R. Knevel[1]. [1]*Leiden University Medical Center, Rheumatology, Leiden, Netherlands*; [2]*Janssen Pharmaceutical Companies of Johnson & Johnson, Discovery Science/ Computational Biology, Beerse, Belgium*; [3]*Leiden University Medical Center, Leiden Computational Biology Center, Leiden, United Kingdom*; [4]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [5]*Newcastle University, Institute of Cellular Medicine, Newcastle, United Kingdom*; [6]*King's College London Centre for Rheumatic Diseases, Department of Inflammation Biology, London, United Kingdom*; [7]*Hospital Universitario de la Princesa (IIS-IP), Rheumatology, Madrid, Spain*; [8]*University of Glasgow, Immunology, Glasgow, United Kingdom*; [9]*Pfizer, Inflammation & Immunology Research Unit, Cambridge, United States of America*; [10]*Karolinska Institutet and Karolinska University Hospital, Rheumatology, Stockholm, Sweden*; [11]*Newcastle upon Tyne Hospitals NHS Foundation Trust, Health and Bioinformatics, Newcastle upon Tyne, United Kingdom*; [12]*University of Glasgow, Infection Immunity & Inflammation, Glasgow, United Kingdom*; [13]*Hospital Clínico San Carlos, Rheumatology, Madrid, Spain*; [14]*Medical University of Vienna, Rheumatology, Vienna, Austria*

Background: Patients who achieve remission promptly could have a specific genetic risk profile that supports regaining immune tolerance. The identification of these genes could provide novel drug targets.
Objectives: To test the association between RA genetic risk variants with achieving remission at 6 months.
Methods: We computed genetic risk scores (GRS) comprising of the RA susceptibility variants[1] and HLA-SE status separately in 4425 patients across eight datasets from inception cohorts. Remission was defined as DAS28CRP<2.6 at 6 months. Missing DAS28CRP values in patients were imputed using predictive mean matching by MICE. We first tested whether baseline DAS28CRP changed with increasing GRS using linear regression. Next, we calculated odds ratios for GRS and HLA-SE on remission using logistic regression. Heterogeneity of the outcome between datasets was mitigated by running inverse variance meta-analysis.
Results: Evaluation of the complete dataset, baseline clinical variables did not differ between patients achieving remission and those who did not (Table 1). Distribution of GRS was consistent between datasets. Neither GRS nor HLA-SE was associated with baseline DAS2DAS (OR1.01; 95% CI 0.99-1.04). A fixed effect meta-analysis (Figure 1.) showed no significant effect of the GRS (OR 0.99; 95% CI 0.94-1.03) or HLA-SE (OR 0.8CRP87; 95% CI 0.75-1.01) on remission at 6 months.

Table 1. Summary of the data separated by disease activity after 6 months.

	all	Remission at 6 months	No remission at 6 months
N	4425*	1558	2430
Age, *mean (sd)*	55.38 (13.87)	5517 (14.09)	55.62 (13.59)
Female %	68.98%	65.43%	70.73%
ACPA+ %	61.94%	63.53%	61.67%
Baseline DAS28, *mean (sd)*	4.76 (1.22)	4.47 (1.23)	5.1 (1.15)

