

Organ-on-Chip Modeling of Rare Ciliopathies: Joubert Syndrome Patient-Derived Kidney Tubuloids for Personalized Drug Screening

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Abstract

Joubert syndrome (JS) renal manifestations lack disease-specific treatments and models. We generated kidney tubuloids from JS patient urine-derived induced pluripotent stem cells and integrated them into a microfluidic organ-on-chip system recapitulating tubular flow and mechanical strain. These tubuloids displayed defective ciliogenesis, abnormal planar cell polarity, and perturbed calcium signaling characteristic of JS. High-content screening of 1,200 FDA-approved compounds identified roscovitine, a cyclin-dependent kinase inhibitor, as a potent rescuer of ciliary length and function. This patient-specific, physiologically relevant platform accelerates drug repurposing for rare ciliopathies and reduces reliance on animal models.

Keywords: organ-on-chip, Joubert syndrome, kidney tubuloids, rare disease modeling, ciliopathies, drug repurposing



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