4 TLR3-MEDIATED INDUCTION OF RO/SSA AND LA/SSB MRNA EXPRESSION IN SALIVARY GLAND EPITHELIAL CELLS

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Background-objectives In-situ over-expression of Ro/SSA (Ro52/TRIM21 and Ro60/TROVE2) and La/SSB mRNAs has been previously described in the salivary gland epithelial cells (SGEC) of Sjögren's syndrome (SS) patients. Recently, Ro52/TRIM21 has been shown to possess a regulatory role in TLR3-mediated inflammatory autoimmune responses. Herein, the authors examined whether TLR3 stimulation is implicated in the regulation of Ro52/TRIM21, as well as of Ro60/TROVE2 and La/SSB mRNA expression by SGEC.

Materials-methods SGEC-lines from SS patients (n=5) and non-SS controls (n=8), were treated with the TLR3-ligand analogue polyinosinic:cytidylic acid (polyI:C, 5 μg/ml) and the TLR4-ligand lipopolysaccharide (LPS, 1 μg/ml, control TLR-treatment) for various time-points. The expression of Ro52/TRIM21, Ro60/TROVE2 and La/SSB mRNAs was analysed by real-time PCR at 0, 6, 12, 24 and 48 h of treatment. The results were normalised by the expression of the HPRT1 gene and calculated by the ΔΔCT method using HeLa as calibrator. Statistically significantly different mRNA expression was evaluated by non-parametric Mann–Whitney analysis.

Results The basal (constitutive) mRNA expression levels of Ro52/TRIM21, Ro60/TROVE2 and La/SSB molecules were similar between SGEC lines from SS patients and controls. La/SSB and Ro60/TROVE2 mRNA levels were significantly upregulated following treatment of SGECs with polyI:C for 48 h (mean fold induction±SE: 1.87±0.19 and 2.38±0.31, respectively; p=0.004 each). PolyI:C was found to be a strong inducer of Ro52/TRIM21 mRNA expression by SGECs at 6 h of treatment (mean fold induction of basal expression±SE: 14.13±4.8, p<0.0001). The polyI:C induced Ro52/TRIM21 mRNA expression remained stable until 12 h of treatment, whereas a further increment was observed at 48 h of treatment (mean fold induction: 33.4±9.8 compared to basal levels). SGECs obtained from SS patients and controls were found to respond similarly to TLR3 signaling. LPS treatment was not found to affect either Ro/SSA (Ro52/TRIM21 or Ro60/TROVE2) or La/SSB mRNA expression.

Conclusion Our findings suggest that TLR3 signaling is implicated in Ro/SSA, and particularly, in Ro52/TRIM21 mRNA expression by SGECs. Further investigation is needed to clarify the mechanisms involved in this regulation.