**not all patients had 6 months data*

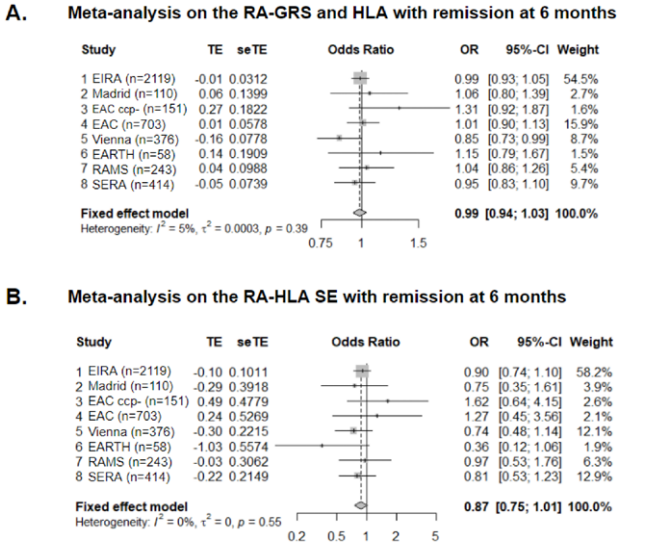

Figure 1. A. Inverse weighted meta-analysis of (**A**) the GRS + HLA and (**B**) the HLA SE. Includes the dataset name (Study), test estimate (TE), the standard error of treatment estimate (seTE), odds ratio (OR), 95% confidence intervals (95%-CI) and the weights of the fixed effect model. I^2 percentage of variation across studies due to heterogeneity. τ^2 states the variance of the true effect size.

Conclusion: In these combined cohorts, RA genetics risk variants are not associated with early disease remission. At baseline there was no difference in genetic risk between patients achieving remission or not. Studies encompassing other genetic variants are needed to elucidate the genetics of RA remission.
REFERENCES:
[1] Knevel R et al. *Sci Transl Med*. 2020;12(545):eaay1548.
Acknowledgements: This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777357, RTCure. This project has received funding from Pfizer Inc.
Disclosure of Interests: Samantha Jurado Zapata: None declared, Marc Maurits: None declared, Yann Abraham Employee of: Pfizer, Erik van den Akker: None declared, Anne Barton: None declared, Philip Brown: None declared, Andrew Cope: None declared, Isidoro González-Álvaro: None declared, Carl Goodyear: None declared, Annette van der Helm - van Mil: None declared, Xinli Hu Employee of: Pfizer, Thomas Huizinga: None declared, Martina Johannesson: None declared, Lars Klareskog: None declared, Dennis Lendrem: None declared, Iain McInnes: None declared, Fraser Morton: None declared, Caron Paterson: None declared, Duncan Porter: None declared, Arthur Pratt: None declared, Luis Rodriguez Rodriguez: None declared, Daniela Sieghart: None declared, Paul Studenic: None declared, Suzanne Verstappen: None declared, Leonid Padyukov: None declared, Aaron Winkler Employee of: Pfizer, John D Isaacs: None declared, Rachel Knevel Grant/ research support from: Pfizer
DOI: 10.1136/annrheumdis-2021-eular.1042

POS0349

SEQUENCE COMPLEMENTARITY BETWEEN SARS-CoV-2 GENOME AND HUMAN NONCODING RNAS ASSOCIATED WITH IMMUNOLOGICAL DISORDERS: AN IN SILICO PIVOTAL STUDY

R. Talotta[1], S. Bahrami[2], M. J. Laska[2]. [1]*University of Messina, Clinical and Experimental Medicine, Messina, Italy*; [2]*Aarhus University, Clinical Medicine, Aarhus, Denmark*

