequencing (NGS) analysis of 302 genes related to primary immune deficiencies and autoinflammatory syndromes was performed.

Results: We selected a subgroup of the CNO patients having the following features: 1) early disease onset (<5 years); 2) all children were initially diagnosed as having tuberculosis (TB) due to bone morphology findings (granulomatous, e.g. tuberculosis-like infection), but had negative TB culture test; 3) initial treatment with combination of 3-4 anti-MBT drugs during 1-2 years was ineffective, and the patient continued to develop new inflammatory bone foci; 4) patients had very severe clinical (fever and systemic arthritis) and radiological signs of disease; 5) all patients were from areas with traditionally high prevalence of consanguinity (table).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EO-CNO</th>
<th>CNO w/o RD</th>
<th>CNO with RD</th>
</tr>
</thead>
</table>
| Onset age, years          | 3.0    | 7.3 (2.8-11.7) | 10.3 (6.2-12.2) | 0.0009
| Fever at onset, n (%)     | 14/22  | 23 (39)    | 5 (25) | 0.03
| Foci number               | 5.0    | 3.0 (1.0-4.0) | 2.0 (1.0-6.0) | 0.048
| Symptomatic arthritis, n %| 20/22  | 33 (56)    | 17 (85) | 0.003
| North Caucasian origin, n%| 22 (100) | 0 (0) | 0 (0) | <0.00001
| Granulomatous inflammation| 22 (100) | 0 (0) | 0 (0) | <0.00001
| Prevalence of CNO         | 1/42,000 | 1.450,000 | 1.375,000 | <0.00001

In the subgroup patients with early onset we performed genetic tests. Rare variants of PID genes were detected in 7/22 (32%) patients. Mutations affecting the genes previously associated with CNO were found only in two patients: one of them carried heterozygous variant IL1RN c.170G>T (p.C57F) and another had IL1RN c.512T>C (p.V171A). No mutation of LPIN2 was revealed. Other detected variants included one pathogenic MEVF p.M694V mutation in heterozygous state and a number of VUS in CD40LG, NLRP12, CR2, NLRP3, IL12B, PLCG2, SH3BP2, CARD14, IRF8, CASP10 and NFKB1A genes.
Conclusion: We have found the unique regional subtype of CNO with early-onset in North Caucasus region with at least 10 times higher prevalence. We have not yet seen similar patients in other nationalities of Russia. Mutations in known genes were detected only in a minor fraction of CNO patients from Dagestan and Chechnya. This work supported by the Russian Foundation for Basic Research (grant No 18-515-57001) and by Japan Medical Research Foundation (grant No 18mrf001).

REFERENCES


Disclosure of Interests: None declared

AB0009 IDENTIFICATION OF A NOVEL POLYMORPHISM OF ERAPI IN A GROUP OF ITALIAN PATIENTS WITH BEHÇET SYNDROME

Nancy Lascaro1, Pietro Leccese1, Salvatore D’Angelo2,3, Teresa Carbone1, Angela Padula1, Giuseppe Martelli1, Maria Carmela Padula1,2,3. 1Rheumatology Institute of Lucania (IReL), San Carlo Hospital, Potenza, Italy; 2Basilicata Ricerca Biomedica (BRB) Foundation, Matera, Italy; 3University of Basilicata, Department of Science, Potenza, Italy

Background: The endoplasmic reticulum aminopeptidase protein 1 gene (ERAP1) was associated to several human diseases, including Behçet syndrome (BS), a multisystemic disorder with unknown etiology. ERAPI1 protein is involved in immune response and its role can be influenced by gene single nucleotide variations (SNVs) with an unclear mechanism [1-5].

Objectives: We aim to genotype ERAPI whole structure searching for SNVs, in 50 consecutive BS patients and 50 sex and ethnically-matched healthy controls (HC) unrelated to each others and/or to BS patients.

Methods: We used both bioinformatics and molecular methodologies. Specific primers for the coverage of all ERAPI1 regions were designed using the NCBI Primer-Blast tool. Genomic DNA was extracted from whole blood and amplified using in vitro PCR. Good-quality PCR amplicons were directly sequenced using the QATC Biotech Sanger sequencing service and bioinformatically analysed using Mutation Surveyor software and NCBI-Blat Nucleotidc on line similarity search tool. SNV functional impact was predicted using on line PolyPhen-2 [6], while the 3D protein prediction was obtained using 3D Protein server [7].

Results: Our study was performed recruiting an explorative cohort of BS patients from Southern Italy, a population caracterized by low disease prevalence. We identified a novel heterozygous SNV at 18169 nucleotide position (NG_027839.1: g.18169A>T; HGVS nomenclature) within the endoplasmic reticulum aminopeptidase protein 1 gene (NP_057526.3:p.Glu183Val; HGVS nomenclature) (Fig. 1b). This is a conserved site involved in the substrate binding, due to its significant role in the anchorage of the N-terminale amin group of the peptides. Because of the different amino acid chemical features, the computational assessment of the protein structure was performed (Fig. 1c) recognizing a change in the protein energy and stability: the SNV was associated to a more stable protein chain (AE=-2.022), probably affecting the enzyme conformational state change and activity, as well as the substrate binding pocket. The amino acid change was predicted to be damaging with maximum score when PolyPhen-2 prediction software was queried (score=1.00) (Fig. 1d).

Conclusion: We found a SNV not previously reported in literature in a relatively small group of Italian BS patients. Our data need to be tested in a larger case-control study. In particular, the link between our SNV and the protein stability is to be assessed in future functional studies.

REFERENCES