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Session : KJTF Symposium 1 (Liver)

Date & Time, Place : November 19 (Sat), 08:40-10:00, Room 5F-1

Session Title : Immune Tolerance

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## **Phase 1/2 multicenter clinical trial of tolerance induction in living donor liver transplantation via induced T cells with suppressing functions**

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Selective immunosuppression to the recipient T cells responding to the donor graft antigen and maintain immune system necessary for homeostasis would be ideal strategy for the transplant patients. And sustain tolerogenic status to the graft despite cessation of immunosuppressant would minimize the risk of adverse life-threatening events related with the medication such as de novo cancer and cardio-and cerebrovascular disease. Since the discovery of CD86 molecule, we have been investigating donor allograft tolerance induced by blocking the T cell costimulatory signals and found donor alloantigen specific regulatory T cells were expanded in that condition and subsequently induce the condition. The donor alloantigen specific regulatory T cell-based therapy, which is generated from recipient mononuclear cells either from spleen or whole blood by cocultured with irradiated donor mononuclear cells in the presence of CD80 and CD86 monoclonal blocking antibodies, successfully prove the therapeutic concept to achieve long term graft survival without any immunosuppressant in the rhesus monkey kidney transplant model. Based on the preclinical safety and efficacy, the first in human clinical research was conducted in living donor kidney transplant and successfully proved the safety of the cell product. And then immunosuppression withdrawal was challenged in living donor liver transplant in single center, in which seven patients out of 10 have been achieved stable clinical graft function without any signs of pathological rejection over 10 years. Based on this result, the Treg cell product has been investigated as a new regenerative medicine in multicenter phase 1 and 2 clinical trial to achieve operational tolerance over a year for the liver transplant patients in Japan. In this session, we will share our experience for this challenge and discuss future perspectives.

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