Amelioration of Skin and Kidney Disease in a Spontaneous Murine Lupus Model via CD6 Modulation

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Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease that can affect multiple organ systems, including the kidneys, skin, and brain. T cells are an important mediator in this end organ damage. CD6 is a co-stimulatory receptor, predominantly expressed on T cells, which binds with activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presentation cells and various epithelial and endothelial tissues. This signaling pathway is vital for T cell activation, proliferation, differentiation and trafficking. We found increased expression of both CD6 and ALCAM in the kidneys of MRL/lpr mice (a spontaneous model of SLE) versus healthy control B6 mice. In a separate experiment, female MRL/lpr mice were aged to 9-10 weeks of age, at which point we began treating with either anti-CD6 antibody (60 ug/dose, intraperitoneally twice per week), isotype control (60 ug/dose, twice per week), or cyclophosphamide (25 mg/kg, once per week). We also included a no treatment group and a group of MRL/MpJ mice, a congenic healthy control strain. Mice treated with anti-CD6 show lower levels of proteinuria and BUN ($p<0.05$), improved survival rates, and decreased renal pathology compared to isotype control mice. Flow cytometry revealed decreased numbers of activated and effector T cells within the kidneys of anti-CD6 treated mice compared to isotype control mice. While there was no difference in anti-DNA levels, anti-CD6 treatment significant improved the spontaneous skin lesions associated with disease progression. Overall, these results indicate that targeting CD6-ALCAM interactions may have promising therapeutic potential within the context of different end organ pathologies within lupus.