Background: Recent evidence shows that human cells may produce several noncoding (nc)RNAs in response to viral infections. Among them, a central role has been attributed to long noncoding (lnc)RNAs, more than 200 nucleotides in length, which are also crucially involved in cancer and autoimmunity. LncRNAs epigenetically control the transcription of genes presiding over cell proliferation, differentiation, migration and apoptosis, by directly or indirectly binding cellular or foreign nucleic acids, including viral genomes.
Objectives: The objectives of this study were to evaluate *in silico* the presence of a nucleotide sequence complementarity between the RNA genome of Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2) and human ncRNA genes and to analyze any associations between SARS-CoV-2 gene-matching ncRNAs and human diseases.
Methods: The FASTA sequence of each of the 11 SARS-CoV-2 isolate Wuhan-Hu-1 genes (ORF1ab, ORF3a, ORF6, ORF7a, ORF7b, ORF8, ORF10, S, E, M, N) was retrieved from NCBI.nlm.nih.gov/gene (reference sequence NC_045512.2). The ensembl.org library for human ncRNA genes was interrogated for any base-pair match and detected human ncRNAs analyzed for their functional activity. Finally, the associations between ncRNAs and human diseases were searched on GWAS databases (https://www.ebi.ac.uk/gwas and https://www.genecards.org).
Results: A total of 252 matches between SARS-CoV-2 genes and human ncRNAs were recorded (ORF1ab: 28; ORF3a: 9; ORF6: 50; ORF7a: 31; ORF7b: 16; ORF8: 23; ORF10: 5; S: 24; E: 17; M: 32; N: 17). With the exception of two small nuclear RNAs (RNVU1-4 and RNU4-74P corresponding to ORF6 and ORF10, respectively), all of them were lncRNAs, mostly expressed in testis and central nervous system under physiological conditions. Percentage of alignment ranged from 91.30% to 100%, with a mean nucleotide alignment length of 17.5±2.4. Polymorphic variants of these transcripts have mostly been reported in patients with neuropsychiatric disorders, cancer and dysmetabolism. Of note, we found 13 and 15 complementarities with lncRNAs associated with immune-mediated diseases Table 1. and immunological pathways (IL-2, IL-6, IL-12, IL-12R, IL-13, IL-17, M-CSF, CXCL-10, TRAIL-R2 and IgG glycosylation), respectively.
Conclusion: This pivotal study shows that SARS-CoV-2 genes contain complementary sequences to human ncRNAs in turn associated with several diseases, including autoimmunity. The biological effects of this interaction remain to be elucidated.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1077

Table 1. SARS-CoV-2 complementary ncRNAs and associated immunological disorders

SARS-CoV-2 gene	LncRNA	Genomic location	Nucleotide alignment length	Alignment percentage	Associated immunological disorder
S	XACT	X:113705866-113705883	18	100%	Crohn's disease
N	LINC01358	1:59082428-59082574	17	100%	Acute Graft-versus-Host Disease
E	COX10-AS1	17:14029229-14029245	17	100%	Systemic lupus erythematosus
ORF8	AC093765.3	4:116752764-116752784	21	95.24%	Ulcerative colitis
ORF6	CDKN2B-AS1	9:22033529-22033546	18	100%	Multiple sclerosis
	CHROMR	2:178433948-178433968	21	95.24%	Multiple sclerosis Psoriasis Atopic eczema
	WAKMAR2	6:137857643-137857657	15	100%	Atopic eczema Hay fever Allergic rhinitis Multiple sclerosis Psoriasis Systemic sclerosis Systemic lupus erythematosus Rheumatoid arthritis
	AC008691.1	5:159362809-159362828 (promoter flank)	20	95%	Sarcoidosis Psoriasis Psoriatic arthritis Sclerosing cholangitis Celiac disease Type I diabetes mellitus Systemic lupus erythematosus Juvenile idiopathic arthritis Ulcerative colitis Crohn's disease Takayasu arteritis Multiple sclerosis
	LMCD1-AS1	3:7953602-7953616 (enhancer)	15	100%	Systemic sclerosis
M	LINC01934	2:181403969-181403984	16	100%	Multiple sclerosis Ankylosing spondylitis Celiac disease Rheumatoid arthritis
ORF7b	XACT	X:113959816-113959831	16	100%	Crohn's disease
	LINC02621	10:62289643-62302335	15	100%	Rheumatoid arthritis
	LINC01991	3:187966255-187966269	15	100%	IgA deficit Atopic asthma Allergic rhinitis

POS0350

EPIONE APPLICATION: AN INTEGRATED GENOTYPE ANALYSIS WEB SERVER FOR CLINICAL GENOMICS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

L. Papageorgiou[1], H. Alkenaris[1], M. Zervou[2], D. Vlachakis[1], G. Goulielmos[2], E. Eliopoulos[1]. [1]*Agricultural University of Athens, Laboratory of Genetics, Department of Biotechnology, Athens, Greece*; [2]*University of Crete, Section of Molecular Pathology and Human Genetics, Department of Internal Medicine, School of Medicine, Heraklion, 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 [1-3]. SLE is a chronic, highly heterogeneous autoimmune disease, characterized by differences in autoantibody profile, serum cytokines, and a multi-system involvement [4]. Epione Application is an integrated bioinformatics web-tool designed to assist medical experts and researchers in the process of diagnosing SLE [5].

