

Overcoming resistance to treatment for breast, bowel, and pancreatic cancer

As cancer progresses, the tumor cells continually change, ultimately resulting in a tumor consisting of a large number of different cell clones with different characteristics. This is referred to as "tumor heterogeneity". In many cases, the cancer cells become resistant to the treatments available.

The interdisciplinary SATURN3 research network aims to study pancreatic, breast, and bowel cancer to unravel the molecular causes that lead to the development of treatment resistance. The goal is to find new ways of preventing resistance and even to overcome it using more efficient treatment methods.

SATURN3 is coordinated by researchers from the German Cancer Consortium (DKTK), Essen University Hospital's West German Tumor Center (WTZ), the Institute for Stem Cell Technology HI-STEM, the German Cancer Research Center (DKFZ), and Technische Universität München (TUM). As part of the National Decade Against Cancer, the German Federal Ministry of Education and Research (BMBF) is providing a total of more than 15 million euros to fund the project over a period of five years.

Even tumors that initially respond well to treatment often start growing again or even spread throughout the entire body through metastasis. This is because cancer cells continually evolve as the disease progresses, differentiating into different cell clones that develop new biological traits. "These newly acquired molecular traits very often enable the cancer cells to evade the effect of drugs that are initially effective. Treatment resistance is the most dangerous side effect of tumor evolution," explained Jens Siveke from the DKTK and WTZ.

Siveke coordinates the new interdisciplinary SATURN3 research network, which aims to investigate the biological background of treatment resistance that arises as a result of the heterogeneity of tumor cells. A total of 13 research institutions are involved in SATURN3.

As part of the National Decade Against Cancer, BMBF has set up a new funding guideline designed to enable promising scientific cooperation projects to investigate these links and hence contribute to developing better treatment options for treatment-resistant tumors. SATURN3 is one of two projects selected for funding.

"BMBF is helping to solve one of the big unsolved questions of cancer research," remarked Michael Baumann, Chair of the DKFZ and co-chair of the Strategy Committee of the National Decade Against Cancer. "The top-level consortiums that can now begin work have good prospects of obtaining results to make crucial progress in cancer medicine."

The scientists participating in the SATURN3 project are focusing on three types of cancer that are still very difficult to treat – and that affect a very large number of people: bowel cancer, pancreatic cancer, and two particularly aggressive forms of breast cancer (triple negative and luminal B).

The salient feature of the SATURN3 concept is that tumor biopsies are not only taken from patients at the initial diagnosis; in addition, tissue samples of the tumors are obtained several times during the course of the disease. The researchers thus also obtain tumor cells that have already become resistant.

The tumor material then undergoes a genetic, epigenetic, and functional analysis for each individual cell separately in order to show the very high level of heterogeneity of the tumors. The research teams involved can draw on the latest analytical technologies, imaging techniques, and artificial intelligence methods established at the consortium's partner institutions.

"We can therefore obtain a time-resolved, multi-dimensional picture of the tumors at single cell level for each patient. This allows us to identify the molecular adaptations by which the cancer cells escape the particular treatment. Once this process has been understood, we might be able to block it in a targeted way," explained Andreas Trumpp from the DKFZ, co-coordinator of SATURN3. „We will be testing the new treatment approaches to overcoming resistance using tumor organoids grown in a petri dish from the tumor material and then examining them in animal models in a further validation step."

As Wilko Weichert from TU München, another co-coordinator of SATURN3, explained, "Our goal is ultimately to identify

molecular changes in the cancer cells that serve as reliable biomarkers for the development of resistance. Early clinical studies are then carried out to examine whether this resistance can be overcome using novel targeted drugs or combinations of drugs." The SATURN3 consortium thus also includes working groups that have considerable expertise in developing clinical study protocols. SATURN3 also receives advice and support from patient representatives, who contribute their experience directly to the research process.

"The treatment resistance caused by tumor heterogeneity poses a huge medical problem. The more precisely we understand these processes in the tumor, the more effectively we can develop strategies that prevent cancer treatment from losing its effectiveness," remarked study coordinator Jens Siveke, summarizing the goals of SATURN3.

Institutions participating in SATURN3 (in alphabetical order):

- Aachen University Hospital
- Cologne University Hospital
- Essen University Hospital
- European Molecular Biology Laboratory (EMBL), Heidelberg
- Freiburg University Hospital
- Georg Speyer Haus Frankfurt
- German Breast Group
- German Cancer Consortium (DKTK)
- German Cancer Research Center (DKFZ)
- Göttingen University Hospital
- Heidelberg University Hospital
- HI-STEM gGmbH
- Regensburg University Hospital
- TU München (TUM) with its University Hospital

Information:

ATURN³: Spatial and Temporal Resolution of Intratumoral Heterogeneity in 3 hard-to-treat Cancers
HI-STEM: Heidelberg Institute for Stem Cell Technology and Experimental Medicine

Press release

18-Nov-2021

Source: German Cancer Research Center

Further information

- ▶ German Cancer Research Center (DKFZ), Heidelberg
- ▶ German Cancer Consortium
- ▶ Westdeutsches Tumorzentrum
- ▶ Technical University of Munich
- ▶ Federal Ministry of Education and Research
- ▶ National Decade against Cancer