University of Zurich[UZH]

Institute for Regenerative Medicine • IREM

InReMed

Innovations in Regenerative Medicine

Monday, May 6th, 13:00 – 14:00

Wagistrasse 12, 9th floor, Founders Lab

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InSphero AG

Versatility of new approach methods – from early drug discovery to risk stratification

In the ever-evolving landscape of drug development, ensuring on-target pharmacological activity and early detection of toxicity in novel chemical entities (NCEs) is crucial to prevent late-stage drug failure. The lack of efficacy and organ toxicity continue to be significant causes of drug failures during clinical trials and post-approval withdrawals. Regrettably, traditional preclinical animal models often fall short in accurately predicting human clinical outcomes due to species differences in drug metabolism and response.

To address this discrepancy, preclinical strategies have advanced, integrating sophisticated human in vitro cell-based models with multi-parametric endpoints. We describe how Micro-physiological systems (MPS), as an integral part of New Approach Methods (NAMs), can be applied throughout the drug development pipeline. This is exemplified by human liver (hLiMTs) and pancreatic islet microtissues (hIsMTs), cultivated from primary human donor cells, emulating tissue architecture and function. They facilitate disease modelling and long-term studies, recapitulating disease phenotype, drug metabolism, and toxicity more accurately than traditional monolayer cultures.

We illustrate the use of complex in vitro hLiMTs to study disease progression under a specific induction scheme and the impact of therapeutic intervention by respective drug candidates. We propose a risk stratification strategy through the identification of population-specific susceptibility to adverse drug effects.

In conclusion, the versatility of new approach methods—from advanced cell-based models to risk stratification—offers potential for enhancing drug efficacy and safety assessment. By harnessing human-centric insights and adopting innovative technologies, we can bolster drug discovery and reduce the risk of late-stage attrition.

Chair: Dr. Melanie Generali