

## Experimental study of combined treatment with tacrolimus and donor splenocytes via the portal vein in small bowel transplantation

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**Abstract :** We previously reported that the combined treatment of perioperative administration of donor splenocytes via the recipient's portal vein (DSPV) and a short-course Tacrolimus significantly prolonged the survival of fully allogenic grafts in rat small bowel transplantation (SBTX). In the present study we examined whether this effect depended on the quantity of the administered alloantigens in DSPV. In addition, we examined the expression of the surface antigen on T cells of the splenocytes and the induced toleragenic factor, according to the tolerant recipients which in our previous report had shown the prolongation of allogenic transplant small bowel graft survival by the combined treatment of DSPV ( $1 \times 10^6$  donor splenocytes) and a short-course Tacrolimus. Donor splenocytes were prepared from Brown-Norway (BN (RT1<sup>u</sup>)) rat spleens for Lewis (LEW (RT1<sup>y</sup>)) recipients. The recipients ( $n=10$ ), treated with a short course of Tacrolimus (0.5mg/kg, 0 to 3 days postoperatively) only showed graft rejection with an average of  $6.3 \pm 1.0$  days postoperatively. However, the combined treatment, consisting of DSPV of  $1 \times 10^6$  donor splenocytes and a short course Tacrolimus significantly prolonged graft survival to  $12.7 \pm 2.1$  days ( $n=12$ ,  $P<0.01$ ). DSPV of less than  $1 \times 10^6$  donor splenocytes ( $5 \times 10^5$  cells and  $2.5 \times 10^7$ ) could not prolong the graft or animal survival under a short-course Tacrolimus treatment. In the tolerant recipients, the CD4 and CD8 percentages of splenocytes were not significantly different from those of control rats or recipients that were treated with short-course Tacrolimus alone. Nevertheless, the percentage of Tcr- $\alpha$   $\beta$ <sup>+</sup> cells expressing IL-2 receptor (R) was significantly lower than in either control rats or the recipients with short-course Tacrolimus. In the suppression assay to one-way mixed lymphocyte response, a toleragenic factor was suggested to the present in the serum of the tolerant recipients. In the present study, it was suggested that the effects of the combined treatment of DSPV and short-course Tacrolimus for the prolongation of graft survival in the rat allogenic SBTX should depended on the quantity of the antigens administered into the portal vein. The beneficial effects of this treatment were reflected in the suppression of IL-2R on the recipient's splenocytes, and tolerogenic factor(s) might subsequently be induced in the tolerant recipient's serum. *J. Med. Invest.* 48 : 157-165, 2001

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## INTRODUCTION

Since the gut is the largest lymphoid tissue in the human body and has specific immunogenicity (1), graft rejection is the most important threat to suc-

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## **Small Bowel Transplantation An Experimental Study In The Rat:**

