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DISEASE MODELING WITH KIDNEY ORGANOIDS FOR TRANSIENT RECEPTOR POTENTIAL CATION CHANNEL 6-MEDIATED FOCAL SEGMENTAL GLOMERULOSCLEROSIS AND TRANSLATING RESEARCH TO SPACE-BASED ORGANOID RESEARCH

Abstract

Space affords humans a unique environment to study diseases without gravity. One organ that is studied in the ISS is the kidney. More specifically, researchers are growing kidney organoids, derived from induced pluripotent stem cells (iPSCs), on a chip system to model kidney-related conditions, including the formation of kidney stones. Organoids are 3D organ-like tissues that are the starting point for more accurately studying human diseases—as opposed to animal models—and potentially manufacturing organs for transplantation. In my research, I determine the effectiveness of the kidney organoid model by studying Focal Segmental Glomerulosclerosis (FSGS), a histological pattern of injury defined by the presence of scarring (sclerosis) in some (segmental) of certain glomeruli (focal) within the kidney. Our study aims to employ promising human-induced pluripotent stem cells (hiPSCs)-derived kidney organoid system to study the TRPC6-mediated FSGS, understand the kidney-in-a-chip system to conduct experiments, determine the effectiveness of kidney organoids in medical research in comparison to traditional mice models, and the potential future use cases of kidney organoids both in space and on Earth.

We prepared hiPSCs from an FSGS patient with TRPC6 (R895C) mutation and prepared kidney organoids. We then examined wild-type and mutant TRPC6 (R895C) kidney organoids using marker protein localization for their tissue arrangement and function to potentially understand the disease mechanism. Then, we compared kidney organoid models to current mice models.

The results showed similar expected collagen IV, cilia (Arl13b), lotus tetragonolobus lectin, and E-cadherin localization patterns between wild-type and R895C kidney organoids, thus conforming normal tissue arrangement with glomeruli and tubule tissues in both wild-type and R895C kidney organoids. However, when we examined podocyte-specific proteins such as nephrin, we noted a normal basolateral localization in wild-type organoids. In contrast, the nephrin exhibited a granular cytoplasmic-enriched localization pattern in R895C kidney organoids. We compared these organoids to mice models and found them to have fetal development, requiring research to improve their maturation.

Overall, it has been found that cells are capable of forming physiologically relevant structures to study chronic kidney diseases in addition to traditional kidney models such as mice models. We found similar structures but different podocyte-specific protein expressions in the mutant versus wild-type organoids. Furthermore, we analyzed the potential for many applications to utilize organoids for analysis in understanding kidney disease mechanisms through a new angle in future medical research on and off Earth and examined the futuristic idea of efficient manufacturing of human tissues in space.