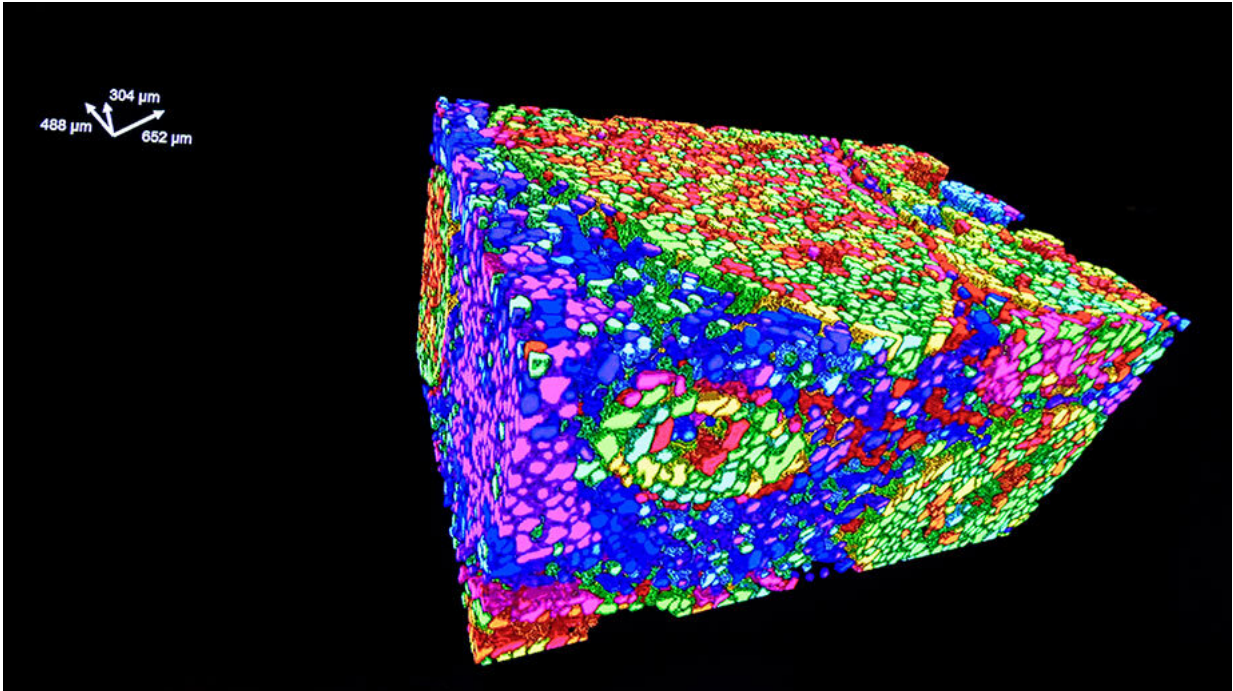


A targeted method to combat cancer

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Cancer tissue visualized in 3D: the cells involved in a tumor can be differentiated using a unique method. Credit: Marc Latzel

By analyzing tumors in unprecedented depth, the Tumor Profiler project represents an important step along the road toward personalized cancer treatments. And the team have already recorded initial successes: In a study focusing on skin cancer, tumors shrank in about one third of patients.

Heinrich B. was seriously ill. His diagnosis: melanoma. The 41-year-old accountant had already been told of multiple metastases in his skin when a computer tomography conducted in 2017 detected offshoots in his lungs too. Hopes were raised by a course of antibody-based immunotherapy, only to be dashed again by a relapse when new metastases appeared. The active cyclist suffered badly from his physical weakness. More sessions of chemotherapy and immunotherapy were unsuccessful. With all therapy options for Heinrich B. exhausted, his doctor no longer knew how to proceed.

Melanoma is the most malignant form of all skin cancers and the fifth most [common cancer](#) in Switzerland. About 3,000 people are diagnosed with the condition every year, men and women being equally affected. 62-year-old teacher Sabine M. was also struggling with a metastatic melanoma. Having remained undetected for so long, the cancer was able to dig into deeper layers of her skin, spread through her body's blood and lymph channels and form its metastases. In such cases, treatment is difficult. The disease had such an impact on her health that the dedicated German teacher could no longer supervise her class through to their Matura exams. She told a friend, "I'm metastasized through and through." She coined the phrase herself, evidence of her desperation.

Every cancer is different

Although Heinrich B. and Sabine M. were both diagnosed with [skin cancer](#), every cancer is different. Traditionally, cancers have always been described using the name of the organ where they first occur, such as skin, breast or bowel cancer. "But we now know that this is not only an outdated view of things, but also one that is not entirely correct," says Andreas Wicki, professor of oncology at UZH and senior consultant physician at the University Hospital Zurich where he is deputy director of the Department of Medical Oncology and Hematology Clinic.

Tumors that originate in different organs, for example, can actually be more similar to one another in biological terms than different types of tumors from the same organ. Currently, about 200 various cancer diseases are known. For many of these cancers, research conducted over recent years has managed to identify the genetic alterations specifically responsible for the tumors. But differences can occur even in the same patient. "This is when metastases differ genetically from the primary [tumor](#)," Wicki explains.

On a [molecular basis](#), therefore, each cancer is unique and characterized by the combination of its mutations. If these differences can be taken into account when oncologists consider treatment, therapies that generate only adverse side effects and no medical benefit can be omitted. Conversely, the risk of failing to prescribe a promising therapy decreases.

