



Title	Monotherapy With Anti-CD70 Antibody Causes Long-Term Mouse Cardiac Allograft Acceptance With Induction of Tolerogenic Dendritic Cells
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論 文 内 容 の 要 旨
Synopsis of Thesis

氏 名 Name	趙 静 (ZHAO JING)
論文題名 Title	Monotherapy With Anti-CD70 Antibody Causes Long-Term Mouse Cardiac Allograft Acceptance With Induction of Tolerogenic Dendritic Cells (抗CD70抗体による単剤療法は、トレロゲン樹状細胞を誘導したマウス心臓同種移植を長期的に受容する)
論文内容の要旨 [目 的(Purpose)] Allograft rejection has been an obstacle for the long-term survival of patients for many years. Current strategies to tackle transplant rejection are not as optimal as expected, especially for long-term treatments. CD70, a tumor necrosis factor (TNF) family member critically expressed on antigen-presenting cells and strongly but transiently up-regulated during lymphocyte activation, represents an important co-stimulatory molecule that induces effective T cell responses. We used an antibody targeting CD70 to investigate the effects in the setting of organ transplantation. [方法ならびに成績(Methods/Results)] Methods: We used a mouse heterotopic cardiac transplantation model to evaluate the effects of treatment with the antibody targeting mouse CD70 (FR70) on transplantation tolerance and its immunoregulatory activity. Results: FR70-treated C3H recipient mice permanently accepted B6 fully mismatched cardiac allografts. Consistent with the graft survival, the infiltration of CD8 ⁺ T cells in the graft was reduced, dendritic cells were differentiated into a tolerogenic status, and the number of regulatory T cells was elevated both in the graft and the recipient's spleen. In addition, naive C3H recipients given an adoptive transfer of spleen cells from the primary recipients with FR70 treatment accepted a heart graft from a matching B6 donor but not third-party BALB/c mice. [総 括(Conclusion)] Our findings show that treatment with FR70 induced regulatory cells and inhibited cytotoxic T cell proliferation, which led to permanent acceptance of mouse cardiac allografts. These findings highlight the potential role of anti-CD70 antibodies as a clinically effective treatment for allograft rejection.	

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨			
This study finds a new target that can be used for transplant patients. As we all know, patients who undergo transplantation will suffer from the transplanted organ rejection or failure. Normally, we need to have them have the drugs to prevent rejection. But for now, none of the drugs can ensure the success of transplanted organs survive. So it demands us to find a new and more targeted drug to prevent organ rejection. Here, this study finds a new target that can be used for these patients. Regulatory T cells (Tregs) and Dendritic cells (DCs) play an important role in transplanted organ rejection. This study observed that by using a novel drug to increase Tregs, and mouse heart transplants survive long-term and show no signs of rejection. This study investigated how the drug works and the questions were addressed: 1) How does this treatment increase Tregs and Tolerogenic DCs? 2) How do Tregs and Tolerogenic DCs arise and function after this treatment? This study has examined the function of these Tregs and Tolerogenic DCs to assess their expression of specific genes. This study also assessed why we see more Tregs and fewer T cells usually seen in rejection and looked at the effect of this antibody on other T cell subtypes. This new treatment strategy not only prevents rejection in the short term but also prevents long-term injury. This is a very exciting prospect as there is currently no treatment available to patients to prevent this long-term injury. We believe that this drug has the potential to be a very important new treatment strategy for heart transplant recipients in the future and may help to make these precious grafts survive longer and function better. This research is worth being granted a doctoral degree (medicine).			