5 MICRORNA (MIRNA) MOLECULES AS CANDIDATE REGULATORS OF RO/SSA AND LA/SSB MRNA EXPRESSION IN SJÖGREN'S SYNDROME

Vasiliki C Gourzi, Efstathia K Kapsogeorgou, Nikolaos C Kyriakidis, Ahsen Morva, Menelaos N Manoussakis, Haralampos M Moutsopoulos, Athanasios G Tzioufas *Laboratory of Immunology, Department of Pathophysiology, School of Medicine, National University of Athens, Athens, Greece*

10.1136/annrheumdis-2011-201239.5

Background-objectives Elevated in-situ mRNA expression of Ro/SSA and La/SSB autoantigens has been observed in the affected salivary glands (SG) of patients with Sjögren's syndrome (SS); however, the regulatory mechanisms implicated in their expression are not defined. MicroRNAs (miRNAs) might be implicated in deregulated Ro/SSA and La/SSB in SS. Herein, the authors sought to investigate the expression of miRNAs that may target Ro/SSA and La/SSB ribonucleoproteins in SS. Therefore, the authors studied the expression of miRNAs, which are predicted to target Ro/SSA and La/SSB mRNAs, in salivary gland epithelial cells (SGEC), peripheral blood mononuclear cells (PBMC) and SG-tissues of SS patients and controls, as well as their association with respective mRNA expression.

Materials-methods The prediction of miRNAs that target the Ro (Ro52/TRIM21 and Ro60/TROVE2) and La mRNAs was performed by miRecords database (http://mirecords.biolead.org). miRNAs and mRNAs expression was analysed in parallel by real-time PCR in total RNA from SGECs, PBMCs and SG-tissues obtained from 11 SS patients and 11 non-SS controls. Significant differences between SS patients and controls, and associations between miRNAs and mRNAs expression, were evaluated by non-parametric Mann–Whitney and Spearman's rank correlation tests, respectively.

Results The miRecords-computational analysis identified several miRNAs that target Ro52/TRIM21 (n=430), Ro60/TROVE2 (n=1258) and La/SSB (n=377) mRNAs. To narrow the number, the analysis was restricted to miRNAs that targeted both Ro/SSA (Ro52/TRIM21 and/or Ro60/TROVE2) and La/SSB mRNAs, and were identified by at least four databases. This approach identified 11 miRNAs (let-7b, miR-16, miR-129-5p, miR-153, miR-181a, miR-200b, miR-200b*, miR-223, miR-483-5p, miR-573, miR-583). Among them, miRs 129-5p, 153, 573 and 583 were not expressed in any of the samples studied and miR-200b* was not detected in PBMCs. The remainder were expressed in SGECs, PBMCs and SG-tissues. Compared to specimens derived from controls, those derived from SS patients manifested significant upregulation of miR-181a in SG tissues (p=0.02), miR-200b in SGECs (p=0.03) and miR-223 in PBMCs (p=0.02). miR-200b levels were negatively associated with Ro52/TRIM21 (r=−0.445, p=0.04), Ro60/TROVE2 (r=−0.454, p=0.04) and La/SSB mRNA expression only in SGECs (r=−0.495, p=0.02).

Conclusions Our findings implicate miR-181a, miR-200b and miR-223 in SS, as well as miR-200b* in the regulation of Ro/SSA and La/SSB mRNAs. Further functional studies are needed to clarify the significance of the deregulated miRNAs in disease pathogenesis and autoantigen expression.