CCR4-deficient mice show prolonged graft survival in a chronic cardiac transplant rejection model.

Abstract:
Chronic graft rejection mediated by cellular immune responses still poses a serious clinical problem in transplant surgery. Chemokines coordinate the recruitment of leukocytes in inflammatory and immune responses. Their precise functions in the rejection of allografts are still ill defined. This study investigates the role of chemokine receptor 4 (CCR4) in acute and chronic cardiac allograft rejection in mice. Allogeneic hearts were transplanted into CCR4 deficient (CCR4(-/-)) and control recipients. Reverse transcription-PCR showed transcription of macrophage-derived chemokine and thymus and activation-regulated chemokine, the cognate chemokine ligands of CCR4, within the graft. Compared to wild-type controls, acute allograft rejection in CCR4(-/-) recipients was only slightly prolonged. In contrast, in a gallium nitrate chronic cardiac allograft rejection model, cardiac graft survival was significantly prolonged in CCR4(-/-) recipients. A relative increase in the percentage of graft infiltrating CD8(+) T cells in CCR4(-/-) recipients was observed 30 days after transplantation and was accompanied by a decrease in CD4(+) T cells. Moreover, the percentage of NK1.1(+)CD3(+) graft-infiltrating cells was significantly reduced on day 5 and day 30 post transplantation. These findings indicate that CCR4 is involved in the recruitment of NK1.1(+)CD3(+) cells into cardiac allografts and clearly establish an
important and novel role for CCR4 in chronic graft rejection.