Titel des Beitrags:
Chemokine receptor Ccr2 deficiency reduces renal disease and prolongs survival in MRL/lpr lupus-prone mice.

Abstract:
MRL/MpJ-Fas(lpr)J (MRL/lpr) mice represent a well-established mouse model of human systemic lupus erythematosus. MRL/lpr mice homozygous for the spontaneous lymphoproliferation mutation (lpr) are characterized by systemic autoimmunity, massive lymphadenopathy associated with proliferation of aberrant T cells, splenomegaly, hypergammaglobulinemia, arthritis, and fatal immune complex-mediated glomerulonephritis. It was reported previously that steady-state mRNA levels for the chemokine (C-C motif) receptor 2 (Ccr2) continuously increase in kidneys of MRL/lpr mice. For examining the role of Ccr2 for development and progression of immune complex-mediated glomerulonephritis, Ccr2-deficient mice were generated and backcrossed onto the MRL/lpr genetic background. Ccr2-deficient MRL/lpr mice developed less lymphadenopathy, had less proteinuria, had reduced lesion scores, and had less infiltration by T cells and macrophages in the glomerular and tubulointerstitial compartment. Ccr2-deficient MRL/lpr mice survived significantly longer than MRL/lpr wild-type mice despite similar levels of circulating immunoglobulins and comparable immune complex depositions in the glomeruli of both
groups. Anti-dsDNA antibody levels, however, were reduced in the absence of Ccr2. The frequency of CD8+ T cells in peripheral blood was significantly lower in Ccr2-deficient MRL/lpr mice. Thus Ccr2 deficiency influenced not only monocyte/macrophage and T cell infiltration in the kidney but also the systemic T cell response in MRL/lpr mice. These data suggest an important role for Ccr2 both in the general development of autoimmunity and in the renal involvement of the lupus-like disease. These results identify Ccr2 as an additional possible target for the treatment of lupus nephritis.

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