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CCR7+CD8+ T cell suppresses effector CD4+ T cell related allo-immune responses in kidney transplantation

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Background: Previously reports showed that $CCR7^+CD8^+$ T cells have suppressive effect on various pathogenic immune cells. The aim of this study is to investigate the regulatory function of $CCR7^+CD8^+$ T cells on allo-reactive effector T cells involved in acute rejection in kidney transplantation.

Methods: We investigated the suppressive effect of $CCR7^+CD8^+$ T cells on T cell proliferation and also inflammatory cytokine induced injury on human primary renal tubular epithelial cells (HPRTEpiC) by FACs analysis and ELISA. Also, we compared the proportion of $CCR7^+CD8^+$ T cells in peripheral blood mononuclear cells by FACs analysis between biopsy proven acute rejection (AR)(n=22) and biopsy proven normal histology (NC)(n=16).

Results: $CCR7^+CD8^+$ T cells significantly decreased the proportion of IFN-g, IL-17/$CD4^+$T cells, and production of IL-17 and IL-2 ($P<0.05$ for each). In contrast, $CCR7^+CD8^+$ T cells increased the production of IL-10/$CD4^+$T cells compared to Th17 condition. Second, $CCR7^+CD8^+$ T cells significantly reduced IL-6, IL-8 and CCL20 secretion from HPRTEpiC, which have been induced by inflammatory cytokines or activated T cells. Also, Our results showed that $CCR7^+CD8^+$ T cells significantly reduced IL-17, IFN-g and IL-2 production from T cells co-cultured with HPRTEpiC. Third, ex vivo analysis of PBMCs isolated from kidney transplant recipients (KTRs) with or without acute rejection, the percentage of $CCR7^+CD8^+$ T cells showed significant decrease in the AR group compared to NC group ($P<0.05$). In contrast, the percentage of $CD28^{null}CD57^+$ T cell and effector memory CD8 T cell ($CD8^+T_{EMRA}$) increased in the AR group compared to NC group. In peripheral blood from total patients groups, $CCR7^+CD8^+$ T cells was inversely correlated with the $CD28^{null}CD57^+$ T cell and effector memory CD8 T cell ($CD8^+T_{EMRA}$).

Conclusion: This study showed that the CCR7+CD8+ T cells effectively regulate effector T cells associated with allograft rejection. It suggests that use of CCR7+CD8+ T cells may be proposed as therapeutic strategy to improve allograft outcome.

Keywords: Acute rejection, CCR7+CD8+T cells, Effector T cells, Kidney transplantation