Personally tailored treatments

For Sabine M. and Heinrich B., a new opportunity arose three years ago when they heard about a study forming part of the Tumor Profiler project. In this study, the Tumor Profiler team vowed to analyze the cancer of each individual patient right down to the cellular and molecular level, with the aim of using the analyses to deliver promising therapy recommendations to the patient's oncologist as rapidly as possible. This could result in new alternatives also for patients like Sabine M. and Heinrich B. who had already exhausted all existing therapy options. Both cancer patients decided to take part in the study. Led by Andreas Wicki, it started with 240 patients, 95 of whom suffered from metastatic melanoma and the rest from metastatic ovarian cancer or acute myeloid leukemia.

Once samples had been taken from biopsies on the study participants, including Heinrich B. and Sabine M., it was important that the sensitive

cells were sent to the seven participating laboratories as quickly as possible; more than a hundred researchers then had about two weeks to evaluate the samples. This was a major logistical challenge, as each of the seven specialized laboratories focused on one specific method. Within the scope of testing, factors being examined included DNA, RNA, proteins in the [cancer cells](#), and cells in the immune system. "What is new and revolutionary about our approach is our combination of analytical methods and our data processing pipeline," Wicki says.

This is how samples from Heinrich B. and Sabine M. reached the laboratory run by Lucas Pelkmans, professor of molecular biology at UZH. He is responsible for carrying out in vitro drug tests. In Switzerland there are about 180 cancer drugs approved by Swissmedic, about 60 of which are regularly used in cancer treatments. The researchers work with known drugs or with a new mix of drugs and test ex vivo how the tumor cells of cancer patients react to them. The aim is to understand which processes in the cell are influenced by which drugs and whether certain drugs, which have not previously been used for the specific type of cancer under examination, work in the specific sample. This is how new treatment options are created. One result from the tests: in certain cases it may be better to use drugs that are approved for other types of cancer than to work with the standard therapy.

Understanding the tumor

In another laboratory, UZH professor Bernd Bodenmiller and his team also analyzed Heinrich B. and Sabine M.'s tissue samples. "We've succeeded in developing a unique method that enables us to visualize dozens of biomarkers in the tissue simultaneously," says Bodenmiller, director of the Department of Quantitative Biomedicine at UZH and professor in the Department of Biology at ETH Zurich.

"We look at the immune cells and the tumor cells and see how they act

in spatial terms and how they potentially communicate." The biomarkers give the researchers a picture of the state of the tumor. "We recognize the components of a tumor and how they interact. This allows us to target and disrupt its function with the use of drugs."

The last links in the chain are the Leonhard Med Secure Scientific Platform Service and Nexus Personalized Health Technologies at ETH Zurich. Here, the data from the seven laboratories are compiled and analyzed with the help of data specialists and algorithms. The ETH data scientists compile the data for the interdisciplinary tumor board. Afterwards, the treating oncologists discuss the new treatment with their patients. "We've developed an advancement in oncology, one that serves the patients," says Mitch Levesque, UZH professor of experimental skin cancer research, one of the researchers involved in the study.

Good news

The work conducted by the Tumor Profiler team was able to help Heinrich B. and Sabine M. too. A few weeks after his biopsy, Heinrich B. received a new immunotherapy based on the laboratories' analyses—and over the next few months, his tumor shrank. It was the same story with Sabine M., who was given a new immunotherapy in combination with a kinase inhibitor: drugs that bind specific enzymes and inhibit their function.

For some of the patients in the study with melanoma, the researchers were able to draw a surprisingly positive conclusion: "We were able to help a third of the cancer patients who'd exhausted all other options by prescribing an individually tailored mix of drugs based on their tumor profiler analysis. Their tumors shrank," Andreas Wicki reports. "And in more than half of the participants, the tumor growth could at least be stabilized." A success story—Heinrich B. and Sabine M., at least, are happy. Heinrich B. can ride his bike long distances again and Sabine M.

is back teaching at school, albeit on a reduced schedule.

Big data in oncology: The Tumor Profiler Project

In the Tumor Profiler project, around a hundred clinicians and researchers from the University of Zurich, University Hospital Basel and ETH Zurich have joined forces in seven specialized laboratories to break new ground in cancer research and treatment. Researchers from University Hospital Zurich are contributing to the project too. Using complementary scientific methods, the researchers analyze samples from cancer patients and pass the results directly on to the treating oncologists.

They're also working on creating a better understanding of the mechanisms of cancer diseases. "The researchers are establishing innovative technologies and developing novel therapeutic approaches based on data-driven medicine," says Beatrice Beck Schimmer, Professor of Anesthesiology at UZH and Vice President Medicine of University Medicine Zurich (UMZH), which funds the project.

The new and truly experimental aspect of the Tumor Profiler project is that virtually every cell is analyzed, including its environment. As a result, data are obtained that are not only of direct help to cancer patients but, due to the vast amounts collected, generate large pools that provide valuable clues to the many and varying types of genetic and molecular cancer.

"Profiling the tumors results in 43,000 individual data points," explains oncologist Andreas Wicki. "The data will enable us able to take the molecular profile of a [cancer](#) patient and derive the perfect therapy."

That, at least, is the long-term goal of the use of big data in oncology. The Tumor Profiler project offers precision medicine tailored to the patient, while promoting data-driven medicine. "All of this has an

incredible impact for our patients, and also for society as a whole," Beck Schimmer concludes.

Provided by University of Zurich

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