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iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells

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ADVANCING CARDIOVASCULAR DRUG DISCOVERY WITH IPSC-DERIVED CARDIAC MODELS

Human iPSC-derived cardiomyocytes (hiPSC-CMs) are increasingly used to support drug safety and discovery, providing human-relevant New Approach Methodologies (NAMs) that can complement and, in some contexts, reduce reliance on animal models. In this talk, I will describe our progression from relatively simple 2D hiPSC-CM assays to more physiologically informative, multicellular cardiac models in both 2D and 3D.

We have established scalable multicellular 2D cultures that combine repeated live cell imaging with machine learning-based analysis to quantify early toxicity pathways and track cell type-specific responses in a label-free manner. This approach enables more clinically relevant exposure scenarios, including repeated or cumulative dosing, and can reveal differential sensitivities across cardiac cell types as well as paracrine signals that shape cardiomyocyte responses. In parallel, we have developed an automated, scaffold-free pipeline for generating reproducible 3D cardiac microtissues from cryopreserved hiPSC-derived cardiomyocytes, endothelial cells, and fibroblasts. This workflow is compatible with standard assay formats and delivers consistent pharmacological responses across independent cell batches, supporting safety pharmacology, arrhythmia disease modelling, and high-throughput screening to identify phenotype-correcting compounds.

Together, these models illustrate how imaging, machine learning, and automation can accelerate the use of complex cardiac NAMs for preclinical research, drug discovery, and safety assessment.