Non-coding RNAs in systemic lupus erythematosus: more than a biomarker?

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Systemic lupus erythematosus (SLE) is a prototype of the systemic autoimmune diseases that occurs predominantly in women of childbearing age. Various organ systems may be involved in patients with SLE and it can lead to increased morbidity and mortality. The pathogenesis of SLE is very complex and involves both genetic and environmental factors. The immune system has many derangements that can affect both the innate immunity and adaptive immune system, leading to loss of self-tolerance. In recent years, transcriptomic and bioinformatic studies have discovered the existence of thousands of non-coding RNAs (ncRNAs). These are functional RNA molecules that are transcribed from DNA but not translated into protein. They are conventionally classified into long ncRNAs (lncRNAs) and short ncRNAs (sncRNAs) with more than or less than 200 nucleotides of the RNA length, respectively. SncRNAs can further be divided into microRNAs (miRNAs) (21–25 nucleotides long), small nucleolar RNAs (snoRNAs), and piwi-interacting RNAs (piRNAs). Recently, lncRNAs and miRNAs have been shown to be involved in the innate and adaptive immune responses. Aberrant expression of miRNAs and lncRNAs has also been found in patients with SLE. Thus, it is not surprising that ncRNAs can also contribute to the immunopathogenesis of SLE. Altered expression of miRNAs in peripheral blood mononuclear cells (PBMCs) or T cells from patients with SLE appeared to be associated with cell signaling abnormalities, altered gene transcription, T cell subset alternation and aberrant cytokine and chemokine release. Our research also demonstrated that overexpression of miR-224 in SLE T cells could suppress the expression of API5 that facilitates the activation-induced cell death of T cells. MiR-524-5p, regulated by Ca^{2+} influx, was found to be overexpressed in SLE T cells and increased miR-524-5p expression was found to correlate with disease activity in SLE patients. The expression level of SNORA12, belongs to the family of small nucleolar RNAs (snoRNAs), was lower in SLE T cells and affected the T-cell function. Therefore ncRNAs could be a biomarker of the monitor disease activity for SLE. In addition, miRNAs- or antisense oligonucleotide (ASO)-mediated therapy has been developed and at least three ASO-mediated therapies have received FDA approval. Therefore ncRNA-based therapy should change the landscape of diseases

management in the near future.