Anti-CD80/86 injection prolongs the graft survival in murine corneal transplantation.

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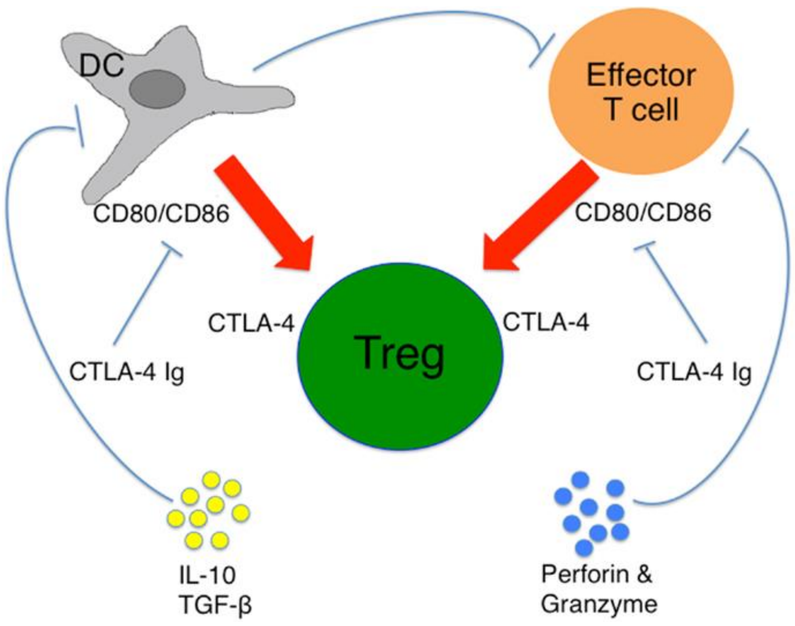
Background



・Corneal Transplantation was performed over 60,000 cases in the world.

・Immflammed graft bed leads to the rejection (40-90%) which called high-risk corneal transplantation.

・Regulatory T cell (Treg) is responsible for immune tolerarnce by suppressing the T cell function, labeled by CD4+CD25+Foxp3+.

・It is clinically important that long-term immune tolerance is established in the transplanted organ

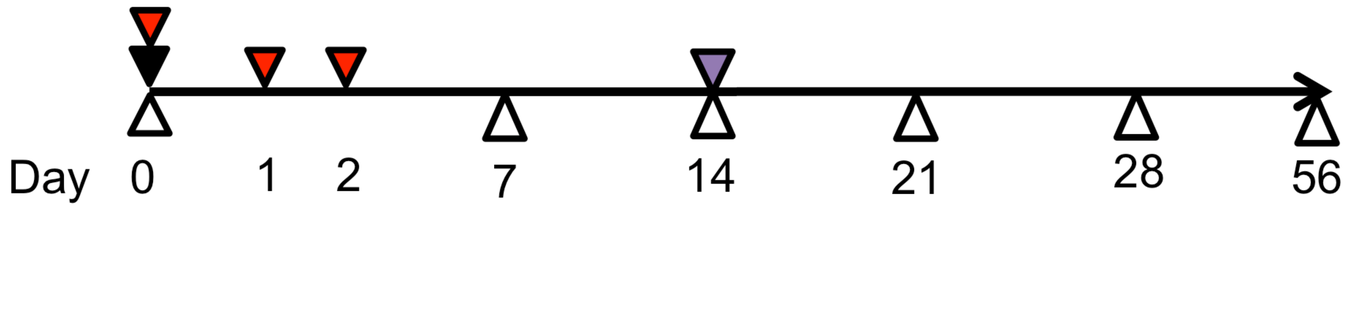
・Anti-CD80 (B7-1) and CD86 (B7-2) expression on antigen- presenting cells (APCs) has led the hypothesis that they might suppress the rejection of corneal transplantation via CD28/CTLA-4 pathways and the APC maturation.

Purpose

To assess the immune responses and the effects on graft survival of anti-CD80/CD86 injection in murine corneal transplantation.

