

**Abstract Type : Oral**

**Abstract Submission No. : OR-1621**

## **Kidney decellularized extracellular matrix hydrogels enhance vascularization and maturation of human iPSC-derived kidney organoids**

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**Objectives:** Human pluripotent stem cells (hPSCs)-derived kidney organoids contain segmented structures with podocytes, proximal tubules, and distal tubules in nephron-like arrangements. However, limited vascularization and immaturity of the nephron-like structures have been yet a major obstacle to overcome. The extracellular matrix (ECM) hydrogel can provide mechanical support and biochemical microenvironment for cell growth and differentiation. Here we report a culture system of hPSCs-derived kidney organoids with kidney decellularized extracellular matrix (dECM) hydrogel.

### **Methods:**

Kidney dECM hydrogel was prepared from porcine kidney tissue. Human iPSCs were differentiated into kidney organoids, which were cultured with kidney dECM hydrogel for 7days. Kidney organoids were also transplanted with kidney dECM in renal subcapsular space of immunodeficient mice.

**Results:** Kidney dECM hydrogel enhanced vascularization of kidney organoids with upregulated vascular endothelial growth factor expression. Kidney dECM hydrogel also upregulated gene expression for podocytes and tubular epithelial cell. Vascularized kidney organoids cultured with kidney dECM hydrogel contained more matured podocytes and renal tubular epithelial cells. Transplantation of kidney organoids with kidney dECM accelerated recruitment of endothelial cells from host mouse kidney and maintained vascular integrity. In transplanted kidney organoids with kidney dECM, the slit diaphragm-like structures were more organized compared to those in without kidney dECM.

### **Conclusions:**

Our data suggest that microenvironment provided from kidney dECM hydrogels promote vascularization and maturation of human iPSC-derived kidney organoids, which can be applied for the development of vascularized form of kidney-on-a-chips and a regenerative therapeutic option for kidney diseases.