Abstract Type : Oral Presentation
Abstract Submission No. : F-005799

Modeling of allograft rejection using human induced pluripotent stem cell-derived kidney organoid system

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Introduction: Kidney organoid derived human induced pluripotent stem cell (hiPSC) has been extensively studies as an alternative cellular model for recapitulating phenotypic and pathophysiologic characters of human disease. In this study, we explored the potential of hiPSC-derived kidney organoid for rejection modeling.

Methods: Using WTC-11 hiPSC, we first evaluated whether IFNr treatment increase the HLA expression in the kidney organoids. Next, we determined if HLA mismatched healthy volunteers PBMC influence HLA expression by co-culture system with kidney organoids. The expression changes of HLA (HLA-ABC and HLA-DR) was detected by analysis of confocal microscopy and flow cytometry. In addition, immunosuppressive effect by tacrolimus was also examined during HLA induction by IFNr or co-culture system.

Results: Treatment of IFNr for 24 h significantly increased the expression of HLA-ABC or HLA-DR with the nephron markers (podocalyxin, lotus tetragonolobus lectin, e-cadherin) in the matured kidney organoids derived WTC-11 hiPSC by confirming confocal microscopy and flow cytometric analysis. Next, after 24h co-culture with HLA-mismatched PBMC and kidney organoids from WTC-11 hiPSC, we analyzed HLA expression after several wash out the PBMC from the kidney organoids. Consistently, the expression of HLA-ABC and HLA-DR was markedly increased compared with non-PBMC treatment and these induction was diminished by tacrolimus treatment dose-dependent manner.

Conclusion: These results showed the evidence that co-culture system with allogeneic kidney organoid and PBMC can be potentially in-vitro transplant rejection modeling. Therefore, this system has possibility of future application for finding a potential risk factors and studying drug screening of allograft rejection.