Objectives: To identify the most credible gene variants and single nucleotide polymorphisms (SNPs), causing SLE using the genomic data provided for the patient and aid the medical expert in SLE diagnosis [5].

Methods: In the present study, we have analyzed more than 70.000 SLE-related publications using data mining and semantic techniques towards extracting the SLE -related genes and SNPs [6]. The extracted knowledge has been filtered, evaluated, annotated, classified, and stored in the Epione Application Database (EAD) (Figure 1). Moreover, an updated gene regulatory network with the genes implements in SLE has been estimated [7]. This was followed by the design and development of the Epione application, in which the generated datasets and results were included. The application has been tested and presented here with WES data from several related patients with SLE [8].

Results: SLE-related SNPs and variants identified in genome-wide association studies (GWAS), whole-genome (WGS), whole-exome (WES), or targeted sequencing information are classified, annotated, and analyzed in an integrated patient profile with clinical significance information. Probable genes associated with the patient's genomic profile are visualized with several graphs, including chromosome ideograms, statistic bars, and regulatory networks through data mining studies with relative publications, to obtain a representative number of the most credible candidate genes and biological pathways associated with the SLE. An evaluation study was performed on 7 patients from a three-generation family with SLE [9]. All the recognized gene variants that were previously considered SLE-associated were properly identified in the output profile per patient, and by comparing the results, new findings have emerged.

Conclusion: The Epione application was designed to assist medical doctor diagnosis from the early stages by using the patients' genomic data [5, 8, 10]. Its diagnosis-oriented output presents the patient profile through which the user is provided with a structured set of results in various categories, which are generated based on the list of the most predictable candidate gene variants related to SLE. This novel and accessible webserver tool of SLE to assist medical experts in the clinical genomics and precision medicine procedure is available at http://143.233.188.162/epione/.

REFERENCES:

[1] Molineros JE *et al.* (2017). Hum Mol Genet 26:1205-1216.
[2] Sciascia S *et al.* (2018). F1000 Res, 2018:1-17.
[3] Gonzalez-Serna D *et al.* (2020). Sci Rep 10:1862.
[4] Harley JB *et al.* (2006). Springer Semin Immun 28:119–130.
[5] Goulielmos GN *et al.* (2018). Gene 668:59-72.
[6] Zhao Y *et al.* (2020). Front Genet 11:400.
[7] Song YL and Chen S (2009). Interdiscip Sci 1:179-186.
[8] Koile D *et al.* (2018). BMC Bioinformatics 19:25.
[9] Albertsen HM *et al.* (2019). Mol Med Rep 19:1716-1720.
[10] Ebrahimiyan H *et al.* (2018). Meta Gene 16:241-247.

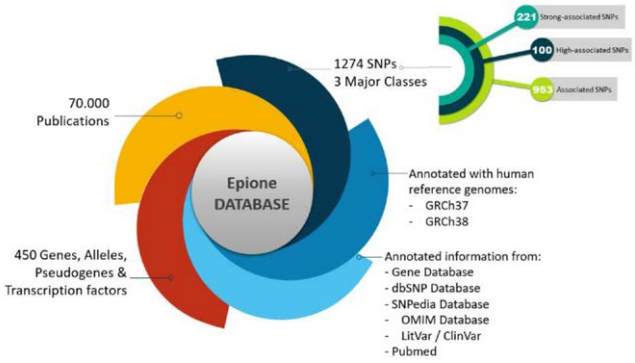

Figure 1. The Epione application database (EAD) for SLE.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.1496