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Title: **Donor Specific Cardiac Allograft Tolerance Without Immunosuppression Following Intrathymic Injection of Donor Alloantigen**

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Induction of donor specific tolerance could prevent the side effects of immunosuppression while improving allograft survival. On day 0, adult male Buffalo ($RT1^b$) rats underwent an intrathymic (IT), portal venous (PV), intrasplenic (IS), or subcutaneous (SQ) injection of $25x10^6$ MHC mismatched Lewis ($RT1^l$), UV-B irradiated Lewis, or syngeneic Buffalo splenocytes, and simultaneously were given 1 cc of rabbit anti-rat lymphocyte serum (ALS) intraperitoneally. 21 days later, a heterotopic Lewis heart was transplanted. Graft survival was evaluated for significance by Kaplan-Meier analysis.

	TREATMENT		Allograft			
Group	IT	ALS	from LEW	Survival Time (days)	MST	p Value vs Control
1	-	-	Heart	6,7,7,8,8	7.2	--
2	-	+	Heart	6,7,7,7,8,9	7.3	NS
3	+ (LEW)	-	Heart	5,6,7	6.0	NS
4	+ (LEW)	+	Heart	6,14,>50(x3),>100(x7),>200(x8)	>176.8	p<0.001
5	+ (UV-B LEW)	+	Heart	>104,>61,10,8	>45.7	0<0.05
6	+ (BUF)	+	Heart	6,7	6.5	NS
7	+ (LEW)	+	2nd Heart (LEW)	>30,>125	>77.5	p<0.05
8	+ (LEW)	+	2nd Heart (ACI)	7,7	7.0	NS

Intrathymic splenic alloantigen injection induced a donor specific tolerance which allowed the cardiac allograft to survive indefinitely in >86% of the recipients without further immunosuppression, while groups receiving antigen injections at other sites (PV, IS, and SQ) rejected cardiac allografts in control time. Prolongation of cardiac allograft survival is specific for the donor antigen given IT since syngeneic or third party antigen does not prolong allograft survival. Microchimerism is unlikely since allograft survival was also prolonged in rats receiving UV-B irradiated Lewis splenocytes which cannot proliferate. Buffalo rats with a long surviving Lewis cardiac allograft after Lewis IT injection subsequently rejected a heterotopic ACI cardiac allograft in a normal fashion, while a second Lewis cardiac allograft was not rejected. Conclusion: IT injection of alloantigen into the adult thymus results in donor specific tolerance during T lymphocyte maturation, thereby allowing long-term cardiac allograft survival without subsequent immunosuppression.

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Title: **Xenogeneic cellular response of human lymphocytes against porcine lymphocytes and isolated pancreatic islets**

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In spite of first clinical trials, very little is known to date about the human cellular response against porcine, i.e., xenogeneic isolated pancreatic islets. Therefore, it was the aim of this study to examine the cell-mediated in vitro response of human responder PBL against porcine stimulator lymphocytes of different lymphatic compartments in the mixed lymphocyte culture (MLC) and isolated porcine pancreatic islets in the mixed lymphocyte islet culture (MLIC). **Results: (1)** In contrast to recent presumptions, a positive cellular response can be observed in the xeno-MLC/MLIC. **(2)** The strength of this response depends on the (lymphatic) stimulator compartment studied (blood > spleen > lymph node > isolated pancreatic islet). **(3)** The strength appears to be also dependent on the individual human lymphocyte donor. **(4)** The MLC/MLIC response appears to correlate with the number of antigen presenting cells, e.g., MHC class II-positive macrophages, within the xenogeneic stimulator cell population (FACS analysis). **(5)** The purity of the isolated pancreatic islet stimulator population greatly influences the MLIC response (crude islets > > handselected islets). **Conclusions: (1)** The selection of the stimulator compartment determines the strength of cellular in vitro responses in the MLC/MLIC. **(2)** Transplantation of porcine pancreatic islets requires careful purification efforts in order to reduce as much graft immunogenicity as possible.