IN VIVO THERAPEUTIC SUCCESS OF MICRORNA-155 (MIR-155) ANTAGOMIR IN A MOUSE MODEL OF LUPUS ALVEOLAR HAEMORRHAGE

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Methods DAH was induced by an intraperitoneal injection of 0.5 mL of pristane. MiR-155 antagonist was intravenously administrated to silence miR-155 expression. Lung tissues were collected for RNA extraction and were embedded in paraffin for sectioning. Gene expression profiling data were analysed using Ingenuity Pathway Analysis. Real time q-PCR was used for single validation. Luciferase reporter assay and RNA-Ago2 immunoprecipitation were performed for target validation.

Results MiR-155 expression was significantly increased in the development of DAH. Disease progression was reduced in miR-155−/− mice and by in vivo silencing of miR-155 using miR-155 antagonist. MiR-155 silencing dampened pristane-induced ectopic activation of multiple inflammatory pathways, and reduced the expression of pro-inflammatory cytokines. Several negative regulators of nuclear factor (NF)-κB signalling were inhibited by pristane, and were re-activated in miR-155−/− mice. In particular, the anti-inflammatory factor peroxisome prolifator-activated receptor-α was identified as a direct target of miR-155.

Conclusions MiR-155 promotes pristane-induced lung inflammation. MiR-155 contributes to ectopic activation of NF-κB signalling pathways by targeting multiple negative regulators. MiR-155 antagonist may be a promising therapeutic strategy for treating acute lung inflammation in lupus.

SEUM IL-18 AS BIOMARKER IN PREDICTING LONG-TERM RENAL OUTCOME AMONG PEDIATRIC-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Methods In a pSLE cohort of 96 patients with an average follow-up period of 10.39±3.31 years, clinical data and laboratory workups including serum IL-18 were collected at time of diagnosis. Nine (9.38%) progressed to end-stage renal disease (ESRD) and 2 (2.08%) died during follow-up. Through multivariate analysis, serum IL-18 level 6 months posttreatment was found to be the most unfavourable factor associating poor clinical outcome despite patient’s initial renal status. The presentation of serum IL-18 in its correlation with SLE global disease activity as well as the presence and severity of LN were all significant (p<0.001, p=0.03, and p=0.02, respectively). The histological classification of LN was not associated with the level of IL-18 among the pSLE patients (p=0.64).

Conclusions The role of serum IL-18 as biomarker representing global disease activity and status of renal flares among pSLE population was shown for the first time. Additionally, we have identified IL-18 at 6 months posttreatment a novel marker for long-term renal outcome prediction.

MICRORNA-21 IS A CRITICAL REGULATOR OF AUTOIMMUNITY THROUGH PROMOTING EFFECTOR AND METABOLIC FUNCTION OF PATHOGENIC TH17 CELLS

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Methods MicroRNA-21 knockout and conditional knockout mice were generated. EAE was induced to study the role of microRNA-21 in pathogenic TH17 cells and they-mediated autoimmune diseases is still unclear. In this study, we systemically dissect the role of microRNA-21 in the differentiation and effector function of pathogenic TH17 cells.

Results In this study, we demonstrate that IL-6-STAT3 signalling induced microRNA-21 is essential for the late stage commitment and maintenance of pathogenic TH17 cells by targeting key regulators. MicroRNA-21-deficient TH17 cells express less pathogenic TH17 signature genes and show less glycolytic activity. Conditional deletion of microRNA-21 in CD4+ T cells protects mice from EAE while loss of microRNA-21 expression by dendritic cells and myeloid cells do not.

Conclusions These findings suggest that microRNA-21 is a novel cell-intrinsic regulator of the commitment and metabolic function of pathogenic TH17 cells. It may be a potential therapeutic candidate with which to reprogram the immune system and help prevent and treat autoimmune diseases.