Meeting Report

No More Monkey Business: Advancing Personalized Medicine with Animal-Free Research – Animalfree Research Forum 2023

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Traditionally, drug development relied heavily on animal testing to gauge safety and efficacy. However, this approach does not always accurately predict human responses to medications due to interspecies differences and individual variations. Moving away from animal testing, medical research is currently shifting towards methods that better reflect human biology. For instance, specialized *in vitro* models made from human-derived cells and tissues, incorporating each patient's unique genetic and environmental aspects, allow for more accurate testing. Moreover, computer modelling offers reliable predictions of drug effectiveness and patient responses. These advancements decrease the chances of adverse drug reactions and assist researchers in identifying the best therapy for each patient. By leveraging animal-free and human biology-relevant methodologies, scientists can create safer, more effective personalized treatments that precisely meet individual patient's needs without relying on animal experimentation.

The role of animal-free methods in medical research and treatments was discussed at the 13th forum of the Swiss-based foundation Animalfree Research. The event was held in Zurich, Switzerland, on November 6, 2023, under the title "No More Monkey Business: Advancing Personalized Medicine with Animal-Free Research". The forum was opened by Dr **Silvia Frey**, Managing Director at Animalfree Research.

Dr **Miriam Zemanova**, Scientific Associate at Animalfree Research, introduced the topic. Dr Zemanova spoke about the history of animal experimentation and the low translatability of biomedical research using animals. She also mentioned that medical treatments are typically designed as a one-size-fits-all approach, which might lead to side effects in some patients. That is why the emerging field of personalized medicine aims to tailor the treatment to the patient's individual characteristics, considering their genetics, lifestyle, biomarkers, or phenotype. Animal-free methods, such as cell cultures and organoids, play a pivotal role in this process because they enable researchers to study human cells and tissues directly.

Dr med. **Christian Schinke**, neurologist at the Charité University Hospital Berlin, presented his research in the talk "Modelling neurotoxicity with human induced pluripotent stem cell (iPSC)-derived sensory neurons". Chemotherapy often causes a nerve condition called chemotherapy-induced peripheral neuropathy (CIPN), resulting in numbness or painful sensations for patients. Dr Schinke developed lab-grown nerve cells that mimic CIPN, which react similarly to how human nerves respond to drugs causing CIPN. These cells helped identify pathways involved in nerve damage and stress response, offering potential targets for preventing CIPN.

PD Dr **Vesna Petkovic**, Project Leader in the Department of Biomedicine at the University of Basel, held a lecture "Human blood-labyrinth barrier (BLB) on a chip: A unique *in vitro* tool for investigation of BLB properties". Hearing loss is a significant global issue often caused by damage to inner ear hair cells due to various factors like aging, noise exposure, or certain medications. Within the inner ear, auditory hair cells and the blood-labyrinth barrier (BLB) are critical for normal hearing, maintaining balance, and protecting against damage and disease. However, delivering treatments to the inner ear is challenging due to its inaccessible location and potential side effects from medications. PD Dr Petkovic developed a chip mimicking the BLB using cells from human temporal bones. This chip offers a way to study how the BLB contributes to both healthy hearing and hearing loss, replacing animal testing and providing a promising tool for developing treatments for hearing impairment.

Dr **Michela Di Filippo**, Researcher at the Department of Dermatology at the University Hospital Zurich, reported on her work in a talk titled "CRISPR/Cas9 modified cells in skin equivalents: A game changer for 3D skin models". Mice have been the primary choice for skin research, but their genetic differences from humans limit translation to human skin conditions. Three-dimensional (3D) human skin models can provide a more accurate representation of human skin, enabling the study of complex tissue-specific effects and disease modelling. The research by Dr Di Filippo utilized a scaffold-free 3D skin model to explore skin inflammation using CRISPR-Cas9 modified cells. This model not only mimicked human skin in structure and gene expression but also revealed insights into skin inflammation mechanisms, offering potential therapeutic targets.

Dr iur. **Vanessa Gerritsen**, Member of the Executive Board at the Foundation for Animals in the Law (*Stiftung für das Tier im Recht*) presented the legal perspective of advancing animal-free research in Switzerland. The Federal Constitution mandates a balance between fundamental rights and economic viability, yet a significant disparity exists in funding allocation between animal testing and principles of animal protection. Despite increased efforts to promote animal-free methods, funding for these approaches remains limited compared to budgets allocated to animal experimentation. Moreover, there is still a lack of systematic evaluation

of experimental methods and research approaches with regard to their actual research benefit. Dr Gerritsen pointed out that the government's funding strategies significantly impact research practices, and therefore they have a major responsibility of aligning these strategies with constitutional principles.

Lastly, Dr **Aysha Akhtar**, M.D., M.P.H., Co-Founder, President and CEO of the Center for Contemporary Sciences, spoke about the replacement of animal testing and the recent legislative changes in the USA. In 2022, the USA enacted a significant legislation known as the FDA Modernization Act 2.0, eliminating the legal mandate for drug and therapeutic testing on animals. Although this law may not bring immediate reductions in animal testing, it signifies an essential initial move towards a new era in medical research. Dr Akhtar addressed the substantial evidence highlighting the shortcomings of animal testing and advocated for its replacement, emphasizing the mutual benefits for both animals and humans. She also discussed the FDA Modernization Act's implications and the necessary future actions to expedite a shift away from animal experimentation, aiming for improved and safer therapeutic approaches.

The forum highlighted the transformative potential of animal-free methods in personalized medicine and was very well received by the participants. We thank all the invited speakers for sharing their experience and knowledge on this topic.

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