TRANSPLANT INTERNATIONAL

LETTER TO THE EDITORS

HLA match in operational tolerance after pediatric living-donor liver transplantation

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Dear Sirs,

We have read the interesting work of Ohe *et al.* [1] regarding operational tolerance (OT) after pediatric living-donor liver transplantation (LT). They investigated a possible correlation between the degree of matching HLA and the OT. The OT is defined as a continued function of transplanted without nonspecific lifelong immunosuppressive therapy. Although it is well demonstrated to influence the rejection and survival in kidney and heart transplantation, the role of HLA matching between donor and recipient in LT is still controversial [2]. HLA-A matching is associated with OT in the population studied, according to improved outcome in kidney transplantation. These results could be not generalized to LT from a deceased donor. Indeed, a recent study has shown that HLA-A mismatching favors a better outcome of LT [3]. In this regard, it can be assumed that HLA matching could allow a more efficient antigen presentation, thus increasing the immune response to viral infections of the transplanted organ. The impact of HLA matching on recurrence of hepatitis C after LT in HCV-infected patients remains controversial. Although HLA matching appears to reduce rejection episodes, it increases the recurrence of HBV and HCV hepatitis [4,5]. The reduced incidence of rejection occurring in better-HLA-matched grafts may lead to reduction of immunosuppressive treatment, which is known to increase HCV-related graft losses. However, despite HLA matching not influencing graft survival, the fibrosis progression is increased in patients with less HLA mismatches [4,5]. Another group reported that HLA-A mismatching increases the risk of recurrent HCV-hepatitis [6]. Finally, the lack of MHC I/II-restricted T-cell response, which can control the spread of postoperative HCV results in a less severe recurrent hepatitis in patients with complete HLA mismatch [7,8]. It could be interesting to evaluate if viral infections and HLA matching are correlated in the same population studied by Ohe *et al.* [1]. In addition, other loci, such as HLA-DQ, HLA-C, and surprisingly, also HLA-DPB1 have been shown to have a negative effect on graft survival. It would be interesting to assess whether HLA matching on these loci influence the OT in this population. The exact OT mechanism involved in transplantation remains unknown. It has been shown that regulatory T cells (Tregs) are present in patients undergoing LT from a living donor and appear to play a key role in the maintenance of tolerance. Although even patients with HLA-A matching present OT, the authors have demonstrated an increased frequency of Treg only in patients with HLA-B mismatch. It would be interesting to examine if the two populations show a different FOXP3 (forkhead box P3) expression that is involved in the development and function of Treg [9]. In addition, to support the hypothesis of a mechanism similar to the development of maternal/fetal tolerance, it would be necessary to assess expression levels of cellular and/or circulating HLA-G both in tolerant and intolerant patients. Indeed, it was been demonstrated a correlation between HLA-G and liver function. In addition, the IL-10 blood production in patients-tolerant could be considered in order to better understand if tolerance mechanisms are similar to those feto/maternal [10].

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Conflicts of interest

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