($p = 0.026$; OR=0.16; 95% CI=[0.03–0.79] and $p = 0.046$; OR=0.2; 95% CI=[0.04–1.00], while for *DRB1*03:01* negative association was revealed only for systemic JIA ($p = 0.03$; OR=0.11; 95% CI=[0.01–0.88]). At the same time the *DQB1*04:02:01* ($p=0.026$; OR=5.88; 95% CI=[1.20–28.72]) and *DRB1*08:01:01* ($p=0.07$; OR=3.94; 95% CI=[1.01–15.39]) allele frequencies were significantly higher in patients with oligoarthritis but not systemic JIA when compared with controls.

Conclusion: High-throughput HLA typing revealed distinct HLA-alleles associated with different JIA subtypes in the Belarusian population as well as some alleles protective both for oligoarthritic and systemic JIA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1346

AB0004 THE ASSOCIATION OF THE RARE RS35667974 IFIH1 GENE POLYMORPHISM WITH SIX AUTOIMMUNE DISEASES: STRUCTURAL BIOLOGICAL INSIGHTS

M. Zervou¹, A. Andreou², G. Goulielmos¹, E. Eliopoulos². ¹University of Crete, Heraklion, Greece, Section of Molecular Pathology and Human Genetics, Department of Internal Medicine, School of Medicine, Heraklion, Greece; ²Agricultural University of Athens, Department of Biotechnology, Athens, Greece

Background: Genome wide association studies (GWAS) have successfully identified novel autoimmune disease-associated loci, with many of them shared by multiple disease-associated pathways but much of the genetics and pathophysiological mechanisms remain still obscure. Considering that most of the potential causal variants are still unknown, many studies showed that the missense variant rs35667974 at interferon induced with helicase C domain 1 (*IFIH1*) gene is protective for type 1 diabetes (T1D), psoriasis (PS) and psoriatic arthritis (PsA), while it was found to be also associated with ankylosing spondylitis (AS), Crohn's disease (CD) and ulcerative colitis (UC). *IFIH1* gene encodes a cytoplasmic RNA helicase that recognizes viral RNA and is involved in innate immunity through recognition of viral RNA [1].

Objectives: To investigate the role of the rare rs35667974 variant of *IFIH1* gene, which resides in exon 14 and changes a conserved isoleucine at position #923 to valine in T1D, PS, PsA, AS, CD and UC [2–4] as well as the mechanism that may affect the function in the protein structure.

Methods: Evolutionary analysis revealed heavily conserved sequence elements among species, indicating structural/functional importance of the mutation at position #923. *In silico* mutagenesis and three-dimensional (3D) homology modeling was used to localize the polymorphism under study on the *IFIH1* protein. The mutant was constructed using molecular modeling with the program Maestro (Schrodinger, LLC) [5]. Molecular mechanics/dynamics studies were applied to validate structural/functional changes caused by the Ile923V substitution. All figures depicting 3D models were generated using the PyMOL molecular-graphics system V.2.2 [6].

Results: Evolutionary and structural analysis revealed that the position of residue Ile923 is located on a protein loop (921–927) directly interacting with mRNA both to the phosphoribose chain and the base pairs. Mutation of Ile to Val at position #923 will directly affect the said interaction with mRNA [7] (Figure 1). Moreover, it has been reported that pre-mRNA or mRNA levels did not correlate with Ile923Val, suggesting that, Ile923Val did not alter the expression of *IFIH1* in a major way [7].

Figure 1. Structural representation of the interferon-induced helicase C domain-containing protein 1 [Homo sapiens] structure (4GL2 from Protein Data Bank) (in green) bound to the double stranded RNA (in orange-yellow). The location of the mutation (Ile923Val) is highlighted in pink. The proximity of the aminoacid 923 to the nucleotide is apparent.

Conclusion: This study represents a comprehensive evaluation of the role of the shared rs35667974 variant of autoimmune locus *IFIH1*, reported to lead to a loss of function phenotype and, as a consequence, reduced levels of *IFIH1* protein and activity that protect against autoimmunity. Structural analysis of rare shared genetic susceptibility or protection loci may provide insight to our understanding of the pathophysiology of autoimmune diseases and the research findings may affect the better management of the diseases under study.

