Literature Reviews–Cells

Luca Inverardi

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Induction of Remission after Donor Leucocyte Infusion for the Treatment of Relapsed Chronic Idiopathic Myelofibrosis Following Allogeneic Transplantation: Evidence for a 'Graft-vs.-Myelofibrosis' Effect

J.L. Byrne, H. Beshti, D. Clark, I. Ellis, A.P. Haynes, E. Das-Gupta and N.H. Russell

British Journal of Hemaetology 2000 Feb; 108(2):430-3.

Complete Remission of Idiopathic Myelofibrosis Following Donor Lymphocyte Infusion After Failure of Allogeneic Transplantation: Demonstration of a Graft-Versus-Myelofibrosis Effect

F. Cervantes, M. Rovira, A. Urbano-Ispizua, M. Rozman, E. Carreras and E. Montserrat

Bone Marrow Transplantation 2000 Sep; 26(6):697-9.

Idiopathic myelofibrosis is a hematological disease of uncertain etiology that leads to progressive anemia and bone marrow fibrosis. No effective therapy is currently available. In severe, progressive cases bone marrow transplantation has been attempted with only partial success. Two recent reports describe a novel, intriguing finding, i.e., a "graft versus myelofibrosis" effect. In both described cases, a transplant of stem cells led to transient amelioration of the hematological pattern, followed by recurrence of the disease. Donor leukocytes were therefore administered. A mild acute GVHD was observed in one case, chronic GVHD was observed in the other. In both patients GVHD was followed by a sizable improvement of the hematological condition with reduction in bone marrow fibrosis and osteosclerosis. These are novel findings suggesting an effect of donor leukocyte infusions on idiopathic myelofibrosis similar to that observed in other hematological malignancies. This observation might add a precious therapeutic tool to our armamentarium for the treatment of this progressive, fatal disease.

Transplantation of Highly Differentiated Immortalized Human Hepatocytes to Treat Acute Liver Failure

N. Kobayashi, M. Miyazaki, K. Fukaya, Y. Inoue, M. Sakaguchi, T. Uemura, H. Noguchi, A. Kondo, N. Tanaka and M. Namba

Transplantation 2000 Jan 27; 69(2):202-7.

Hepatocyte transplantation has appealing features for the treatment of acute liver failure. Bioartificial liver devices have been preliminarily tested with encouraging results. One of the important limitations to a more widespread use of such devices is the need for the use of xenogeneic hepatocytes because of the scarce availability of human cells. An immortalized but functionally highly competent human hepatocyte cell line might solve the problem of human hepatocyte availability and make the bioartificial liver a valuable and easily available tool for clinical trials. Kobayashi and associates have utilized the large T antigen of SV40 to immortalize primary human fetal hepatocytes. Immortalized cells were preliminarily tested in rats to ascertain their efficacy in preventing hyperammonemia and encephalopathy after sub-total hepatectomy. Transplanted immortalized human hepatocytes indeed protected the recipient animals determining significantly prolonged survival after 90% hepatectomy. Unlimited availability of human hepatocytes for treatment of acute liver failure and possibly other pathological conditions may be of exceptional clinical utility.

A Murine Model of Allogeneic Adrenocortical Cell Transplantation: Perspectives for the Treatment of Addison's Disease in Humans

V. Ellerkamp, T.J. Musholt, S.H. Klebs, P.B. Musholt, G.F. Scheumann, J. Klempnauer and M.W. Hoffman

Surgery 2000 Dec; 128(6):999-1006.

Hormone substitution for the treatment of Addison's disease (adrenocortical insufficiency) provides inadequate replacement, especially in stress situations, where regulated secretion by the cortex is not properly mimicked by exogeneous hormone administration. Allogeneic transplantation of adrenocortical cells represents therefore an intriguing possibility. Ellerkamp and associates describe an animal model of adrenocortical cell transplantation, where immunological responsiveness to the tissue is analyzed in some detail. Interestingly, immune recognition of MHC class I disparate cells by lymphocytes is remarkably inefficient, suggesting an intrinsic immunomodulatory property of adrenocortical cells. Natural candidates for this immunomodulation are the corticosteroids secreted by adrenocortical cells. Experiments performed to address this very issue, on the other hand, provide evidence for additional mechanisms of immunomodulation by adrenocortical cells. These intriguing observations highlight some potentially unique immunological features of adrenocortical cell transplantation.

Transplanted Fetal Striatum in Huntington's Disease: Phenotypic Development and Lack of Pathology

T.B. Freeman, F. Cicchetti, R.A. Hauser, T.W. Deacon, X.J. Li, S.M. Hersch, G.M. Nauert, P.R. Sanberg, J.H. Kordower, S. Saporta and O. Isacson

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Transplantation of neural and stem cells holds promise as a viable approach for the treatment of neurodegenerative diseases. A paradigm of neurodegenerative diseases is represented by Huntington's chorea. It is a fatal untreatable disease characterized by progressive loss of neurons in the nucleus striatum. In a clinical trial of fetal striatal

neuron transplantation, the exploration of these premises was undertaken. A patient died 18 months after transplantation of causes unrelated to the procedure. Post-mortem histological analysis of the transplanted cells revealed their persistence and typical morphology of developing striatum. Remarkably, no histological evidence of immune rejection was observed. Also, transplanted cells exhibited a normal phenotype, namely the absence of protein aggregates of mutated hungtintin, the hallmark of the disease. These important findings provide direct evidence of survival of transplanted fetal neurons in the brain of a patient 18 months post-transplant.

Luca Inverardi, M.D.
Diabetes Research Institute
University of Miami
1450 Northwest 10th Avenue
Miami, Florida, USA 33136
Tel.: 305.243.2954
Fax: 305.548.4404
email: linverar@med.miami.edu