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Mechanisms of apoptotic cell-mediated IL-10 production in patients with systemic lupus erythematosus

Huan Ning and Ling Gu
Saint Louis University School of Medicine, USA

Introduction: Systemic lupus erythematosus (SLE) is characterized by production of autoantibodies and hyperactive B cells. Interleukin-10 (IL-10), a B cell growth factor, is increased in SLE patients and its levels correlate with autoantibody production and the severity of disease. The mechanisms of IL-10 overproduction in SLE patients, however, are largely unknown. We hypothesized that IL-10 overproduction in SLE patients is due, at least in part, to apoptotic cell activation of monocytes/macrophages through suppression of poly (ADP-ribose) polymerase 1 (PARP-1) activity.

Methods: Twenty-six SLE patients and fifteen healthy volunteers were enrolled. IL-10 levels in serum and culture supernatants from monocytes were measured by ELISA. Apoptosis of peripheral blood mononuclear cells isolated from both groups were determined by FACS analysis. The PARP-1 activity was measured by Universal chemiluminescent PARP-1 Assay and its effects on IL-10 transcription determined by co-transfection with the IL-10 promoter into human monocytes. Comparisons were performed with Student t test.

Results: IL-10 levels were increased and associated with increased apoptotic cells in SLE patients compared with healthy controls. PARP-1 activity was reduced in SLE patients and suppressed in monocytes by apoptotic cells in a dose-dependent manner. IL-10 gene transcription was suppressed by over-expressing PARP-1 while enhanced by knocking-down with shRNA. Mutation of the E998K in the PARP-1 protein almost completely abolished its suppressive effects.

Conclusion: The increased apoptotic cells in SLE patients lead to IL-10 production in monocytes through suppressing the PARP-1activity. Higher IL-10 promotes heightened autoreactive B cell responses and immune complex-mediated pathology in SLE patients.