AUTOIMMUNE CONNECTIVE TISSUE DISEASES

FN14 DEFICIENCY AMELIORATES ANTI-DSDNA IGG-INDUCED GLOMERULAR DAMAGE IN SCID MICE

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Background: Many studies have demonstrated that anti–dsDNA IgG is closely associated with lupus nephritis. Recently, it was found that activation of fibroblast growth factor-inducible 14 (Fn14) signaling pathway damages glomerular filtration barrier in MRL/lpr lupus-prone mice. However, MRL/lpr mice have high titers of serum autoantibodies other than anti-dsDNA IgG.

Objective: The aim of this study was to further explore the effect of Fn14 deficiency on anti-dsDNA IgG-induced glomerular damage in severe combined immunodeficiency (SCID) mice that have no endogenous IgG.

Materials and Methods: Fn14 deficiency was generated in SCID mice. The murine hybridoma cells producing control IgG or anti-dsDNA IgG were intraperitoneally injected into mice. In two weeks, the urine, serum, and kidney tissue samples were harvested from mice at sacrifice.

Results: It showed that the injection of anti-dsDNA IgG, but not control IgG hybridoma cells, induced proteinuria and glomerular damage in SCID mice. Between the wild-type (WT) and knockout (KO) mice injected with anti-dsDNA IgG hybridoma cells, the latter showed a decrease in both proteinuria and glomerular IgG deposition. The histopathological changes, inflammatory cell infiltration, and proinflammatory cytokine production were also attenuated in the kidneys of the Fn14-KO mice upon anti-dsDNA IgG injection.

Conclusions: Therefore, Fn14 deficiency effectively protects SCID mice from anti-dsDNA IgG-induced glomerular damage.