



Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care

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Abstract Topic : Diabetic Kidney Disease + Metabolic Abnormality-related Kidney Disease

Kidney Proximal Tubule-on-a-Chip Model for Lipotoxic Kidney Injury and Therapeutic Evaluation

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Objectives : Obesity promotes the accumulation of circulating free fatty acids (FFAs), which induce lipotoxic injury in renal proximal tubules and contribute to the development of metabolic kidney disease. However, conventional animal models and two-dimensional cultures do not adequately reproduce the proximal tubule–vascular interface or the microenvironment associated with lipotoxic stress. This study aimed to develop a physiologically relevant kidney proximal tubule-on-a-chip model to recapitulate FFA-induced lipotoxic injury and to evaluate its potential as a platform for therapeutic assessment.

Methods : A kidney proximal tubule-on-a-chip was established by co-culturing human renal proximal tubule epithelial cells and endothelial cells under microfluidic flow conditions to reconstruct the tubular–vascular interface. Lipotoxic stress was induced by treatment with FFAs. Pathological responses were evaluated by assessing intracellular lipid accumulation, expression of pro-inflammatory cytokines, and alterations in epithelial barrier integrity associated with tight junction proteins. To explore the translational applicability of the platform, a clinically relevant positive control compound and an advanced biopharmaceutical candidate are being applied under lipotoxic conditions.

Results : The kidney proximal tubule-on-a-chip reproduced key features of FFA-induced lipotoxic injury. FFA treatment resulted in increased intracellular lipid accumulation, elevated pro-inflammatory cytokine expression, and disruption of epithelial barrier integrity associated with tight junction proteins. Treatment with a clinically relevant positive control compound attenuated lipid accumulation and inflammatory responses and partially restored epithelial barrier integrity in the lipotoxic injury model.

Conclusions : This kidney proximal tubule-on-a-chip provides a physiologically relevant in vitro model of FFA-induced lipotoxic kidney injury. The platform demonstrates pharmacological responsiveness and may serve as a useful tool for therapeutic evaluation and preclinical screening of advanced biopharmaceutical candidates.

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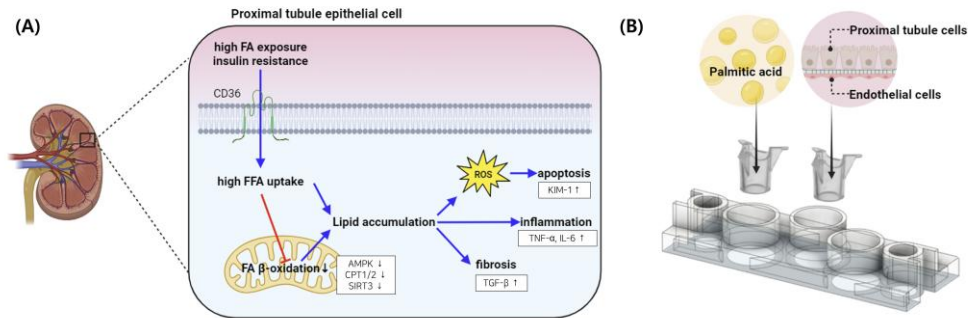


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