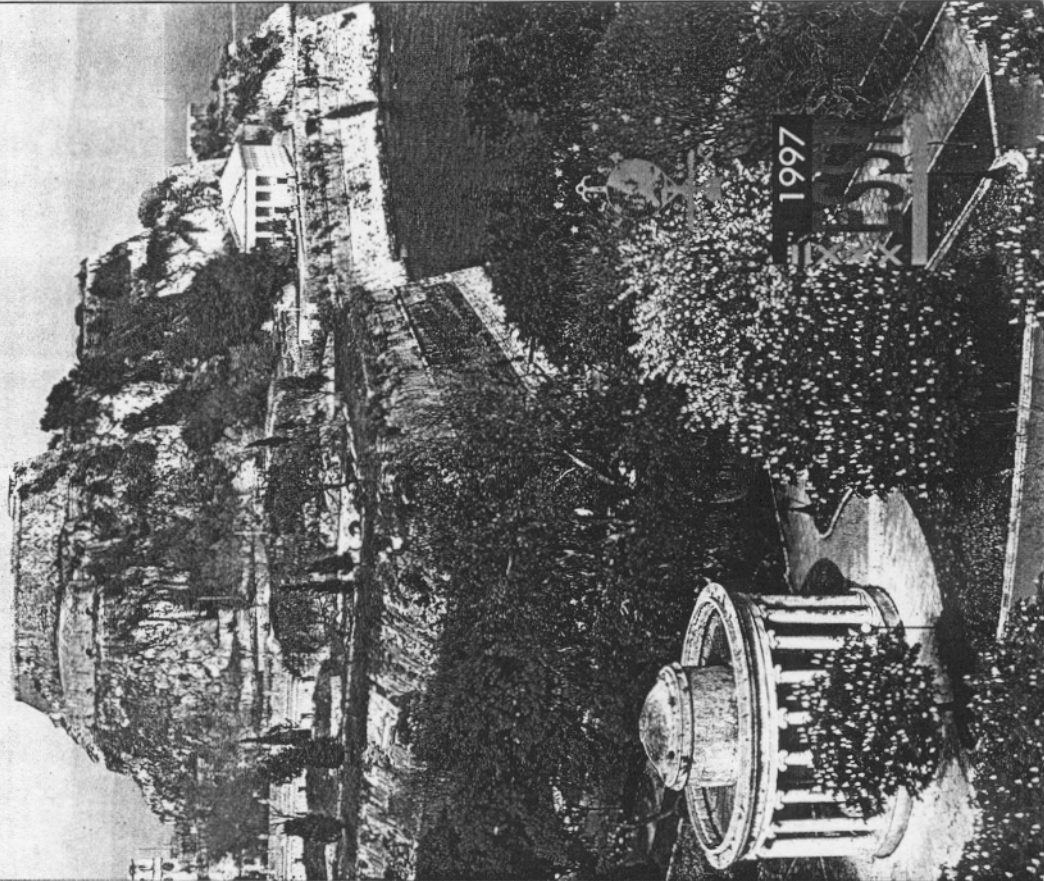


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P-73 Immunotolerance in Hepatocellular Transplantation

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Inoculation of allogeneic bone marrow and glomeruli into the thymus has induced a certain degree of tolerance improving subsequent allografts survival. In other hand, hepatocellular transplantation (HCT) is a feasible technique with hepatocyte's survival, functionalism and regenerative capability well established. In the present study, the efficacy of intrathymic allogeneic hepatocyte inoculation in promoting specific tolerance was tested by assessing the effect of this strategy on the survival of subsequent allogeneic splenic HCT.

Methods. Syngeneic adult male WAG rat (250 g) were used as donors for HCT. Young WAG and Sprague-Dawley male rats (70–80 g) were used as recipients. Hepatocytes were obtained by enzymatic digestion with collagenase, following the technique described by Seglen. Under ether anesthesia, 3×10^6 hepatocytes were inoculated into each thymic lobe, through a cervicotomy. HCT was carried out 15 days later, inoculating into the thymus and the spleen 20×10^6 hepatocytes. Animals were sacrificed on days 1, 5, 7 or 15, and the presence of hepatocytes in the thymus and the spleen was assessed by optic and immunofluorescent microscopy. Three series of 10 animals were formed: WAG-WAG, WAG-SD and WAG-SD plus immunosuppression (CsA 20 mg/kg i.p. and dexamethasone 6 mg/kg on days -2, -1 and 0 prior to intrathymic inoculation).

Results. Fifteen days after intrathymic syngeneic HCT, morphologically normal hepatocytes may be seen in the thymus. Allogeneic hepatocytes inoculated into the thymus do not survive more than 7 days, and a subsequent HCT into the spleen is rejected. Intrathymic allogeneic HCT associated to a short course of immunosuppression induced a certain degree of tolerance, as demonstrated by the presence of morphologically normal hepatocytes in the splenic pulp seven days after transplantation.

Conclusions. Intrathymic cellular transplantation may be useful to induce allotolerance for hepatocellular transplantation.