The Protection From Humoral Rejection Given by a Liver Xenograft Is Species-Specific and Non-MHC Restricted

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WE transplanted B10.BR (H-2^k) mouse livers into 3- to 4-week-old LEW rats (RT1^l) and obtained greater than 100 days graft survival in over 50% of the recipients concomitantly treated with FK 506. However, in spite of FK 506 therapy, heart xenografts in the same model were rejected in 2 days. Furthermore, stable liver recipients that had been off FK 506 for 1 month when challenged with B10.BR or Balb/C (H-2^d) hearts rejected them (12.4 ± 3.6 and 11.8 ± 2.1 days, respectively) by cellular mechanisms, whereas third-party hamster hearts were lost to humoral rejection in 3 to 4 days. Heterophilic antibodies present in rat recipients of primary B10.BR heart xenografts not only lysed B10.BR but also Balb/C mouse lymphocytes with the same intensity, suggesting that species specificity rather than MHC antigens may be more important in this model. This observation was further supplemented by the failure of the antibodies in the serum from recipients that had rejected a B10.BR heart graft to block the expression of class I antigens (H-2^k) in B10.BR splenocytes. It is noteworthy that the complement (C) in our long-surviving liver recipients, which had become mouse-type after grafting, produced weak lysis of mouse lymphocytes while efficiently killing hamster cells. Given this apparently species-specific protective effect of a liver xenograft, it is tempting to speculate that the humoral response against the xenograft is species rather than MHC-restricted, which may be an outcome of species restriction of C inhibition.

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