shown that the largest factor influencing disease susceptibility is genetics. Genome-wide association studies have successfully characterized genetic variants that are associated with RA, with the vast majority of them mapping to non-coding regulatory elements. Understanding the mechanisms by which this phenomenon leads to disease is essential to translate results from genetic association studies to the clinic.

Objectives: There is evidence showing that autoimmune diseases are the consequence of erroneous wiring of the regulatory circuitry between enhancers and their target genes. The aim of this study is to characterize non-coding regions containing RA-associated variants, in order to determine the genes and pathways by which these regions act to increase the risk of disease.

Methods: We isolated CD4⁺ T-cells from blood obtained from RA patients. We stratified patients in two subgroups, high disease activity (DAS28>5.1, n=18) and low disease activity (DAS28<3.2, n=33). All samples were genotyped using Illumina Infinium Exome-24 v1.0 BeadChip arrays. RNA-Seq Libraries were generated for matching RNA samples using the Lexogen QuantSeq Library Prep kit and sequenced on an Illumina NextSeq500. For a subset of 6 samples (3 high disease activity and 3 low disease activity patients), capture Hi-C was performed to characterize chromatin interactions between all RA associated loci and their potential target genes.

Results: We observed numerous chromatin interactions between RA variants and potential causal genes. Preliminary results show that a number of disease-associated SNPs interact with compelling candidate genes situated several megabases away. Whilst some of these chromatin interactions are common to both patients groups, subsets of them are specific to each disease subgroup, which are correlated with differential gene expression.

Conclusion: These results suggests that there might be different biological pathways contributing to disease in RA patients with inactive disease compared to patients with high disease activity.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3211

FRI0006

PROTECTIVE ROLE OF THE PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) RS2495477 POLYMORPHISM IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SUBCLINICAL ATHEROSCLEROSIS

Sara Remuzgo-Martínez¹, Fernanda Genre¹, Verónica Pulito-Cueto¹, Alfonso Corrales¹, Javier Llorca², Verónica Mijares¹, Leticia Lera-Gómez¹, Virginia Portilla¹, Iván Ferraz-Amaro³, Santos Castañeda⁴, Oreste Gualillo⁵, Javier Martín Ibanez⁶, Ricardo Blanco¹, Raquel López-Mejías¹, Miguel A. González-Gay^{1,7}. ¹Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander, Spain; ²Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander, Spain; ³Division of Rheumatology, Hospital Universitario de Canarias, Tenerife, Spain; ⁴Rheumatology Department, Hospital Universitario de La Princesa, IIS-IPrincesa, Madrid, Spain; ⁵SERGAS (Servizo Galego de Saude) and IDIS (Instituto de Investigación Sanitaria de Santiago), The NEIRID Group (Neuroendocrine Interactions in Rheumatology and Inflammatory Diseases), Santiago University Clinical Hospital, Santiago de Compostela, Spain; ⁶Instituto de Parasitología y Biomedicina "López-Neyra", CSIC, PTS Granada, Granada, Spain; ⁷School of Medicine, University of Cantabria, Santander, Spain

Background: RA is associated with the development of cardiovascular (CV) disease and subclinical atherosclerosis¹. The presence of carotid plaques assessed by ultrasonography studies is a surrogate marker for subclinical atherosclerosis². Proprotein convertase subtilisin/kexin type 9 (PCSK9) is involved in homeostasis of cholesterol, a traditional CV risk factor related to RA and atherosclerosis^{1,3}. PCSK9 polymorphisms can both increase and decrease the risk of CV disease in patients with atherosclerosis³. Moreover, PCSK9 levels have been also related with CV risk⁴. However, there is little information on PCSK9 in RA.

Objectives: To assess the role of several PCSK9 polymorphisms in RA and subclinical atherosclerosis in RA as well as to determine if these ones may influence on PCSK9 mRNA and protein levels.

Methods: PCSK9 rs2479409, rs11583680, rs2483205, rs2495477 and rs562556 polymorphisms were genotyped in 1,169 Spanish RA patients, who met the 1987 ACR and the 2010 ACR/EULAR criteria for RA⁵⁻⁶, and 528 healthy controls. Associations were estimated using odds ratios (OR) and 95% confidence intervals (CI). The potential association between PCSK9 polymorphisms in both RA and controls and the presence/absence of carotid plaques in RA was evaluated by logistic regression. PCSK9 mRNA expression and PCSK9 serum levels were

determined by qPCR and ELISA, respectively. All results were adjusted by sex, age and traditional CV risk factors.

