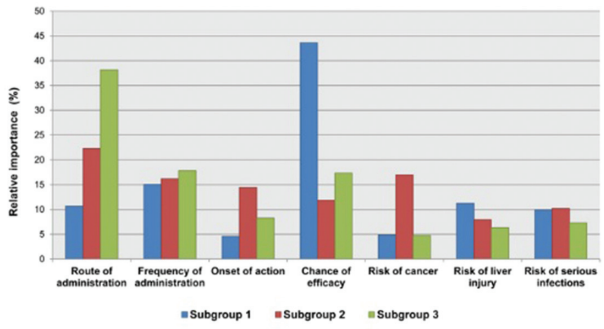

Abstract OP0281-HPR – Figure 1 Relative importance of attributes for each subgroup

Conclusions: DCE data revealed that RA patients had different preferences for DMARD characteristics, which resulted in the identification of three subgroups. Integrating preferences of these subgroups in patient-tailored treatment decisions and the effect on medication adherence should be part of future research.

REFERENCE:

[1] Pasma A, et al. Arthritis Res Ther 2015;1–10. doi:10.1186/s13075-015-0801-4

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.2906

FRIDAY, 15 JUNE 2018

From gene to function

OP0282 NEW SYSTEMIC SCLEROSIS RISK LOCI IDENTIFIED THROUGH A META-GWAS STRATEGY

E. López-Isac[1], M. Acosta-Herrera[1], S. Assassi[2], C.P. Simeón[1], P.E. Carreira[1], I. Castellví[1], N. Ortego-Centeno[1], L. Beretta[3], C. Lunardi[4], A. Gabrielli[5], G. Moroncini [5], N. Hunzelmann[6], T. Witte[7], J.H. Distler[8], A. Franke[9], A. E. Voskuyl[10], J. de Vries-Bouwstra[11], C. Wijmenga[12], R. Hesselstrand[13], A. Nordin[14], A.-M. Hoffmann-Vold[15], A. Herrick[16], J. Worthington[16], C.P. Denton[17], M.A. Brown[18], on behalf of Australian Scleroderma Interest Group, Y. Allanore[19], on behalf of French GENESYS Consortium, T.R. Radstake[20], C. Fonseca[17], M. D. Mayes[21], J. Martín[1], on behalf of Spanish Scleroderma Group. *[1]Instituto de Parasitología y Biomedicina López Neyra (CSIC)., Granada, Spain*; *[2]The University of Texas Health Science Center–Houston, Houston, Texas, USA*; *[3]Referral Center for Systemic Autoimmune Diseases, Milan*; *[4]Università degli Studi di Verona, Verona*; *[5]Università Politecnica delle Marche and Ospedali Riuniti, Ancona, Italy*; *[6]Cologne University, Cologne*; *[7]Hannover Medical School, Hannover*; *[8]University of Erlangen-Nuremberg, Erlangen*; *[9]Christian-Albrechts-University of Kiel, Kiel, Germany*; *[10]VU University Medical Center, Amsterdam*; *[11]Leiden University Medical Center, Leiden*; *[12]University Medical Center Groningen, Groningen, Netherlands*; *[13]Lund University, Lund*; *[14]Karolinska Institute, Stockholm, Sweden*; *[15]Oslo University Hospital, Oslo, Norway*; *[16]The University of Manchester, Manchester*; *[17]Royal Free and University College Medical School, London, UK*; *[18]University of Queensland Diamantina Institute, Queensland, Australia*; *[19]Paris Descartes University, Paris, France*; *[20]University Medical Center Utrecht, Utrecht, Netherlands*; *[21]The University of Texas Health Science Center–Houston, Housron, Texas, USA*

