or using other stimuli, i.e. IL-4 and TNF-α, indicating a specific function for the rs3761847 polymorphism in unstimulated and LPS+IFNγ-activated monocytes.
Conclusions: Our findings suggest that there is no relationship between invasive capacity of RASF or expression of TRAF1-C5 genes and genotype at rs3761847. In contrast, we report an association of the rs3761847 genotype and TRAF1 expression in monocytes. These data underline the importance of studying genotype-phenotype associations in the different cell types relevant for RA pathogenesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6066

THU0015 INVESTIGATION OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) IN GREECE: NEW SUSCEPTIBILITY LOCI

M.I. Zervou[1], D.G. Dimopoulou[2], E. Eliopoulos[3], M. Trachana[4], P. Pratsidou-Gkertsi[4], A. Andreou[3], A. Garyfallos[2], G.N. Goulielmos[1]. *[1]Medical School, University of Crete, Heraklion, Crete; [2]4th Department of Internal Medicine, Hippocratio Hospital, Aristotle University of Thessaloniki, Thessaloniki; [3]Biotechnology, Agricultural University of Crete, Athens; [4]1st Department of Pediatrics, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Background: Juvenile idiopathic arthritis (JIA) is an autoimmune disease characterized by persistent chronic arthritis, in which both genetic and environmental components are involved [1]. Different genetic variations have been reported as risk factors for JIA, but a difficulty of the replication of results in different ethnic backgrounds indicates the existence of an ethnic heterogeneity of genetic factors for JIA.
Objectives: We sought to validate three single nucleotide polymorphisms (SNPs), namely *PTPRC* (rs10919563), *TYK2* (rs34536443) and *PRKCQ* (rs4750316), previously found to be associated with JIA [2–4], and to investigate whether the 27-bp VNTR polymorphism on intron 4 of *eNOS,* which is associated with various autoimmune diseases so far [5], is associated with risk for JIA in Greece.
Methods: The sample set consisted of 125 JIA patients and 221 healthy controls from Northern Greece. Genotyping of the three SNPs was performed with Taqman primer-probe sets, using a Real-Time PCR platform (Applied Biosystems, ViiA™ 7 Real-Time PCR System), while *eNOS* VNTR polymorphism was genotyped by PCR. Odds ratios (OR) and 95% confidence intervals (CI) were calculated and the statistical difference in allele distribution was assessed by means of x^2 test or Fisher's exact test. Bioinformatic analysis was performed using BlastP, Pymol and Maestro and Desmond (Schrodinger Inc.).
Results: A case–control association study was conducted enrolling 4 successfully genotyped markers. *eNOS* only was found to be associated with JIA. Genotype a/a and allele "a" were more common in individuals with JIA than in controls ($p<0.0001$, OR=0.15, 95% CI 0.065–0.37 and $p<0.0001$, OR=0.34, 95% CI 0.23–0.49, respectively). No associations with JIA were detected for *TYK2, PTPRC* or *PRKCQ*. Aiming to investigate the structural consequences and the structure/function relationships accompanying the Pro1104 to Ala (rs34536443) mutation on TYK2 protein, bioinformatics analysis was performed. Combining 3D-modeling and Molecular Dynamics simulations we have noted changes in structural flexibility, affecting the functionality of the kinase domain of TYK2.
Conclusions: This study demonstrated for the first time that *eNOS* VNTR polymorphism is associated with susceptibility to JIA, thus suggesting that the risk allele "a" may confer susceptibility to clinically distinct disorders. Apart from the previously reported evidence for the role of *PTPRC* rs10919563, *PRKCQ* rs4750316 and *TYK2* rs34536443 in an increased risk for JIA, our results demonstrate no association of these genes with JIA in the Greek population. However, the lack of association of *PTPRC* SNP with JIA is in line with previous data reported from cohorts in US and Australia. Taken together, the results highlight the importance of comparative studies in different populations, considering that replication of previously identified markers is paramount to determine which SNPs represent true risk loci, thus pointing towards key disease pathways which warrant further study.
References:
[1] Ravelli and Martini (2007). Lancet 369:767–78.
[2] Hinks et al (2010). Ann Rheum Dis 69:1049–53.
[3] Hinks et al. (2012). Ann Rheum Dis 71:1117–21.
[4] Hinks et al (2013). Nat Genet 45: 664–9.
[5] Vazgiourakis et al (2007). Lupus 16:867–74.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2258

THU0016 A COMPREHENSIVE CONTRIBUTION OF GENES OF THE HYPOXIA INDUCIBLE FACTOR-1 ALPHA SIGNALING PATHWAY TO KNEE OSTEOARTHRITIS SUSCEPTIBILITY

J. Fernandez-Torres[1,2], G.A. Martínez-Nava[1], A. López-Reyes[1], Y. Zamudio-Cuevas[1], D. Clavijo-Cornejo[1], K. Martínez-Flores[1], M.C. Gutiérrez-Ruíz[2], L.E. Gómez-Quiroz[2], C. Pineda[1]. *[1]Laboratorio de Líquido Sinovial, Instituto Nacional de Rehabilitacion; [2]Cellular Physiology Laboratory, Universidad Autónoma Metropolitana-Iztapalapa, Mexico City, Mexico*

