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Metabolic Changes in the Recipient After Successful Liver Xenotransplantation in the Rat

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MOST hepatic functions are genetically determined and, after liver transplantation, the hepatic parenchyma retains its species specificity. Therefore, in the hamster-to-rat liver xenotransplantation model,[1] we assessed the phenotypic changes of the serum protein profile in the recipient, as well as the functional compatibility between the xenoproteins and the recipient environment. Upon serum protein electrophoresis from a normal rat, a xenotransplanted (OLTX) rat, and a hamster, it was evident that the protein profile of the OLTX rat was closer to the hamster than to the rat. In particular, the rat albumin migrated less than hamster albumin, and an OLTX rat at 180 days after transplantation clearly showed hamster albumin. Six days after transplantation OLTX rat serum samples contained albumin with mixed migration characteristics.

Combining electrophoresis and immunofixation techniques we demonstrated the band of migration of complement in the area of the β_2-globulins. The OLTX showed a complement band with the same characteristics of the hamster, confirming that in the transplanted rat the main source of complement was of hamster liver origin.

By double immunodiffusion assay, using antibodies against rat IgG, it was demonstrated that the IgG in the transplanted rat remained recipient-type. To study the interaction between the hamster complement present in the OLTX serum and the rat IgG, we performed a hemolytic assay. In that test, the OLTX complement was able to lyse SRBC with rat antibodies, with the same efficiency as normal rat complement.

Another possible functional interaction between donor and recipient proteins was studied on the OLTX bile. The IgA, that have recipient origin because it is produced by the lymphoid tissue, has to be transported into the bile by the secretory component (SC), a membrane protein produced by the biliary epithelium and so of donor origin. With radial immunodiffusion performed in agar containing goat antirat IgA, we tested rat, hamster, and OLTX rat bile and demonstrated the presence of the same amount of rat IgA in the bile of a normal rat and in the bile of an OLTX rat. Immunohistochemical analysis of a hamster liver graft stained for IgA showed a distribution of IgA along the perisinusoidal space, and a granular pattern of staining in the cytoplasm. It seemed to suggest preferential binding to receptors (SC) for these immunoglobulins.

In conclusion: (1) after liver xenotransplantation, hepatic serum proteins show donor phenotype; (2) molecular chimerism does not necessarily preclude normal protein function; and (3) donor proteins seem able to functionally interact with the recipient environment.

So far, no incompatibilities with a normal life have been identified after liver transplantation in the hamster-to-rat model.

REFERENCE

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