Background: In systemic sclerosis (SSc), previous GWASs have identified several *loci* associated with the disease, but their rate of discovery has been limited due to modest sample sizes. Extensive collaborative efforts have enabled us to gather the largest cohort of SSc patients. In the present study, we have performed a large meta-GWAS taking advantage of our well-powered cohort.
Objectives: To continue unravelling the complex genetic component of SSc.
Methods: The complete set of individuals enrolled for this study comprised a total of 26 679 genome-wide genotyped individuals of European ancestry. PLINK and EIGENSTRAT were used for quality control and population stratification adjustments. Genotype imputation was performed with IMPUTE2 and the 1000 Genome Project Phase 3 as reference panel.
Results: Twenty-three *loci* reached the genome-wide significance level (*p*-value<5×10–8) in our large-scale meta-analysis. Twelve out of the total significant signals represented new associations and involved novel pathways in the pathophysiology of the disease. Significant enrichment was observed for epigenetic marks of active promoters and active enhancers in critical cell types for the disease. In addition many of the interrogated variants correlated with eQTLs thus altering gene expression.
Conclusions: Using a large meta-GWAS, we have identified twelve novel associations for SSc susceptibility and confirmed several previously reported risk *loci*. These results considerably increase our understanding of the genetic basis of SSc and shed light on the pathogenesis of the disease providing important information to discover new therapeutic targets genetically validated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.5151

OP0283 CROSS-DISEASE META-ANALYSIS IN FOUR SYSTEMIC AUTOIMMUNE DISEASES TO IDENTIFY SHARED GENETIC ETIOLOGIES

M. Acosta-Herrera[1], M. Kerick[1], D. Gonzalez-Serna[1], C. Wijmenga[2], A. Franke[3], L. Padyukov[4], T. Vyse[5,6], M.E. Alarcon-Riquelme[7], M.D. Mayes[8], J. Martin[1], on behalf of The Myositis Genetics Consortium, Scleroderma Genetics Consortium. *[1]Institute of Parasitology and Biomedicine Lopez-Neyra, Granada, Spain*; *[2]Department of Genetics, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands*; *[3]Institute of Clinical Molecular Biology, Christian-Albrechts-University of Kiel, Kiel, Germany*; *[4]Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden*; *[5]Division of Immunology, Infection and Inflammatory Disease*; *[6]Division of Genetics and Molecular Medicine, King's College London, London, UK*; *[7]Centro de Genómica e Investigación Oncológica (GENYO), Pfizer-Universidad de Granada-Junta de Andalucía, Granada, Spain*; *[8]The University of Texas Health Science Center–Houston, Houston, USA*

Background: Cross-disease genome-wide association studies (GWAS) in autoimmune diseases (AIDs) has become a powerful tool to expose new genetic variants associated with disease susceptibility and to reveal shared biological mechanisms in the pathophysiology of these conditions.
Objectives: The goal of our study was to identify shared genetic etiologies by performing a large-scale meta-analysis of four systemic AIDs in individuals from European-descent populations, including rheumatoid arthritis [4595 cases and 3372 controls], systemic lupus erythematosus [3154 cases and 8775 controls], systemic sclerosis [2255 cases and 4407 controls] and myositis [1674 cases and 3150 controls]
Methods: PLINK and EIGENSTRAT were utilised for quality control and population stratification adjustments. Genotype imputation was performed using Minimac in the Michigan Imputation Server and the Haplotype Reference Consortium as reference panel.
Results: We meta-analysed ~6.5 million single nucleotide polymorphisms (SNPs) (MAF >1%, Rsq >0.3) across the four diseases and were able to identify 27 genome-wide significant independent loci with at least two diseases leading the association. Our new findings include five unreported shared risk loci: *NAB1*, *KPNA4-ARL14*, *DGQK*, *LIMK1*, and *PRR12*. The results from the meta-analysis were functionally enriched in transcription factor binding sites, promoter and enhancer histone marks and DNase cleavage hotspots in immune cell lines, as well as in epithelial and epidermal cell lines. This is consistent with the clinical manifestations across diseases related to the immune system and the connective tissue. Interestingly, several associated variants were able to modify the expression of the nearest genes and constitute shared expression quantitative trait loci across diseases.
Conclusions: These studies offer the opportunity to uncover new biological pathways, address patient classification based on their molecular taxonomy and provide an opportunity for drug repositioning by targeting shared mechanisms across diseases.
Acknowledgements: Partially funded by EU/EFPIA Innovative Medicines Initiative Joint Undertaking PRECISESADS (115565), The Ministry of Economy and Competitiveness (SAF2015–66761 P), Consejería de Innovación, Ciencia y Tecnología, Junta de Andalucía (P12-BIO-1395), and Juan de la Cierva fellowship (FJCI-2015–24028).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.2876