Results: Significant differences in the allele frequencies of PCSK9 rs2495477 between RA patients and controls were found (minor allele: OR=0.55, 95% CI=0.34-0.89, p=0.01). A significant association between minor allele of rs2495477 and carotid plaques was also disclosed in RA patients (OR=0.72, 95% CI=0.56-0.92, p=0.01). PCSK9 levels were significantly decreased in RA patients carrying rs2495477 minor allele compared to controls (97.8 ± 104.9 vs 235.8 ± 93.5 ng/mL, p=0.001). None of the five PCSK9 polymorphisms influenced on its expression.

Conclusion: Our study showed for the first time that PCSK9 rs2495477 confers protection against RA susceptibility and the development of sub-clinical atherosclerosis in RA patients. Furthermore, rs2495477 decreased PCSK9 serum levels in RA that may be crucial to control the disease.

REFERENCES:

- [1] Autoimmun Rev. 2016; 15: 1013–30.
- [2] Ann Rheum Dis. 2014; 73: 722–7.
- [3] J Am Coll Cardiol. 2005; 45: 1611–9.
- [4] Atherosclerosis. 2016; 252: 50–60.
- [5] Arthritis Rheum. 1988; 31: 315–24.
- [6] Arthritis Rheum. 2010; 62: 2569–81.

Acknowledgement: Study supported by ERDF and PI15/00525 (ISCIII). Personal funds, SR-M: RD16/0012/0009 (ISCIII-ERDF); FG: Sara Borrell fellowship CD15/00095 (ISCIII-ESF); VP-C: PREVAL18/01 (IDIVAL); VM and RL-M: Miguel Servet type I CP16/00033 (ISCIII-ERDF,ISCIII-ESF).

Disclosure of Interests: Sara Remuzgo-Martínez: None declared, Fernanda Genre: None declared, Verónica Pulito-Cueto: None declared, Alfonso Corrales: None declared, Javier Llorca: None declared, Verónica Mijares: None declared, Leticia Lera-Gómez: None declared, Virginia Portilla: None declared, Iván Ferraz-Amaro: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Oreste Gualillo: None declared, Javier Martín Ibanez: None declared, Ricardo Blanco: None declared, Raquel López-Mejías: None declared, Miguel A. González-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker's bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi.

DOI: 10.1136/annrheumdis-2019-eular.2383

FRI0007

IDENTIFICATION AND VALIDATION OF PLASMA MICRO-RNA 425-5P AND -451A AS MICRO-RNAs ASSOCIATED WITH CARDIOVASCULAR DISEASE RISK OBSERVED IN RHEUMATOID ARTHRITIS PATIENTS

PARADES SILVIA¹, Delia Taverner², Raimon Ferre³, Josep Maria Alegret⁴, Lluís Masana⁵, Joan Carles Vallve⁵. ¹Hospital Universitari Sant Joan, Department of Rheumatology, Reus, Spain; ²Hospital Universitari Sant Joan, Department of Rheumatology, Reus, Spain; ³Hospital Universitari Sant Joan, Internal Medicine, Reus, Spain; ⁴Hospital Universitari Sant Joan, Department of Cardiology, Reus, Spain; ⁵Rovira i Virgili University, Lipid Research Unit, Reus, Spain

Background: Cardiovascular disease (CVD) risk is increased in Rheumatoid arthritis (RA) patients, and therefore, improved approaches for its early detection are needed. An accelerated atherosclerosis is considered the cause of the increase CVD risk. As microRNAs (miRNAs) are increasingly recognized as critical regulators in atherosclerosis and possess excellent stability in plasma, this study focused on using miRNAs as noninvasive CVD risk biomarkers in RA patients.

Objectives: To identify plasmatic miRNAs in RA patients that can facilitate earlier diagnosis of CVD and provide insight regarding the increase risk for CVD observed in these patients.

Methods: A discovery and validation studies were performed. To discover miRNAs candidates, we first compared plasmatic profiles of 754 miRNAs in 7 RA patients without CVD, in 7 patients with acute myocardial infarction (AMI) but without RA, and in 7 healthy controls matched for age and for classical CV risk factors. miRNAs commonly expressed in the two group of patients but differentially expressed from the controls were selected as miRNA candidates for validation. Selected miRNAs were validated in independent serum samples from 214 RA patients (validation cohort) by studying its association with subclinical atherosclerosis measured by carotid intima-media thickness (cIMT). Plasma profile of miRNAs in the discovery study was analyzed using validated TaqMan Open Array miRNA panels which enables the quantification of 754 human miRNAs.