Small Bowel Transplantation Jan M. van Oosterhout, 1982      *Organtransplantation in Rats and Mice* Wolfgang Timmermann, Heinz-Jochen Gassel, Karin Ulrichs, Robert Zhong, Arnulf Thiede, 2012-12-06 Main focus of the new book will be the description and discussion of rat and mouse models for organ transplantation Various microsurgical techniques will be presented which allow transplantation of functional organs in syngeneic systems In particular the extremely difficult methods necessary for organ transplantation in mice will be presented and evaluated Besides these practical aspects the book will also cover the theoretical sides of organ transplantation like the immunobiology of allotransplantation Special emphasis will be given to the resurgent field of xenotransplantation The results from xenograft models developed in the recent years using rats or mice will be reviewed and their impact on future human xenotransplantation will be discussed      *Microsurgical Models in Rats for Transplantation Research* Arnulf Thiede, Eberhard Deltz, Rainer Engemann, Horst Hamelmann, 2012-12-06 Preclinical experimental transplantation research that is based on microsurgical models in rats fulfills two indispensable conditions for modern organ transplantation research Almost all organ grafts can be performed on the rat with an amount of technical effort that is still justifiable Thus transplantation models that are analogous to human organ transplantation can be developed tested and evaluated This fulfills a necessary condition from the standpoint of surgery With the species rat we have a great variety of genetically different inbred strains From the immunological point of view this is an indispensable prerequisite for the investigation of preclinical transplantation models that can be expected to produce controllable reproducible results In vivo experimental results can be supplemented by and correlated to in vitro tests Lately these experimental results are being greatly expanded and more precisely defined by the application of immunohistological methods that have been established recently in Kiel In this book we hope to present a cross section of the microsurgical models in use today and of current immunological and immunohistological models Furthermore we wish to record the present state of microsurgical organ transplantation research and to show its relationship to the current state and development of clinical organ transplantation A special aspect of our Kiel research group is the long term well functioning interdisciplinary cooperation between surgery immunology and pathology Through this cooperation we attempt to provide an atmosphere in which theoretical and practical viewpoints can mutually influence each other      **Cumulated Index Medicus**, 1996      **Handbook of Animal Models in Transplantation Research** Donald V. Cramer, Luis G. Podesta, Leonard Makowka, 2024-11-01 Handbook of Animal Models in Transplantation Research is a new surgical handbook that provides detailed information concerning the transplantation of a variety of tissues in experimental animals The text provides a practical guide for experienced investigators to develop new surgical transplantation models for application in a laboratory setting Each chapter gives consistent descriptions of the anatomical considerations the surgical model and potential applications of the procedure The organ systems covered include the heart and or lung liver small bowel kidneys and bone

marrow The species selected for representation of each experimental model is based upon the usefulness and frequency of the model for studies in transplantation research This book is important for all experimental surgeons transplantation biologists and students of surgical research *Index Medicus* ,2004 Vols for 1963 include as pt 2 of the Jan issue Medical subject headings Research Awards Index ,1983 *Gastroenterology Abstracts and Citations* ,1977 **Research Grants Index** National Institutes of Health (U.S.). Division of Research Grants,1970 **Tissue Engineering Using Ceramics and Polymers** Aldo R. Boccaccini,J Gough,2007-10-31 Technology and research in the field of tissue engineering has drastically increased within the last few years to the extent that almost every tissue and organ of the human body could potentially be regenerated With its distinguished editors and international team of contributors Tissue Engineering using Ceramics and Polymers reviews the latest research and advances in this thriving area and how they can be used to develop treatments for disease states Part one discusses general issues such as ceramic and polymeric biomaterials scaffolds transplantation of engineered cells surface modification and drug delivery Later chapters review characterisation using x ray photoelectron spectroscopy and secondary ion mass spectrometry as well as environmental scanning electron microscopy and Raman micro spectroscopy Chapters in part two analyse bone regeneration and specific types of tissue engineering and repair such as cardiac intervertebral disc skin kidney and bladder tissue The book concludes with the coverage of themes such as nerve bioengineering and the micromechanics of hydroxyapatite based biomaterials and tissue scaffolds Tissue Engineering using Ceramics and Polymers is an innovative reference for professionals and academics involved in the field of tissue engineering An innovative and up to date reference for professionals and academics Environmental scanning electron microscopy is discussed Analyses bone regeneration and specific types of tissue engineering **Essentials of Experimental Surgery** H Gregerson,S Lindkaer Jensen,F Moody,M Shokouh-Amiri,1996-05-28 This book covers all aspects of experimental gastrointestinal research including anatomy physiology surgical procedures and animal experimental models As well as being a useful reference guide to established scientists it serves as an ideal introduction to the field of gastroenterology By consulting the book the appropriate animal species and experimental model can be chosen for physiological and pathophysiological studies **AMB** ,1997 **Hepato-gastroenterology** ,2004 **Journal of Comparative Neurology** ,1924 Publishes papers on the anatomy and physiology of the nervous system Preference is given to papers which deal descriptively or experimentally with the nervous system its structure growth and function **Manl of Microsurgery** Sun Lee,1985-08-22 **Excerpta Medica** ,1991 *Experimental Surgery and Physiology* Robert J. Adams,1988 Pediatric Surgery Kenneth J. Welch,1986 **Experimental Modulation and Suppression of Anti-allograft Immune Response** Öyvind Östraat,1997 **Biological Systems** Barbara Jasny,Daniel Koshland,1990

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