

## **"Der Simulierte Mensch" and the Charité 3<sup>R</sup> perspective**

Berlin is a spotlight of Germany's biomedical science, which translates into many animal experiments ("capital of animal experimentation"). Berlin's scientific and political community shares the idea that those who need animal experiments bear a special responsibility for the intense development of alternative methods. This goes hand in hand with the realization that modern alternative methods have enormous potential for the further development of basic biomedical research and translation. Consequently, politicians took this up in 2016, intending to make Berlin the "capital of alternative methods":

The joint activities resulted in three main developments: Charité established Charité 3<sup>R</sup> in 2018 to structurally anchor 3Rs in Charité's internal biomedical science. In 2018, the Technische Universität Berlin and the Charité acquired funding for a new research building, "Der Simulierte Mensch" opening in 2024. In 2020, universities and non-university partners established the Berlin-wide Einstein 3R Centre (EC3R). All three activities were initiated by the scientific community and are strictly science-driven.

Charité 3R is structured in three pillars. Pillar 1: scientific and political communication on animal experiments and alternatives. Pillar 2: Education and support to promote the 3Rs. Pillar 3: direct research funding in all 3R aspects. An independent review is always carried out, usually through the involvement of external reviewers.

Der Simulierte Mensch is a joint research building of TU Berlin and Charité. It houses interdisciplinary scientific projects aiming to simulate human physiology and pathophysiology at subcellular, cellular, and organ/organoid level, which is reflected by the laboratory levels of the buildings with their specific technological platforms. Two additional levels are designed for science communication and interaction with stakeholders from Berlin's biomedical science.

The EC3R bundles the 3R activities of Berlin partners in the areas of communication and education. Joint training strategies are implemented, and barrier-free access to partner events is ensured. Six scientific replacement projects were reviewed and selected after a Berlin-wide call to further develop organoids as disease models. All activities focus on improving quality and usability of models for biomedicine.

All parties involved must work together to develop robust and forward-looking alternatives for biomedicine. The stakeholders are convinced that, in addition to ethical and legal reasons, there are good scientific reasons for consistently pushing forward with alternatives. Research into alternatives must be conducted with such high quality that scientists turn to these methods on their own initiative for scientific reasons. Overall, 3R research can significantly strengthen Berlin as a science location by opening up scientific perspectives and spin-offs.