REFERENCES:

- [1] Nejentsev S *et al.* (2009). *Science* 324:387–389.
- [2] Smyth DJ *et al.* (2006). *Nat Genet.* 38: 617–619.
- [3] Li Y *et al.* (2010). *J Invest Dermatol* 130:2768–2772.
- [4] Ellinghaus D *et al.* (2016). *Nat Genet* 48:510–518.
- [5] Schrödinger Release 2017-1: Maestro, Schrödinger, LLC, New York, NY, 2017.
- [6] Schrödinger LLC: The PyMOL Molecular Graphics System 2016 version 2.2.
- [7] Wu B *et al.* (2013). *Cell* 152:276–289 [8] Downes K *et al.* (2010). *PLoS One* 5:e12646.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1388

AB0005 IDENTIFICATION OF KEY GENES AND PATHWAYS FOR PSORIASIS BASED ON GEO DATABASES BY BIOINFORMATICS ANALYSIS

X. Sun¹, S. X. Zhang^{2,3,4}, S. Song^{2,3,4}, T. Kong¹, C. Zheng¹, L. Cheng¹, S. Feng⁵, G. Shi⁶, X. Li^{2,3,4}, P. F. He⁷, Q. Yu^{1,7}. ¹Shanxi Medical University, School of Management, Taiyuan, China; ²The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; ³Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China; ⁴Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China; ⁵Shanxi Medical University, School of Humanities and Social Science, Taiyuan, China; ⁶Shanxi Medical University, Basic Medical College, Taiyuan, China; ⁷Shanxi Medical University, Institute of Medical Data Sciences, Taiyuan, China

Background: Psoriasis is an immune-mediated, genetic disease manifesting in the skin or joints or both, and also has a strong genetic predisposition and autoimmune pathogenic traits¹. The hallmark of psoriasis is sustained inflammation that leads to uncontrolled keratinocyte proliferation and dysfunctional differentiation. And it's also a chronic relapsing disease, which often necessitates a long-term therapy².

Objectives: To investigate the molecular mechanisms of psoriasis and find the potential gene targets for diagnosis and treating psoriasis.

Methods: Total 334 gene expression data of patients with psoriasis research (GSE13355 GSE14905 and GSE30999) were obtained from the Gene Expression Omnibus database. After data preprocessing and screening of differentially expressed genes (DEGs) by R software. Online tool Metascape³ was used to analyze Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis of DEGs. Interactions of proteins encoded by DEGs were discovered by Protein-protein interaction network (PPI) using STRING online software. Cytoscape software was utilized to visualize PPI and the degree of each DEGs was obtained by analyzing the topological structure of the PPI network.

Results: A total of 611 DEGs were found to be differentially expressed in psoriasis. GO analysis revealed that up-regulated DEGs were mostly associated with defense and response to external stimulus while down-regulated DEGs were mostly associated with metabolism and synthesis of lipids. KEGG enrichment analysis suggested they were mainly enriched in IL-17 signaling, Toll-like receptor signaling and PPAR signaling pathways, Cytokine-cytokine receptor interaction and lipid metabolism. In addition, top 9 key genes (CXCL10, OASL, IFIT1, IFIT3, RSAD2, MX1, OAS1, IFI44 and OAS2) were identified through Cytoscape.

Conclusion: DEGs of psoriasis may play an essential role in disease development and may be potential pathogenesis of psoriasis.

REFERENCES:

- [1] Boehncke WH, Schon MP. Psoriasis. *Lancet* 2015;386(9997):983-94. doi: 10.1016/S0140-6736(14)61909-7 [published Online First: 2015/05/31].
- [2] Zhang YJ, Sun YZ, Gao XH, *et al.* Integrated bioinformatic analysis of differentially expressed genes and signaling pathways in plaque psoriasis. *Mol Med Rep* 2019;20(1):225-35. doi: 10.3892/mmr.2019.10241 [published Online First: 2019/05/23].
- [3] Zhou Y, Zhou B, Pache L, *et al.* Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. *Nat Commun* 2019;10(1):1523. doi: 10.1038/s41467-019-09234-6 [published Online First: 2019/04/05].