Complement and Target Cells Belong to the Same Species After Liver Xenografting: Protection From Hyperacute Rejection

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LIVER xenografting implies that most of the complement (C) in the recipients will be produced by the graft. It is known that membrane-bound proteins have the property of homologous restriction; ie, they inhibit MAC-mediated lysis only when the terminal C components are from the same species as the cells on which these proteins are expressed.[1] To test the hypothesis that this could be a mechanism of protection from hyperacute rejection, we transplanted hamster hearts into stable hamster-to-rat liver xenograft recipients (OLT). Minutes later, hyperimmune serum (HS) obtained from untreated hamster heart xenograft recipients was given intravenously (IV)—either unaltered or C-inactivated by heating at 56°C for 30 minutes. Survival of the hamster hearts is shown in Table 1. Different dilutions of absorbed sera were tested in their ability to lyse hamster or mouse lymphocytes in a C-dependent cytotoxicity assay. Hamster serum did not lyse hamster cells. While antihamster HS and normal rat serum produced efficient lysis of hamster lymphocytes, that produced by OLT serum was poor. In contrast, OLT serum caused efficient lysis of mouse target cells. In conclusion, the homology of C and target cells represents a novel mechanism of protection that the liver confers to other organs.

REFERENCE

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Table 1. Survival of Hamster Heart Xenografts in Liver Xenograft Recipients Injected With Active or Decomplemented Rat Antihamster Hyperimmune Serum

Heart Recipients (Immunosuppression)	Transferred Hyperimmune Serum			
	Active	(MST ± SD)	Inactive	(MST ± SD)
1. Normal LEW* (none)	2, 2, 2, 3, 3 min	(2.4 ± 0.5)	8, 10, 15, 18, 32 min	(16.6 ± 9.4)
2. LEW rat (CyP 8 mg/kg per day × 10 + FK 506 1 mg/kg per day × 30)†	2, 2, 3, 3, 4 min	(2.8 ± 0.8)	6, 12, 12, 21, 28 min	(15.8 ± 8.6)
3. OLT rat‡,§ (CyP + FK 506)	7, 8, 12, 16, 32 min	(15.1 ± 10.1)	23, 23, 25, 27, 28 days	(25.2 ± 2.2)

*LEW rat recipients normally reject hamster hearts in a mean of 3.0 days.

†Pretreatment. This kind of pretreatment normally extends survival of hamster hearts beyond 3 days.

‡LEW rats that received a hamster liver transplant 40 to 60 days before and were immunosuppressed with CyP and FK 506 as in group 2 for 30 days, with no treatment thereafter. The preexisting liver xenografts were not adversely affected at the time of heart rejection using inactivated HS. With active HS, the livers of 4 of 5 rats underwent humoral rejection in less than 24 hours, and the fifth rat survived another 50 days.

§When unaltered (n = 5) or decomplemented (n = 5) normal rat serum was given instead of HS. Heart xenograft survival was unaffected in group 1 (3 days) and in group 3 (25 days).