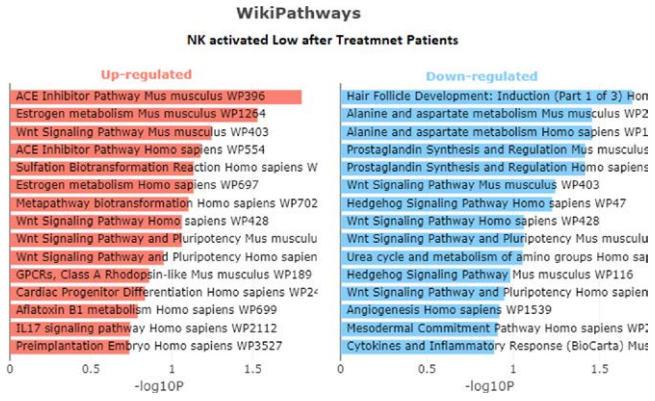

Figure 2. Top wikiPathways enriched in the patients with decreased percentage of synovial infiltrating activated NK after 6 months of tDMARD therapy compared to those who showed increased or unchanged percentage.

Conclusion: Synovial tissue NK cells, resting mast cells, plasma cells and M1 macrophages play major role in response to tDMARD. Genes related to WNT signaling, estrogen metabolism and IL17 signaling can help stratification of patients for a more effective personalized medicine in RA.

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AB0011 INFLUENCE OF IL17A GENE ON THE PATHOGENESIS OF IMMUNOGLOBULIN-A VASCULITIS

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Background: Cytokines signaling pathway genes represent a key component of the genetic network implicated in the pathogenesis of Immunoglobulin-A vasculitis (IgAV) [1], an inflammatory vascular pathology. *Interleukin (IL)17A* is a genetic risk *locus* for autoimmune diseases, such as giant cell arteritis [2] and spondyloarthritis [3].

Objectives: To determine the potential influence of *IL17A* on IgAV.

Methods: Five *IL17A* tag polymorphisms (rs4711998, rs8193036, rs3819024, rs2275913 and rs7747909) were genotyped in 360 Caucasian patients with IgAV and 1,003 sex and ethnically matched healthy controls.

Results: No statistically significant differences between patients with IgAV and healthy controls were observed when each *IL17A* genetic variant was analyzed independently. Similarly, no statistically significant differences between patients with IgAV and healthy controls were found when the five *IL17A* polymorphisms were evaluated combined conforming haplotypes. In addition, there were no statistically significant differences in genotype, allele and haplotype frequencies of *IL17A* when patients with IgAV were stratified according to the age at disease onset or to the presence/absence of gastrointestinal or renal manifestations.

Conclusion: Our results do not support an influence of *IL17A* on the pathogenesis of IgAV.

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AB0012 ROLE OF IRF5 GENE ON THE PATHOGENESIS OF IMMUNOGLOBULIN-A VASCULITIS

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Background: Interferon signaling pathway plays a relevant role in autoimmunity. Genetic variants in the *interferon regulatory factor (IRF) 5* gene, that encodes the major regulator of the type I interferon induction [1], have been related to the development of several inflammatory diseases [2].

Objectives: To determine the influence of *IRF5* on Immunoglobulin-A vasculitis (IgAV), an inflammatory vascular disease.
Methods: Three *IRF5* polymorphisms (rs2004640, rs2070197 and rs10954213) representative of 3 different haplotype blocks were genotyped in 372 Caucasian patients with IgAV and 876 sex and ethnically matched healthy controls.
Results: No statistically significant differences between patients with IgAV and controls were observed when each *IRF5* polymorphism was analyzed independently. Similarly, no statistically significant differences between patients with IgAV and controls were found when *IRF5* polymorphisms were evaluated combined conforming haplotypes. Additionally, there were no statistically significant differences in genotype, allele and haplotype frequencies of *IRF5* when patients with IgAV were stratified according to the age at disease onset or to the presence/absence of gastrointestinal or renal manifestations.
Conclusion: Our results do not support an influence of *IRF5* on the pathogenesis of IgAV.
References:
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[2] Arthritis Res Ther 2014; 16: R146.
Acknowledgments: This study was supported by European Union FEDER funds and "Fondo de Investigaciones Sanitarias" (grant PI18/00042) from 'Instituto de Salud Carlos III' (ISCIII, Health Ministry, Spain). RL-M is a recipient of a Miguel Servet type I programme fellowship from the ISCIII, co-funded by the European Social Fund (ESF, `Investing in your future´) (grant CP16/00033). SR-M is supported by funds of the RETICS Program (RD16/0012/0009) (ISCIII, co-funded by the European Regional Development Fund (ERDF)). VP-C is supported by a pre-doctoral grant from IDIVAL (PREVAL 18/01). LL-G is supported by funds of PI18/00042 (ISCIII, co-funded by ERDF).
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AB0013

