Identification of MicroRNA Predictive of Treatment Response in Lupus Nephritis

S Hasi*, A Hadavar, H Zhou, N Birmah, M Tandon, A Aliev. National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, USA; National Institutes of Health, National Institute of Dental and Craniofacial Research, Bethesda, USA; National Institutes of Health, National Institute of Dental and Craniofacial Research NIDCR, Bethesda, USA

Background and aims High dose corticosteroids and cyclophosphamide are commonly used to treat LN. Although effective in preventing end stage renal disease (ESRD) in most cases, significant long-term side effects such as infections, increased risk of malignancy, and infertility are common and are related to the duration of therapy or the cumulative dose of medications. There are currently no markers that can reliably determine response or refractoriness to treatment at an individual level. MicroRNAs are small, non-coding RNAs responsible for post-transcriptional regulation, have been shown to have altered expression levels in a variety of diseases suggesting their potential use as biomarkers. We propose miRNAs can be predictive markers for response to cyclophosphamide.

Methods RNA was isolated and analysed via TaqMan Array MicroRNA 384 well Cards, from formalin-fixed paraffin embedded (FFPE) renal biopsies of two cohorts of patients with LN who were subsequently treated with cyclophosphamide with at least 2 years of follow up history. Patients who responded to cyclophosphamide based on urinalysis criteria of proteinuria less than 1 gram were classified as responders while those that did not fit the criteria were classified as non-responders. Significantly differentially expressed miRNAs, determined via 2^ΔΔCt method, from the first cohort were validated by the second cohort.

Results Six significantly up-regulated miRNAs, hsa-miR-30c-2-3p, hsa-miR-29b-1-5p, hsa-miR-195-3p, hsa-miR-424-3p, hsa-miR-1260a, and hsa-miR-1248 were found in responders. Conclusions These miRNAs may act as prognostic markers of renal outcomes and treatment response, which can establish a more personalised treatment of lupus nephritis in the future.

Usefulness of Soluble PD-1 in Patients with Systemic Lupus Erythematosus

S Hirahara*, Y Katsumata, Y Kawaguchi, H Yamanaka. Tokyo Women’s Medical University, Institute of Rheumatology, Tokyo, Japan

Background and aims Programmed cell death protein 1 (PD-1/CD279) is a cell surface receptor that belongs to the extended CD28/CTLA-4 family and is expressed on T cells and pro-B cells. PD-1 plays an important role in down regulating the immune system by preventing the activation of T-cells. Soluble PD-1 (sPD-1), which is produced by the alternative splicing, can functionally block the regulatory effect of membrane-bound PD-1 on T cell activation. We aimed to retrospectively evaluate the usefulness of sPD-1 in patients with systemic lupus erythematosus (SLE).

Methods We measured the levels of sPD-1 by enzyme-linked immunosorbent assay (ELISA) kit in sera of patients with SLE (n=59) and systemic sclerosis, and healthy controls, and compared them. We also analysed the association between the levels of sPD-1 and clinical information in patients with SLE.

Results The levels of sPD-1 in SLE patients with SLEDAI-2K≥6 were significantly higher than those in SLE patients with SLEDAI-2K<6, patients with systemic sclerosis, and healthy controls (p<0.05 in all comparisons), whereas there was no significant difference in other comparisons. In SLE patients, the levels of sPD-1 were moderately correlated with the titers of anti-ds DNA antibodies and SLEDAI-2K, and were moderately and inversely correlated with the levels of C3 and C4. In addition, the levels of sPD-1 were significantly higher in SLE patients with arthritis, mucosal ulcers, fever, leukopenia, or anaemia than those without (p<0.05 in all comparisons).

Conclusions The present study suggested that sPD-1 can serve as a new biomarker reflecting disease activity in patients with SLE.