Background: The hallmark of osteoarthritis (OA) is the breakdown of articular cartilage. Articular cartilage is an avascular tissue, and this generates a hypoxic microenvironment. Hypoxia inducible factor-1α (HIF-1α) is the main transcriptional regulator of cellular and developmental response to hypoxia.
Objectives: The present study was designed to investigate whether genetic polymorphisms of the HIF-1α signaling pathway are involved in the development of knee OA.
Methods: A total of 243 unrelated Mexican-mestizo individuals comprising 93 knee OA patients and 150 healthy controls were recruited into the study. 42 genetic polymorphisms from 22 genes involved in the HIF-1α signaling pathway (*PIK3R1*, *AKT2*, *GSK3B*, *IL6*, *AGER*, *HIF1A*, *EGLN1, VHL*, *HIF1AN*, *VEGFA*, *EPO*, *NOS2*, *NOS3*, *IGF1*, *EGF*, *EDN1*, *MMP1*, *MMP3*, *MMP13*, *CA*, *COL2A1*, *COL3A1*) were genotyped in cases and controls using TaqMan-based allelic discrimination assays.
Results: After adjusting for age, sex and admixture, significant associations with knee OA were found for 7 SNPs in the case-control study. The following genotypes and alleles were associated with protection against OA: the CT genotype of the *HIF1AN* rs11190613 polymorphism (OR=0.44, 95% CI=0.19–1.0, *P*=0.05); the AA genotype of the *VEGFA* rs1570360 polymorphism (OR=0.14, 95% CI=0.02–0.69, *P*=0.016); the GT genotype and T allele of the *VEGFA* rs729761 polymorphism (OR=0.47, 95% CI=0.22–1.0, *P*=0.05; and OR=0.51, 95% CI=0.27–0.97, *P*=0.041, respectively); the GA genotype of the *COL2A1* rs1793953 polymorphism (OR=0.40, 95% CI=0.20–0.79, *P*=0.008); and the GG genotype and G allele of the *CKM* rs4884 polymorphism (OR=0.34, 95% CI=0.14–0.84, *P*=0.019; and OR=0.51, 95% CI=0.32–0.82, respectively). Otherwise, the CT genotype of the *COL3A1* rs2138533 polymorphism (OR=2.89, 95% CI=1.28–6.5, *P*=0.01); and the GA genotype of the *IGF1* rs35767 polymorphism (OR=2.22, 95% CI=1.11–4.43, *P*=0.024) were associated with an increased risk of OA. However, by using of epistatic interactions between HIF-1α pathway polymorphisms, we found that the gene-gene interaction had a synergistic effect over the estimated OR-values (see table).

a	b	OR_i	OR_c*	P_{int}
VEGFA rs1570360	*COL3A1* rs2138533			
GG	CC	1		0.027
	CT	2.89	4.51	
	TT	1.24	11.1	
COL3A1 rs2138533	*IGF1 rs35767*			
T	G	1		0.037
	A	1.49	3.26	
CKM rs4884	*COL3A1 rs2138533*			
A	C	1		0.036
	T	1.27	4.08	
COL2A1 rs1793953	*HIF1AN* rs11190613			
A	T	1		0.05
	C	0.71	0.35	

OR_i = initial OR-value; OR_c* = combined OR-value obtained by "b" column interaction with "a" column; P_{int} = *P*-value of the intreraction.

Conclusions: In this study we could observe that the gene-gene interaction of the HIF-1α signaling pathway highly increases the risk of developing OA, with the exception of *COL2A1* and *HIF1AN* interaction which had a protective role against OA. Further studies are needed to validate this results.
References:
[1] Fernández-Torres J, et al. Polymorphic variation of hypoxia inducible factor-1 A (HIF1A) gene might contribute to the development of knee osteoarthritis: a pilot study. BMC Musculoskelet Disord 2015; 16:218.
[2] Rodríguez-Fontanela C, et al. Assessment of osteoarthritis candidate genes in a meta-analysis of nine genome-wide association studies. Arthritis Rheumatol 2014; 66:940–949.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2131

THU0017 COMBINATION OF EGFR AND BLYS GENE EXPRESSION IN LUPUS NEPHRITIS

L.A. Mas[1,2], S. Retamozo[2,3], F. Bonisconti[1,2], E.V. Palomino[1,2], J.P. Pirola[2,3], V. Saurit[2,3], A. Alvarellos[2,3], T. Alvarellos[1,2]. *[1]Immunogenetics, Hospital Privado. Universitario de Córdoba; [2]Instituto Universitario de Ciencias Biomédicas de Córdoba; [3]Rheumatology, Hospital Privado. Universitario de Córdoba, Cordoba, Argentina*

Background: Lupus nephritis (LN) is a severe complication of Systemic Lupus Erythematosus (SLE). Non-invasive biomarkers are needed for diagnosis of LN and to identify patients at risk of a renal flare (1). Thus the presence of biomarkers associated with inflammation, tissue damage or cell activation in the urine of patients with LN may be a useful tool in the evaluation of LN patients.
The glomerular filtration rate (GFR) is considered the best overall index of renal function in health and disease. Because GFR is difficult to measure in clinical practice, most clinicians estimate the GFR (eGFR) from the serum creatinine concentration (2).
B Lymphocyte Stimulator (BLyS) is a cytokine that fosters B cell activation, antibody production, B cell - T cell interaction and plasma cell survival. These events have been demonstrated to play a role in patients with LN (3).
Objectives: We evaluated urinary levels of BLyS as biomarker for LN and their relationship with eGFR.