WITH PIPETTE AND LAPTOP

On the road to precision medicine

Separated DNA fragments in an experiment: cutting-edge biochemistry methods enable physicians to decode their patients' genes. This knowledge helps them find targeted treatments for their patients with better prospects of success.

Top researchers around the world are leading the fight against cancer. But every tumor is different – and just as unique as every patient is, which is why it is important to analyze the genetic differences between tumors and the effect that they have on the progression of this widespread disease. To help them perform such analyses, scientists at Bayer are increasingly using supercomputers and methods drawn from the field of bioinformatics. The vast quantities of information that they process are known as "big data" in medical research. "Lots of advances have been made in cancer treatment, but I don't believe in a one-size-fits-all therapy. The idea is rather to provide each patient with a therapy suited to his or her individual needs," says Dr. David Henderson, coordinator of the OncoTrack project in the Innovative Medicines Initiative (IMI) for Bayer's Pharmaceuticals Division. The IMI is a public-private partnership between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA), which provides funding amounting to EUR 5 billion to support biomedical research.

In the context of this project, Bayer scientists are working with more than 20 collaboration partners, including other pharmaceutical companies and academic scientists, to investigate the tumors of colorectal cancer patients down to the smallest detail. They are looking for the origins of the differences between individual patients. The first step: "In addition to the routine diagnostic data, we also collect all of the patients' clinical data," says Henderson. This process generates nearly one terabyte of biomedical data per study participant.

For example, the researchers read the DNA sequence of the primary tumor – in other words the cancer cells that were the original source of the disease. They then compare this genetic code with the secondary tumors, known as metastases, that developed later. "When cancer occurs, a cell picks up several mutations. This enables it to bypass the control mechanisms that normally prevent unchecked cell growth," explains Henderson. The

"For certain diseases, genetic information may soon be part of every patient's diagnosis and therapy"

Dr. John Butler-Ransohoff, responsible for the Harmony project at External Innovation & Alliances, Bayer

Bayer scientist Dr. David Henderson is conducting research to find out which gene variants make colorectal cancer particularly dangerous.

tumor accumulates an ever increasing number of harmful genetic mutations. Using their analyses, the scientists are able to trace the development path of the disease. "The different mutations influence the course of the illness and also determine whether a medication is effective for a patient or not," says Henderson.

Biomarkers could be an indicator for how cancer progresses

Together with his interdisciplinary team of oncologists, geneticists and bioinformatics experts, Henderson wants to determine which characteristics – such as mutations – are commonly associated with which disease patterns and serve as triggers for the disease itself. These genetic features, known to scientists as biomarkers, could be an indicator of how the disease is most likely to progress for the respective patient. "Ultimately, our goal is to divide the patients into subgroups and provide each individual with the optimum form of therapy," explains Henderson. The project, funded by EUR 16 million from the European Union and the same amount from the involved pharmaceutical companies, began in 2011 and will continue through 2016. "We are on the home stretch now. Over the past years we have been able to establish several animal models," says Henderson, summarizing his team's achievements. Nevertheless, cancer researchers consider the current status quo nothing more than a milestone on the journey to their ultimate goal. "In this project we tested how to handle large, heterogeneous sets of patient data records," continues Henderson. This enabled the researchers to verify their method. "So far we have only worked with 300 patients, but we now want to expand our approach to a larger number of participants."

The experts in IMI's Harmony project, scheduled to be launched in January 2017, will work with a potentially one hundred times larger study group. "A pan-European conglomeration of research institutions is enabling us to access up to 50,000 anonymized patient records," says Dr. John Butler-Ransohoff, the person responsible for Harmony in External Innovation & Alliances at Bayer. This patient information comes directly from medical practice – from children and adults with specific forms of leukemia. "With Harmony, we specifically consider potential differences between children and adults in the data analyses as these diseases can have totally different causes in children and will then have to be treated differently as well," adds Butler-Ransohoff. The scientists and computer specialists are therefore analyzing the relevant DNA of patients and monitoring the progression of their disease over the course of several years. "We are trying to determine what the patients with similar disease patterns have in common," says Butler-Ransohoff. For this, the scientists can examine the entire DNA in minute detail, searching for genetic biomarkers. "Using these biomarkers," says Butler-Ransohoff, "we can divide patients into different genetic groups that might all be associated with the same, specific disease pattern." The oncologists hope this will enable them to choose for each patient the therapeutic option that promises the best chance of success with the fewest side effects.

Up to 50,000

anonymized patient records

are being analyzed by the experts in IMI's Harmony project in the search for biomarkers.

Source: Bayer

Sequencing a human genome now costs less than US$ 1,000

Both projects illustrate what the medicine of the future is all about: understanding each patient better and taking their specific DNA into account to select the optimum course of therapy. "The first sequencing of a human genome cost millions of dollars. Today that same procedure costs less than 1,000 dollars, and the price continues to drop. For certain diseases, genetic information may soon be part of every patient's diagnosis and therapy," explains Butler-Ransohoff. This trend is evident in fields outside of cancer research too. Bayer researchers are turning to geneticists and IT specialists in the search for new therapies for cardiovascular patients as well. "The opportunities for collecting medical data and the IT resources for evaluating it are steadily expanding," says Henderson. Basic research is yielding a stream of new approaches that are ultimately finding their way into clinical practice. "This is helping us to gain an increasingly better understanding of diseases and enabling us to offer patients targeted treatment," says Henderson. ■