Creating Personalized Cancer Treatments Using "Mini-Tumors" and a Digital Twin

The BMBF is funding a research project by the University of Bonn and ESQlabs that is aiming to improve colon cancer treatment.

Funded by the Federal Ministry of Education and Research (BMBF), a collaborative project involving the University of Bonn, the company ESQlabs and the University Hospital Bonn is seeking to refine the therapy recommendations given to colon cancer patients. To this end, "ISPOT-K" is merging organoids taken from patients with the power of digital twin technology.

The diagnosis may be identical, but the progression of colon cancer is never the same from patient to patient: how the tumor spreads and what therapy and drugs will work will vary from one to the next.

Traditional cancer treatments are typically based on personal information such as age and sex, cancer types and staging, histological information and selected genetic data. However, none of this gives a clear indication about how a patient will respond to a particular treatment. This is where the team from the University of Bonn and ESQlabs comes in with its novel idea. The "ISPOT-K" team combines organoid-based tests and computational models to create a digital twin of every single colon cancer patient and thus propose the most effective course of therapy with the fewest and least severe side effects.

Digital twins based on "mini-tumors"

3D organoids are made from tissue that is grown in such a way as to imitate the structure and function of a human organ. The working group led by Assistant Professor Elena Reckzeh is based at the University of Bonn's LIMES Institute and specializes in this experimental organoid technology. The group cultivates samples of tumor tissue taken directly from colon cancer patients in order to turn them into 3D organoids in the laboratory. These "mini-tumors" are then exposed to a range of cancer drugs so that predictions can be made as to how the patient will respond to treatment. Patients are being recruited with the help of Professor Tim Vilz from the Colorectal Surgery and Proctology team at the University Hospital Bonn.

In a second step, the data obtained from the 3D organoid is combined with detailed molecular and physical information from the patient. This computational modeling is being done by Professor Jan Hasenauer's working groups under the overall leadership of Dr. Dilan Pathirana from the Bonn Center for Mathematical Life Sciences at the University of Bonn. They are focusing on modeling intracellular signaling pathways that are relevant to cancer, including drug reactions and quantifying uncertainties. The research being done by the two working groups lies at the interface between the Modelling and Life & Health Transdisciplinary Research Areas (TRAs) at the University of Bonn and is also benefiting from the expertise offered by the Hausdorff Center for Mathematics and ImmunoSensation^2 Clusters of Excellence.

Digital twin helps optimize dosage recommendations

Meanwhile, integrating data into the digital twin is the core expertise of MPSlabs, a dedicated business unit of ESQlabs specializing in quantitative systems pharmacology, physiologically based pharmacokinetic (PBPK) modeling and digital twin solutions based on microphysiological systems (MPSs). The digital twin can be used to simulate how a particular tumor would respond to various treatments so that the best possible dosage strategy can be recommended. "Our vision is a data-driven workflow that starts with organoid testing and ends with an in silico simulation—essentially a

'virtual patient' guiding physicians toward the most effective therapy," explains Dr. Christian Maass, who leads the business unit MPSlabs and is a principal scientist with ESQlabs.

"ISPOT-K has the potential to revolutionize personalized colon cancer treatment," Jr. Prof. Elena Reckzeh adds. "We envision this powerful combination delivering the safest and most effective therapy possible, tailored to the individual situation of every single patient."

More effective treatment, fewer animal studies

Going forward, the patient-specific drug recommendations made by the digital twin may enable the costs of cancer therapy to come down by reducing the use of ineffective generic treatments and ensuring that every patient is given the right dose of their medication. ISPOT-K aims to provide a platform not only for personalized medicine but also for drug development pipelines in order to optimize drug candidates at an early stage. Hence, these findings could help to reduce the need for animal testing during preclinical drug development in the future, because researchers might be able to resolve some issues—such as toxic side effects or the lack of an effective treatment—before conducting animal experiments.

Institutions involved and funding secured

The project, which is now under way, has a project volume of €1.7 million. The BMBF is providing €1.1 million in funding to ISPOT-K, around €700,000 of which is going to the University of Bonn. The University Hospital Bonn is also involved in the project alongside the University of Bonn and ESQlabs.

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Images:

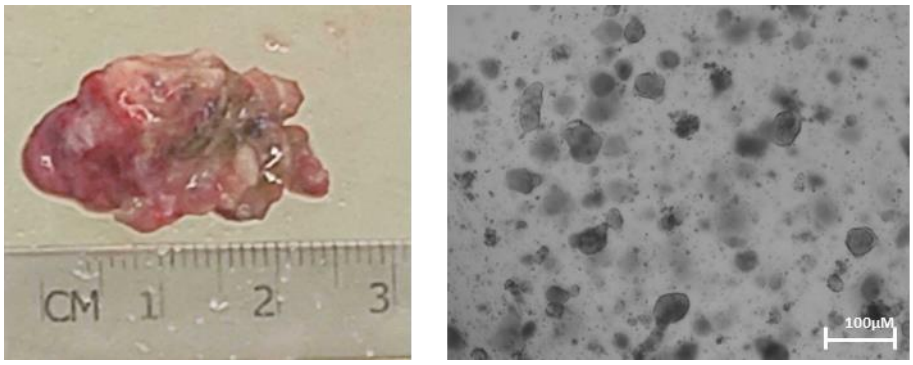

Image: Left: Tumor tissue from patients. Right: Tumor organoids generated from the tumor tissue, viewed through a bright-field microscope. Scale: 100 µm = cross-section of a human hair. ©Images: Jasmitha Boovadira Poonacha, from the working group led by Assistant Professor Elena Reckzeh.