LETTER TO THE EDITOR
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Induction of Donor-Specific Tolerance: Is This Achievable?

To the Editor,

The final goal of transplant physicians is the induction of donor-specific tolerance (DST), in which the host permanently accepts the graft, but immunity against other antigens is maintained. There have been reports of successful induction of DST in rodent models. However, the majority of studies have focused primarily on the inhibition of costimulatory signals that regulate the activation of T cells, and belatacept, a high-affinity variant of CTLA4-IgG, is the only biological drug that has been applied to human organ transplantation [1]. Antigen-presenting cells (APCs) are activated by the innate immune response, and mature APCs are the key regulators of rejection through activation of the acquired immune response. Therefore, the control of APC maturation is the key step in induction of DST in the field of organ transplantation. Previously, we reported induction of DST through control of APC maturation [2]. However, we were not able to delineate the underlying mechanisms, nor apply the methods to other models of transplantation.

Recently, Jung et al. [3] reported a significant contribution where they showed successful induction of DST through the control of APC maturation. They developed a way to maintain APCs in a semi-arrested state by administration of an antibody ligating a particular epitope on intercellular adhesion molecule 1 (ICAM-1). Signaling through ICAM-1 is important for the activation of APCs. They evaluated the effect of semi-arrested APCs on xenogeneic grafts in humanized mice and non-human primates. Thus, they provided a feasible method that may assist the realization of the DST concept. Further work will likely be connected to clinical trials.

However, care should be taken when interpreting these results and applying them directly to humans. The study was performed not on 'organs' but, rather, on a 'group of cells', because 'group of cells' induces a milder immune response, as compared to that against an organ. Moreover, a thorough method for screening various microorganisms in xenogeneic species has not yet been developed. Therefore, the safety issue remains to be resolved. Despite these limitations, this study provides new insight and will help overcome the problem of non-specific immunosuppression. Furthermore, this study may facilitate control of immune responses more meticulously and safely by providing a method of controlling the immune response at the site of interest.

Keywords: Donor-specific tolerance; Antigen-presenting cells; Intercellular adhesion molecule 1

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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