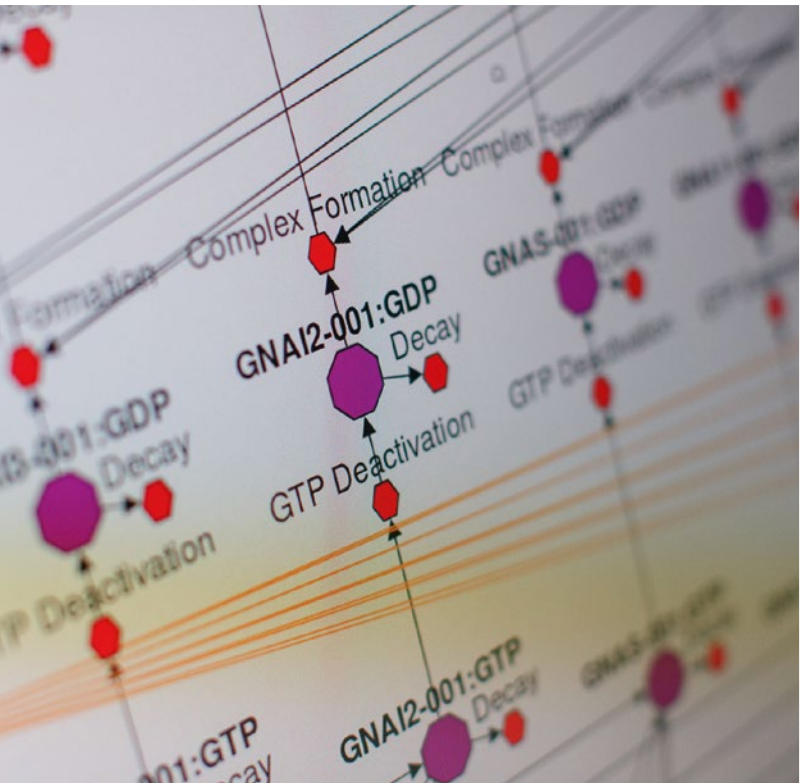
A crash test dummy for medicine

Preparations for sequencing: First, standard laboratory work (large picture and top right). Then, the digital twin (bottom right) is presented based on the molecular compounds.

Photo: Michael Rathmayr



Digital twins help in the research of tumors and the development of new drugs – and can spare patients wrong treatments. A visit to pioneers of digital medicine.

COPY —— Isabell Spilker

Four futuristic looking beehives stand in the front garden of the Adlershof Technology and Startup Center in Berlin, Germany. Here, bees produce delicious honey in the same way their ancestors did in ancient times. Honey has long been valued for its healing power, above all in natural medicine, and has been tested time and again over ten thousand years. Scientists in the building complex next door are researching completely new recovery procedures and applications: They are developing technologies that can revolutionize our healthcare system. This is where man's digital twin is being created.

The company Alacris Theranostics was founded in 2008 as a spin-off of the Max Planck Institute for Genetics. It began its work after a first round of funding in 2011. The goal of Alacris Theranostics is truly personalized medicine. A person's digital twin can be created from different data, mainly from sequenced DNA, to serve this purpose. A simulation with this data serves as a kind of virtual crash test for different scenarios, currently mainly in the field of tumor diseases.

"Our point is to look at how the individual patient and the particular tumor reacts to certain drugs," says Dr. Bodo Lange, Managing Director of the company. Personalized medicine means administering matching medicine to individual patients. So far, only groups of patients are addressed, not individuals. Which is not good enough for him. "Many drugs do not work very efficiently – only one-third of patients respond to drug-based cancer therapies." This is bad for the patient and bad for the healthcare systems, especially when you look at the numbers across all clinical scenarios: up to 200,000 people lose their lives in Europe every year due to so-called adverse drug reactions. Knowing critical information about the genes of a cancer patient would dramatically reduce the number of patients who are unwillingly exposed to the side effects (and costs) of an ineffective drug.

TUMORS ON THE MOLECULAR LEVEL

20 employees, including physicists, biologists, medical-technical assistants, and bioinformaticians, are constantly working on implementing the idea in the laboratories and offices of Alacris Theranostics. Every tumor, every patient provides new information. Scientists sequence DNA from blood and tumors to do so. On the computer, 14 bioinformaticians then evaluate the concrete cases and create models of individual tumors. While the data is stored on a 800-terabyte server, their screens display cryptic plans and mark individual dots with numbers. "You can see small parts of the overall complexity at the molecular level," explains Lange.

"All individuals are different," says Professor Hans Lehrach, Austrian geneticist and Emeritus Director of the Max Planck Institute for Molecular Genetics in Berlin. Alacris and the digital medical twin owe their existence to his genius, perseverance, and restlessness. Lehrach has founded several biotech companies and worked at institutes such as Harvard University in Boston, the European Molecular Biology Laboratory in Heidelberg, and the Imperial Cancer Research Fund in London to help decipher the human genome – and at 72 years old he is still not ready for retirement.

A patient's right arm is put in a cast, although he broke his left arm, simply because studies show a higher frequency of right arm breaks among patients. With such a drastic example, Lehrach describes the status of data-driven medicine. "Medications are molecular entities that interact with the human organism differently from disease to disease and human to human. Until now, doctors have not been able to see the molecular networks very well, and thus had a prediction problem." The only reasonable solution is to create a model for testing the digitized version of different drugs to apply the best available therapy and to exclude unwanted side effects as a prophylactic measure. In other words, to improve the quality of life and healing prospects of patients.

PATIENTS OF THE FUTURE

After sequencing, doctors have a detailed tumor profile and a specific recommendation as to which drug is suitable – be it unexpected or only approved in other countries. Participants in Alacris studies in collaboration with university hospitals, or wealthy private patients, are the only ones who have the chance to receive such a diagnosis.

Insurers do not usually pay the cost of such analyses of around 10,000 euros – with a few exceptions from Switzerland or the USA. "The problem is actually that we need to examine more patients to make it more cost-effective," sums up Lehrach. "The European healthcare systems spend 4.5 billion euros a day – in large part for drugs that do not work and cause only side effects. That is a massive problem!" Lehrach has joined 200 partners in his international "DigiTwin" research initiative and is currently

Professor Hans Lehrach is the spiritual father of humankind's digital twins. He was involved in sequencing the human genome from the beginning.

The digital twin of man – the sum of many equations

working on another submission to the European Commission for about one billion euros. His goal: this technology should be part of normal diagnostics.

The scientists are also thinking beyond tumor diagnostics: “In the long term, every human should have their digital twin available, from birth to old age, that becomes better and better through life with all the information.” Heart rate, complete blood count, metabolic data – all collected data feed the twin and not only help the doctor to find the optimal therapy, but also to set up training plans for a marathon, for example.

ANIMAL EXPERIMENTS ON DIGITAL MICE

The digital twin is also important for research and development. “We can test hundreds of medications on a virtual patient,” confirms Lange. “And one drug that is currently being developed, on thousands of patients.” This allows researchers to exclude patients from clinical trials who are unlikely to have a response. “We can even perform animal testing on the digital twins of mice – and only at the end perform the actual test on a minimum number of animals,” explains Lehrach.

Is this what medicine will look like in the future? For Lehrach, the digital twin may not be the only correct answer to this question. “But it is the best.”

The computers need 24 hours after DNA sequencing to test 90 drugs in the respective model on the basis of approx.

10,000

differential equations.

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Dr. Bodo Lange has been running Alacris Theranostics in Berlin since the first round of financing in 2011.

Photos: Michael Rathmayr