Novel human cell models in drug development:
How 3D, Organoids & Organs on Chips can improve and renew current paths - and our vision for the future

Prof. Dr. .Adrian Roth

Principal Scientific Director
PHC Safety Interface, Product Development Safety

F. Hoffmann-La Roche Ltd

Adrian is a molecular biologist by training and since August 2020 is Principal Scientific Director Personalized Healthcare Safety within Roche's Clinical development organization. The focus is on bringing innovative new scientific approaches, including microphysiological systems, genetics & genomics or digital tools into clinical testing with a focus on personalized, patient-centric solutions that aim at optimizing the benefit/risk ratio.
Before assuming this role, Adrian has been the Global Head of Roche's Investigative Safety Department within Roche's Early Research & Development organization overseeing all cell based pre-clinical safety support in ADME & Toxicology. He also holds a Professorship at the University of Basel, Switzerland and has authored numerous publications.
His team provided support to all therapeutic areas across all modalities using cellular tools addressing key questions in DMPK & Safety. The focus has been prioritization of drug candidates early on to allow candidate selection, de-risking of findings by mechanistic understanding in later stages, Entry-into-human enabling and providing regulatory compliant packages.
Throughout his career, a key area of focus and strong interest of Adrian has been the establishment of modern human cell models such as 'Organs on Chips', Organoids or Microphysiological Systems which his team has introduced for pre-clinical safety assessment at Roche and now are explored as a way to support also programs at the clinical stage to better understand individual safety risks, to predict outcomes and to stratify patient subgroups at risk.

ABSTRACT

Using human-relevant, translational in vitro models has been widely considered to reduce attrition during drug discovery and development. Over the past decade a considerable hype emerged regarding the transformative potential of microphysiological systems for pharmaceutical research; yet - while it is agreed that such models could bring value – currently, mostly proof-of-concept studies are available and widespread application is still lacking. Thus, while acknowledging the opportunity and value such human relevant cell systems could provide, the adoption by pharma companies is moderate. Realizing the full potential of these models will need more clear use-cases demonstrating clinical translation, improvements on technical ease of use and greater collaboration between stakeholders. Furthermore, it is proposed that refining existing platforms for specific contexts of use where significant gaps exist in drug development will help broader application, rather than unrealistic claims that microphysiological systems can right away replace the complete drug discovery engine at once. Key advantages of such tissue systems over traditional pre-clinical models, e.g. the ability to mimick human-specific biology such as immunology or defined contexts of rare diseases should be further exploited to establish more use cases that demonstrate true added value. Modeling & analytics can help with back- and forward translation using real world data. Furthermore, the ability to generate patient-derived tissue models will allow personalization of treatments and support precision medicine approaches in clinical trials.