

## 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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## **Table of Contents Small Bowel Transplantation An Experimental Study In The Rat**

1. Understanding the eBook Small Bowel Transplantation An Experimental Study In The Rat
  - The Rise of Digital Reading Small Bowel Transplantation An Experimental Study In The Rat
  - Advantages of eBooks Over Traditional Books
2. Identifying Small Bowel Transplantation An Experimental Study In The Rat
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Small Bowel Transplantation An Experimental Study In The Rat

- User-Friendly Interface
- 4. Exploring eBook Recommendations from Small Bowel Transplantation An Experimental Study In The Rat
  - Personalized Recommendations
  - Small Bowel Transplantation An Experimental Study In The Rat User Reviews and Ratings
  - Small Bowel Transplantation An Experimental Study In The Rat and Bestseller Lists
- 5. Accessing Small Bowel Transplantation An Experimental Study In The Rat Free and Paid eBooks
  - Small Bowel Transplantation An Experimental Study In The Rat Public Domain eBooks
  - Small Bowel Transplantation An Experimental Study In The Rat eBook Subscription Services
  - Small Bowel Transplantation An Experimental Study In The Rat Budget-Friendly Options
- 6. Navigating Small Bowel Transplantation An Experimental Study In The Rat eBook Formats
  - ePub, PDF, MOBI, and More
  - Small Bowel Transplantation An Experimental Study In The Rat Compatibility with Devices
  - Small Bowel Transplantation An Experimental Study In The Rat Enhanced eBook Features
- 7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of Small Bowel Transplantation An Experimental Study In The Rat
  - Highlighting and Note-Taking Small Bowel Transplantation An Experimental Study In The Rat
  - Interactive Elements Small Bowel Transplantation An Experimental Study In The Rat
- 8. Staying Engaged with Small Bowel Transplantation An Experimental Study In The Rat
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers Small Bowel Transplantation An Experimental Study In The Rat
- 9. Balancing eBooks and Physical Books Small Bowel Transplantation An Experimental Study In The Rat
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection Small Bowel Transplantation An Experimental Study In The Rat
- 10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
- 11. Cultivating a Reading Routine Small Bowel Transplantation An Experimental Study In The Rat
  - Setting Reading Goals Small Bowel Transplantation An Experimental Study In The Rat

- Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Small Bowel Transplantation An Experimental Study In The Rat
  - Fact-Checking eBook Content of Small Bowel Transplantation An Experimental Study In The Rat
  - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
  - Utilizing eBooks for Skill Development
  - Exploring Educational eBooks
- 14. Embracing eBook Trends
  - Integration of Multimedia Elements
  - Interactive and Gamified eBooks

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