

Donor dendritic cells after liver and heart allotransplantation under short-term immunosuppression

SIR,—Donor (LEW) dendritic cell dissemination into recipient (BN) tissues was assessed in rats 16, 30, and 70 days after orthotopic liver transplantation (n = 3) and 30 days after intra-abdominal heart transplantation (n = 4), according to previously described surgical techniques.¹ Intramuscular FK 506 (1 mg/kg) was given to liver recipients daily for 7 days, but continued for 14 days in heart recipients because of the greater vulnerability to rejection of cardiac compared with hepatic grafts.² The same doses were then continued twice a week. Immunolabelling with a mouse monoclonal antibody, L-21-6, which recognises the invariant chain of LEW and most other rat strains, but not BN class II MHC antigen,³ allowed the distinction of donor from recipient cells.

L-21-6+ (donor) dendritic-shaped cells were detected in lymphoid tissues of the non-rejecting LEW-BN liver recipients at 16, 30, and 70 days. These cells were restricted to the periarterial lymphatic sheaths of the spleen, and the paracortex of mesenteric, cervical, and intrathoracic lymph nodes, but diminished with time (figure). Occasional cells were also detected in the thymic medulla and non-lymphoid organs, such as the heart and skin, but not the brain. Liver allografts showed mild mononuclear infiltration with increased numbers of mast cells, but there was no evidence of parenchymal damage or obliterative arteriopathy. Residual donor (L-21-6+) dendritic cells were present in portal tracts and beneath the terminal hepatic venules at all time points examined.

Despite a longer period of daily FK 506 treatment, heart allografts had obliterative arteriopathy, indicating low-grade graft rejection. As in the liver transplants, the mild cellular infiltrate in heart allografts contained increased numbers of mast cells. An estimated one quarter of the normal quantity of dendritic cells in the cardiac graft interstitium and around blood vessels was identified as the persistent L-21-6+ (donor) phenotype. Unlike liver recipients, heart recipients had only rare donor dendritic cells in their spleen and lymph nodes, none in thymus, and none in non-lymphoid tissues, skin, lung, native heart, adrenal glands, kidneys, liver, intestines, and brain.

When liver transplantation was done across the immunologically more difficult ACI-BN strain barrier (n = 3), donor cell dissemination to extrahepatic tissues at 30 days resembled that after

LEW-BN cardiac allotransplantation. Donor dendritic cells persisted irregularly in the liver grafts but were sparse or undetectable at extrahepatic sites.

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Donor dendritic cell repopulation in recipients after rat-to-mouse bone-marrow transplantation

SIR,—Bone-marrow-derived dendritic cells are powerful antigen-presenting cells, which are 100-times more effective than macrophages in activating T lymphocytes in mixed-lymphocyte culture¹ and in intact animals.² These cells are pivotal in the generation of the T-cell repertoire, including provision of the appropriate ligand for negative selection of potentially autoreactive T lymphocytes.³ We now describe the tissue distribution of donor dendritic accessory cells in fully xenogenic (F344 rat → B10 mouse) radiation bone-marrow chimeras that were permanently tolerant to donor-specific xenoantigens, yet fully reactive to third-party mouse and rat lymphoid cells.^{4,5}

Laboratory animals were typed for chimerism by flow cytometry, and 3 per group were killed for a complete tissue survey at 1, 2, 3, 4, 6, and 8 weeks and at 8 months after reconstitution. Immunohistochemical staining for rat-derived dendritic cells (class II bright) was with the monoclonal antibody L-21-6 directed at the invariant chain of the rat class II molecule without cross-reactivity in mouse cells (provided by Dr Yuichi Iwaki, University of Pittsburgh).



Donor-recipient histological changes one month after rat liver allotransplantation under FK 506 immunosuppression.

Periarterial lymphatic sheath of spleen (left); thymic medulla (right). Immunoperoxidase stain with L-21-6 monoclonal antibody and haematoxylin counter stain ($\times 300$ - $\times 500$).