The Simulated Man

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Currently, experimental animals are primarily used for:

- Gaining scientific knowledge in basic biological research,
- Research into the onset and progression of a disease, and for
- Toxicity testing of new therapeutic strategies.

The development of human models covering these three areas of application will make an important contribution to avoiding and reducing animal experimentation and thus, in this question, insinuates itself into the concept of the State of Berlin.

The knowledge we can gain with the help of new human models can be divided into three subgroups.

1)
The human body consists of **organs and tissues** in which cells interact with each other and with their unique extracellular matrix. This interaction forms the basis for their specific functional capabilities.
The further development of complex 3D cell cultures (using bioprinting and/or microfluidics) enables the creation of that functional unit, the organoid.
These organoids then simulate an aspect of our complex organism and allow us to explore the strictly choreographed interaction of different cell types of a tissue.

2)
Our body consists of more than 300 different **cell** types. The tasks and functions of each one has not yet been sufficiently researched. With the help of current technologies, such as CyTOF (Cytometry Time of Flight), for example, from one single patient biopsy, each individual cell can be examined, in parallel, for approximately 40 characteristics and properties. And this can be done at a speed of 500-1000 cells per second.
In this way, new tumor markers can be identified without the use of a laboratory animal.

3)
Advances in genome sequencing technologies now allow high-throughput analyses within a few days to hours. This makes it possible to analyze large groups of people (of different genders, ages and ethnic origins) and to compare them with the data from an afflicted patient group. A clinical picture can thus be depicted in much more detail and can be a trend-setter for possible therapeutic approaches.
Even if (almost) all cells from a person carry the same genetic information, they differ in the type and quantity of proteins they synthesize in order to be functional in their organ or tissue. With the help of proteomics, this unique **subcellular** profile can be analyzed and compared with databases. This enables the identification of new protein complexes and/or interaction partners.

The research project "**The Simulated Man**" (German: Der Simulierte Mensch, Si-M) was jointly applied for by the Technical University of Berlin (TU Berlin) and the Charité University Medicine Berlin (Charité). The initiators are Prof. Andreas Thiel (Charité) and Prof. Roland Lauster (TU Berlin). Both are experts in their fields of regenerative immunology and technologies for advanced 3D cultivation.
Only with the resources of the Charité and the TU Berlin can this special research project be realized; it stands at the interface of engineering sciences and medicine. In the building, scientists from both institutions will work together to simulate the functions of human cells and tissues with new technologies from 3D cultivation, multi-organ chips or 3D bioprinting.

Figure 1: Animated interior view of the research building "The Simulated Man" from a draft (rights: Architectural office HDR GmbH).

In contrast to already existing collaboration projects, the joint development of the model "side by side" will be practiced in the same laboratory environment of the building.
In this way, both the development of organ models and the technological developments can be adapted and optimized at the same time. Thus, the building is not separated in the middle and half of it is occupied by scientists from the Charité or the TU Berlin. Rather, only those scientists from both institutions will move in who have applied for a joint cooperation project and have financed it with third-party funds. They will work in a laboratory and an office, will be able to use the latest equipment and technologies of the Si-M and thus realize their vision in a goal-directed manner.

At the Institute for Biotechnology of the TU Berlin, new technologies have been established which play a major role in the concept; these are found in the areas of 3D cultivation of human cells, microfluid-coupled systems and bioprinting. In addition, the institute has extensive expertise in the fields of protein- and RNA-technologies.
With the BIH Centre for Regenerative Therapies (BCRT), the Charité has a strong engine for new research priorities. The main focus is on oncological, immunological and regenerative questions.

The coupled simulation of several human tissues opens up completely novel research approaches with high clinical relevance, particularly in the field of new cancer therapies and infections. The two disciplines come together in the field of immunotherapies for cancer in an exemplary fashion.
The new research building will be completed in 2023 and is divided thematically and structurally into three levels: "tissue and organs", "cell" and "subcellular". Each of these floors is equipped with German Research Foundation-funded state-of-the-art equipment.

Young scientists in particular can develop their innovative ideas quickly and efficiently and put them into practice.
Thanks to the flat hierarchies of the Si-M, young working group leaders can exchange ideas and interpret experimental results as equals with luminaries from the Si-M.

The research building "The Simulated Man" can thus act as a driving force for the upcoming paradigm shift in the medical biosciences.

Figure 2: Animated frontal view of the research building, “The Simulated Man“ from the draft (Rights: Architectural office, HDR GmbH)

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