Methods

・Corneal Transplantation, Tx（Donor: C57BL6　8week♂, Recipient:　BALB/c　8week♂ ）
・Group：① low-risk control Tx (control), ②control with anti-CD80/86, ③ high-risk Tx (HR), ④ HR with anti-CD80/86, N=6
・Injection：　IP（Anti-CD80 50ug+Anti-CD86 50ug /100uL）
・Evaluation：per 1 week by microscopy, at day 14 post-transplantation for flowcytometry (draining lymph nodes, dLNs), CD4+CD25+Foxp3+Treg, CTLA-4, CD11cMHCⅡ）



Results

Fig 1. Increased the graft survival in HR with anti-CD80/86 injection

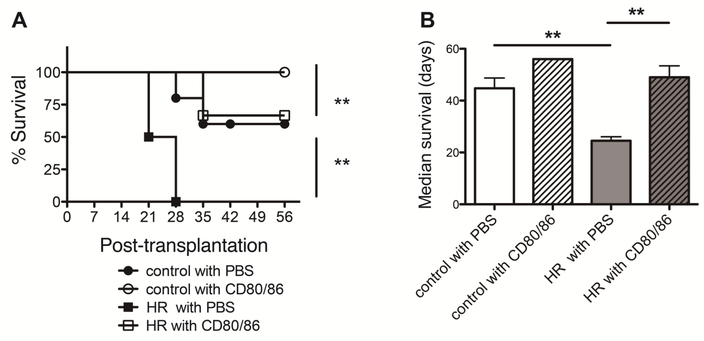


Fig 2. Decreased the graft opacity and neovascularization in HR with anti-CD80/86 injection

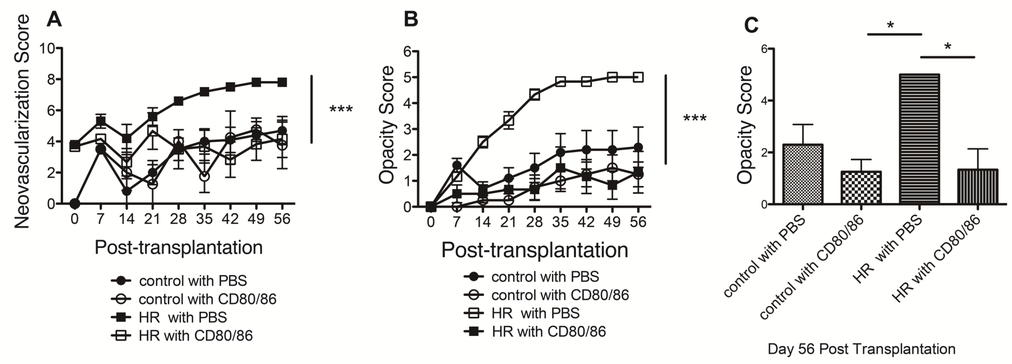


Fig 3. Anti-CD80/86 administration increased MFI expression level of CTLA-4 in dLNs of HR-anti-CD80/86 compared to HR-PBS

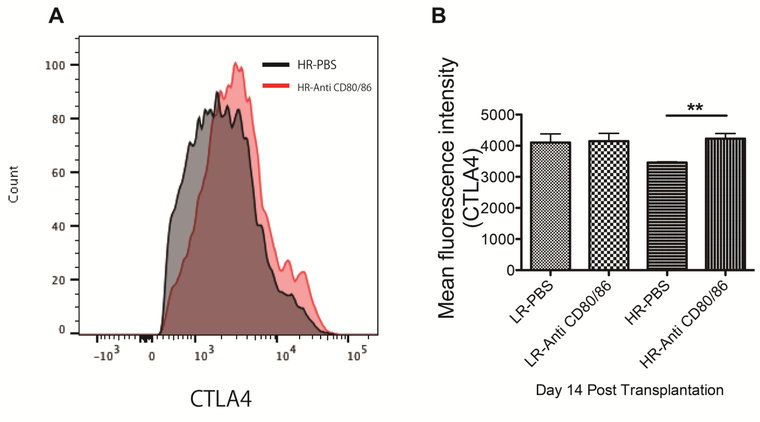
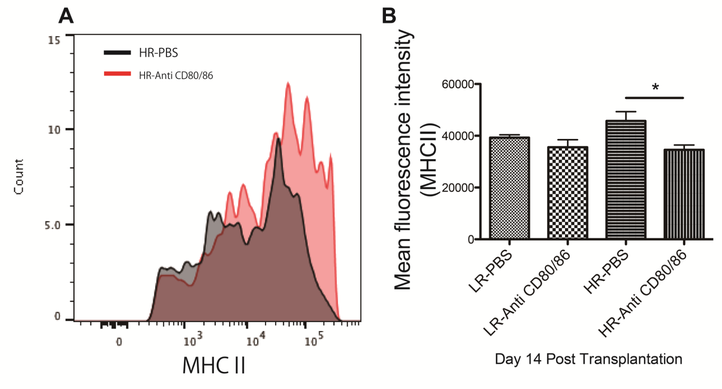


Fig 4. The MFI expression of MHC class II in CD11c⁺ DCs of HR-anti-CD80/86 was reduced compared to HR-PBS



Conclusion

We found the blockade of CD80/86 at the time of transplantation induced long term allograft survival via CTLA-4 activation and MHC class II deactivation.

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