CD6 Modulation Ameliorates Immune Complex-Mediated Glomerulonephritis

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Lupus nephritis (LN) is a serious end organ complication of systemic lupus erythematosus (SLE) in which T cells are thought to play an essential role. CD6 is a co-stimulatory receptor on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presentation cells and epithelial and endothelial tissues. The CD6-ALCAM pathway plays an integral role in modulating T cell activation and trafficking, and increased levels of CD6 are associated with pathogenic T cell responses. To assess the role of the CD6-ALCAM pathway in LN pathogenesis, we tested a monoclonal antibody against CD6 in a short-term, validated, inducible murine model of lupus nephritis known as nephrotoxic serum nephritis (NTN). NTN mice were treated 3x per week with an anti-CD6 mAb (10D12, 60ug/dose, n=23) or with vehicle control (n=23). Healthy mice were also included as a control (n=12). Mice treated with the anti-CD6 mAb displayed decreased levels of proteinuria ($p<0.001$) and significantly improved BUN levels ($p<0.01$) compared to vehicle control mice. Histology also significantly improved with anti-CD6 treatment ($p<0.05$). RT-PCR revealed significantly decreased levels of VCAM and RANTES in the kidneys of treated mice, while anti-inflammatory IL-10 was increased, compared to vehicle control mice. Flow cytometry analysis indicated decreased accumulation of both renal-infiltrating activated T cells (CD4+CD25+CD69+, $p <0.01$) inflammatory macrophages ($p<0.05$). Overall, these results indicate that the CD6-ALCAM pathway is an important driver of inflammation and pathology in LN and, thus, a promising therapeutic option that is more selective than the immunosuppressive therapies currently offered.