Poster

[P25-8] P25-8: Immunosuppressive drugs (3): Biomarkers and pharmacokinetics

Chair: Hideyuki Motohashi, Japan

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[P25-8-4] The regulatory effects of tacrolimus- and sirolimus-based immunosuppressive regimens on Tfh and Tfr cells in kidney transplant recipients

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Background

Tacrolimus and sirolimus, routinely used in renal transplant recipients, are known to dampen the immune response to donor antigens by nonspecifically inhibiting T cells proliferation. As subsets of CD4+ T cells, T follicular helper cells (Tfh) and T follicular regulatory cells (Tfr), play counter roles in regulating B cells in germinal center reactions (GCs) and are reported to be closely related to antibody-mediated rejection (ABMR). However, whether the presence of immunosuppressive drugs impact their proportion and function in periphery blood remains to be determined. Here we investigated the variation of Tfh and Tfr cells phenotypically and functionally in renal transplant recipients (RTs) with different immunosuppressive treatments.

Methods

The frequency of circulating Tfh and Tfr cells as well as the expressions of Tfh related molecules including inducible costimulatory molecule (ICOS), programmed cell death protein 1 (PD-1) and interleukin-21 (IL-21) were analyzed by flow cytometry in 26 RTs treated with tacrolimus-based regimen (TAC), 15 with sirolimus-based regimen (SRL) and 16 healthy volunteers (HC).

Results

The percentage of blood Tfh cells and the expression level of PD-1 on Tfh cells were significantly elevated in TAC group compared with those in SRL and HC groups. Whereas, no difference was found among three groups in regard of IL-21 and ICOS expressions in Tfh cells. In addition, the number of Tfr cells was significantly elevated in TAC group compared with that in HC group, instead of SRL group. The ratio of Tfr to Tfh in TAC group and SRL group remained comparable to that in HC group.

Conclusions

Our study indicated that the quantity of circulating Tfh cells was significantly elevated in tacrolimus treated RTs, while their ability to secret IL-21 haven’t been altered, which may result from the inhibitory function of the simultaneous increasing of PD-1 on Tfh cells and Tfr cells in tacrolimus-treated RTs. In addition, sirolimus can control the quantity of Tfh cells more significantly than tacrolimus, suggesting a superiority of sirolimus in preventing ABMR and maintaining the immune tolerance in RTs.