

Prevention of Sensitization and Hyperacute Rejection in Liver and Heart Xenografts by FK 506 Plus Donor Antigens

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WE have observed that FK 506 (FK) prevented the induction of hyperacute rejection (HAR) in hamster-to-rat liver (OLT_X) and heart (HT_X) transplant models and analyzed the mechanisms. 1.5×10^7 hamster hepatocytes (HC) or a minced heart as source of xenoantigens were given to prospective recipients on day -6, with or without FK (1 mg/kg/d \times 6). OLT_X and HT_X were performed on day 0.

Xenoantigen alone induced HAR that correlated with high titer of complement-dependent cytotoxic antibody (CDC). Additionally, immunosuppression with FK resulted in prevention of HAR and improved survival of OLT_X recipients in the first 3 postoperative weeks ($P < .05$), with evidence of reduced antibody in the grafts. Even though FK did not eliminate total IgM amount and natural antibody titers, target-specific IgM, which is responsible for HAR, was reduced in the antigen + FK-treated group as compared with that with antigen alone. Furthermore, the sera from long-term survivors of OLT_X did not inhibit CDC

activity of sera obtained from animals experiencing HAR. This is contrary to reports by Braun et al.¹ who showed an inhibitory effect of serum from an immunosuppressed patient, postulating a possible role for anti-idiotypic antibodies. This preliminary evidence suggests that the inhibition of xenoantigen-specific IgM production by FK seems to play an important role in the acceptance of xenografts.

REFERENCE

1. Braun WE, Klingman L, Stewart RW, et al: Transplantation 46:153, 1988

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