HLA ASSOCIATION WITH SYSTEMIC SCLEROSIS (SSc) IN NORTH INDIAN POPULATION AND FAMILIAL INHERITANCE PATTERNS

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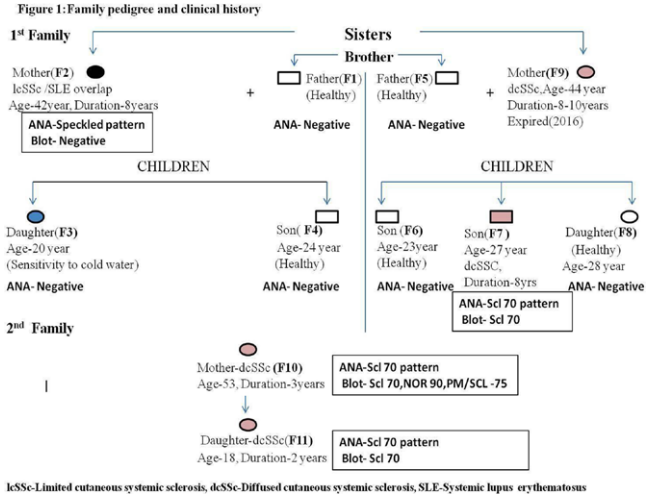
Background: It is widely believed that SSc develops in an individual with a permissive genetic makeup.Genetic influences have long been suspected to impact SSc. In families with a history of SSc, the incidence of disease can range from 1.5 to 1.7% (1). There are several reports of familial occurrence and certain alleles of the HLA system have been associated with the disease (2).No Indian data pertaining to genetic basis of systemic sclerosis is present. Understanding the genetic basis of the disease will help us in defining the biomarkers of the disease in the population that can help in early diagnosis and prognosis.
Objectives: To study HLA association with Systemic sclerosis (SSc) in North Indian Population and its genetic susceptibility to familial systemic sclerosis.
Methods: A total of 150 SSc patients diagnosed by following ACR and EULAR criteria and 150 control subjects, were genotyped for HLA-A, B, DRB1, DQB1 loci by Luminex® 200 Instrument (USA). The association of alleles with disease susceptibility was tested by Chi-square test and Fisher's exact test.
HLA Typing for HLA class I (A, B, C) and II(DR,DQ,DP) for familial study of systemic sclerosis in 2 families was performed by Next Generation Sequencing(NGS) with illumina MiniSeq using MIA FORA NGS Kits from IMMUCOR. Antinuclear patterns (ANA) and specific antibodies were detected by indirect Immunofluorescence and Immunoblot (Euroline, Germany).
Results: Strong disease associations were observed for haplotypes A*24(OR=1.7;< 0.02), A*32(OR=2.8;< 0.02), B*35(OR=1.7;< 0.03), DRB1*11(OR=2.1;< 0.007). The reduced frequencies of haplotypes A*68(P< 0.05), DRB1*10(P< 0.05), DRB1*12 (P<0.00) among patients suggested a protective association. There was no statistical association found with HLA DQB*1.
Through NGS we observed that in the 1st family haplotypes HLA –A*11, 32, 24; B* 51, 55, 35; C*-14, 04; DRB1*15, 04; DQB1*05, 03; DPB1*04, 26 appears in affected family members with serological abnormalities.In the 2nd family both mother and daughter had same set of haplotypes except DQB1 with serological abnormalities. The haplotypes DPB1*04 was present in all the diseased individuals of both the families (Fig. 1 and table 1).

Table 1. NGS HLA typing report

	A	B	C	DRB1	DQB1	DPB1
F1	11 24	35 15	04 04	15 15	05 05	02 26
F2	11 32	51 55	14 04	15 04	05 03	04 04
F3	11 24	35 55	04 04	15 15	05 05	26 04
F4	32 11	51 15	14 04	15 04	05 03	02 04
F5	24 33	35 44	04 07	15 07	05 02	26 14
F6	11 24	35 55	04 04	15 15	05 05	04 26
F7	11 24	35 55	04 04	15 15	05 05	04 26
F8	24 32	51 35	14 04	04 15	03 05	26 04
F9	11 32	51 55	14 04	15 04	05 03	04 04
F10	11 33	44 52	07 12	11 07	02 03	04 13
F11	11 33	44 52	07 12	11 07	03 03	04 13

Fig. 1



Conclusion: The risk alleles A*24, 32; B*35; DRB1*11 were found to be associated with North Indian cohort of SSc, while the protecting alleles were A*68; DRB1*10, 12.These risk alleles were present in the SSc affected family members and the protective alleles were absent in the same. Surprisingly, even healthy members carried the same risk alleles but did not manifest the disease or have serological evidence of the same. We have not excluded occurrence of disease at a later age, as presently the healthy siblings are young. Thus our study indicates that though HLA association are found with SSc but many other factors like HLA (HLA *C, DPB1*) or non HLA genes as wells as epigenetic factors might also play a role in disease manifestation and severity.
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