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

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Background and aims Diffuse alveolar haemorrhage (DAH) is a rare but life-threatening complication of systemic lupus erythematosus (SLE). Pristane-treated B6 mice develop severe DAH within 2 weeks of treatment. MicroRNA-155 (miR-155) is a pleiotropic microRNA that plays a crucial role in the regulation of immune responses. The purpose of this study was to examine the role of miR-155 in the development of DAH in pristane-induced lupus using miR-155-knockout (miR-155/-) mice and miR-155 antagomir to silence miR-155.

Methods DAH was induced by an intraperitoneal injection of 0.5 mL of pristane. MiR-155 antagomir 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 antagomir. 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)-kB signalling were inhibited by pristane, and were re-activated in miR-155-/- mice. In particular, the anti-inflammatory factor peroxisome proliferator-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-kB signalling pathways by targeting multiple negative regulators. MiR-155 antagomir may be a promising therapeutic strategy for treating acute lung inflammation in lupus.

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

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Background and Aims An urge of biomarker identification is needed to better monitor lupus nephritis (LN) disease activity, guide clinical treatment, and predict patient’s long-term outcome. With the proinflammatory effect and its association with inflammasomes, the significance of interleukin-18 (IL-18) among pediatric-onset systemic lupus erythematosus (pSLE) patient.

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 disease onset and 6 months after treatment despite their initial renal status. Through Cox regression analysis, the parameters at baseline and at 6 months posttreatment were carefully analysed.

Results Average age of all cases was 12.74±3.01 years old and 65 of them underwent renal biopsy at the 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.