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Reduction of chronic rejection of renal allografts by anti-transforming growth factor beta antibody therapy

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Background: Chronic rejection (CR) is the dominant cause of kidney transplant failure, and is characterized by vasculopathy, glomerulopathy, tubular atrophy and interstitial fibrosis. To date, there is no effective therapy for CR. Transforming growth factor beta (TGF-β) has been demonstrated to a fibrotic factor in the pathogenesis of renal fibrosis. This study was designed to test the efficacy of anti-TGF-β monoclonal antibody (1D11) in the prevention of CR of renal allografts.

Material/Methods: The kidney transplantation was performed in male Lewis rats ($RT1^{l}$) receiving allogeneic donor kidneys from male Fisher 344 ($RT1^{lv1}$) rats. Recipients were treated with either anti-TGF-β antibody (1D11, 5 mg/kg) or anti-verotoxin antibody (13C4, 5 mg/kg) as control antibody three times a week. The severity of CR in the renal allografts was assessed by histological examination. The graft function was determined by the levels of proteinuria, serum creatinine and blood urea nitrogen (BUN) in recipients.

Results: Here, we showed that the proteinuria of recipients following the time course of anti-TGF-β antibody treatment was significantly lower than that of those receiving control antibody treatment ($P = 0.0002$). At the end of 12-week treatment, histological examinations indicated the severity of CR in the grafts was reduced by anti-TGF-β antibody treatment, evidenced by the fact that the scores of mononuclear cell infiltration and interstitial fibrosis and the number of injured tubules, glomeruli and interlobular aterioles or ateries were lower in anti-TGF-β antibody-treated group than those in control antibody-treated group ($P < 0.05$). The beneficial effect of anti-TGF-β antibody treatment on preventing CR of renal allografts was also confirmed by its protection of graft function, indicated by lower levels of serum creatinine and BUN in anti-TGF-β antibody-treated recipients compared to those in control antibody-treated recipients ($P < 0.05$).

Conclusion: Our data demonstrate that anti-TGF-β antibody (1D11) treatment significantly reduces CR of renal allografts in a preclinical model, suggesting the therapeutic potential of anti-TGF-β antibody (1D11) for treating CR of kidney transplants in patients.

Biography

Qiunong Guan is a research assistant in the Department of Urologic Sciences at the University of British Columbia (Vancouver, Canada). She completed graduate studies in Biology with M.Phil. degree from the University of Wales at Swansea (UK), and had been working as a research assistant in many research laboratories, including Dr. S. Sriram's lab in the Department of Neurology at Vanderbilt University (USA) and Dr. A. Jevnikar's lab in the Department of Medicine at the University of Western Ontario (Canada) before she moved to Vancouver. She has co-authored 22 full original research publications in peer-viewed journals.

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