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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 variants¹ 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 DAS28CRP (OR 1.01; 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)	55.17 (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

A. Meta-analysis on the RA-GRS and HLA with remission at 6 months

B. Meta-analysis on the RA-HLA SE with remission at 6 months

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:

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

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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 (RNU1-4 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.

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