reduced miR-21 levels by 45%. Moreover, silencing of PD-1, using a specific siRNA, was associated with 4.5-fold up-regulation of miR-21. Experiments are underway to elucidate the mechanisms of transcriptional regulation of miR-21 by mediators downstream to PD-1 and to correlate PD-1 genotypes with miR-21 expression.

Conclusions PD-1 may exert its anti-proliferative effects through suppression of miR-21 and breakdown of this pathway in lupus can disturb the balance between immune activation and tolerance. Our data suggest that both genetic and epigenetic factors regulate T cell hyperactivity in SLE.

18 REGULATION OF T CELL HYPERACTIVITY IN SLE: THE NEGATIVE CO-STIMULATORY MOLECULE PD-1 REGULATES MIR-21 EXPRESSION IN SLE T LYMPHOCYTES

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Background and objectives Polymorphisms to PD-1, a negative regulator of T cell function involved in peripheral tolerance, increase the susceptibility to SLE. The authors sought to define the mechanisms involved by exploring its effects on miR-21 expression known to promote T cell hyperactivity in lupus.

Materials and methods PD-1 expression levels were quantified by real time PCR in purified CD4⁺ T cells. Ambion miR-Vana Kit and primers were used for the detection of miR-21. T cells were stimulated with plate-bound anti-CD3/anti-CD28 mAb and PDL1.Ig was used for PD-1 crosslinking. Silencing of PD-1 was performed with a specific siRNA.

Results Under basal conditions, freshly isolated T cells from active lupus patients had 2.3-fold higher miR-21 levels compared to healthy T cells. Combined anti-CD3/anti-CD28-stimulation induced higher miR-21 levels in SLE T cells than in controls (mean 4.0-fold vs 1.6-fold, respectively), suggesting aberrant regulation of miR-21 expression in SLE. PD-1 mRNA and miR21 levels correlated with disease activity. There was an inverse correlation between PD-1 mRNA and miR-21 levels in SLE patients ($r^2=-0.93$) suggesting a co-regulation. This was documented by stimulating SLE T cells with anti-CD3/anti-CD28 in the presence or not of PDL1.Ig. PD-1 cross-linking