Expert interview

Genome analyses: "Germany lags behind dramatically"

Today, around 6,000 genetic diseases can be diagnosed using genetic tests. Genetic testing enables the accurate identification of diseases especially when symptoms are unclear, and also allows statements to be made about disease progression. However, restrictive regulations considerably hinder the use of genetic diagnostics in Germany - and it is patients who pay the price. BIOPRO spoke with Dr. Dr. Saskia Biskup, a human genetics specialist and co-founder of the Tübingen-based company CeGaT. The company specialises in genetic diagnostics and has won numerous awards for the concept.

Dr. Biskup, who uses your diagnostic services?

People who have been suffering from a disease for years, but whose condition could not be diagnosed. Such people often have a rare disease and have seen countless doctors. On average, it takes around seven years to diagnose a rare disease. Genome analyses can reduce the time taken to a few weeks. Patients who appear to have exhausted all treatment options are increasingly coming to see us. We examine the tumour and look for possible therapeutic approaches.

Dr. med. Dr. rer. nat. Saskia Biskup is a specialist in human genetics and managing director of CeGaT GmbH. © CeGaT

How does genome analysis work?

We recommend that patients attend a consultation which may bring to light incidental findings, for example risk factors for other diseases that are unrelated to the matter in hand. In this case, the patient has to decide whether he or she wants information about these risk factors or not.

A blood or saliva sample is sufficient for a diagnostic test. We isolate the DNA, amplify the desired DNA regions and decipher the genetic material. We also carry out data analysis and diagnosis. DNA analysis is done with next-generation sequencing methods, i.e. high-throughput methods that can be used to sequence genomes within a matter of days.

And how do you examine tumour patients?

As far as cancer patients are concerned, we remove and sequence tumour tissue and compare it with the patient's healthy tissue. This enables us to identify tumour-related mutations. Each tumour is different, and depending on the underlying mutation, patients may require different therapies or respond differently to therapies. The goal is to find a therapy that fits a patient's specific requirements. This helps reduce unnecessary side effects and increases the success rate of therapies.

Where do we currently stand with regard to the use of human genetics for patient diagnosis and treatment in Germany?

In Germany, meaningful diagnostic tests cannot be offered to the majority of patients: since July 2016, doctors are only allowed to invoice the health insurance companies for sequencing up to 25,000 of the three billion base pairs in the human genome. This corresponds to about four genes. However, as many as 1,000 genes are known to cause mental disabilities. We then have to wait an entire year before we can sequence the next four genes. It's an insane situation that costs the healthcare system huge amounts of money. Thanks to technical progress we would be able to look at millions of DNA positions for the 2,000 euros that it costs to sequence four genes. In other countries, a trio, i.e. the sequencing of the exomes of father, mother and child covering around 60,000 genes costs around 2,500 euros. Germany dramatically lags behind international developments.

Does this mean that the use of diagnostic services involving genetic tests is more advanced in other countries?

Far more advanced. The Netherlands are among the pioneers in this field. There, comprehensive genetic diagnostics is a matter of course. The Netherlands publish more, and are more innovative. France is currently setting up a large-scale genome programme that aims to sequence around 240,000 total genomes by 2020. And England has almost completed its 100,000 genomes project. In the USA, laboratories involved in diagnostics require accreditation, while in Germany, many methods and procedures can be used and invoiced without quality assurance.

What does the restrictive regulation in Germany mean in practice?

The 25,000 positions are a joke. I'm looking forward to the time when the powers-that-be who set this limit will finally realise this. Not only does it take much longer to diagnose a disease, it is also more costly. The whole thing is particularly hard to swallow when a child comes to us with an unexplained mental and/or physical retardation. As a matter of fact, such children account for around half of the patients that seek advice from us. In such a case, a trio examination would be the perfect thing to do. This has long been standard in many countries. If we could sequence the genome of the father, mother and child, it would be a tremendous help for us when it comes to identifying changes in the child's DNA. Trio examinations help us detect the cause of a mental disorder in up to 45 percent of the children that we test. This is a really good rate that will improve rapidly as the phenotype-genotype databases on disease-causing gene variants grow week on week and are made available to people working in the fields of research and diagnostics.

Rapid diagnostics brings only advantages: the healthcare system saves the costs incurred by additional, sometimes invasive, and often ineffective examinations in patients with rare diseases that are carried out over the seven years that it usually takes to diagnose a rare disease. And for the patients, knowing what disease or condition they have is the first step towards managing a

disease.

What happens with these children or other patients with unclear symptoms?

When the family is well-informed and well-off, they can pay for the examination out of their own pocket. Alternatively, we can apply for authorisation to analyse more than 25,000 genome positions. In this case, we have to explain the therapeutic relevance of the planned examination. This is impossible to do, as we first need a diagnosis. I have written hundreds of applications, most of which were dismissed on very flimsy grounds. Patients with private insurance cover have a clear advantage.

What about therapies?

In principle, a therapy can only be put in place if the underlying genetic cause of the disease is known. This means that people suffering from rare diseases cannot be offered immediate treatment. However, people with rare diseases are extremely relieved to finally know what has caused their long-term condition. They can then seek therapy from experts in their particular disease and share information and experiences with others. And the odyssey of seeing one doctor after another without finding an answer is finally over for them.

What do you think needs to change for patients in Germany to have better human diagnostics options?

Staff of CeGaT GmbH decode genetic information using high-throughput sequencers. © CeGaT

In theory, each of the 250 human geneticists in Germany can put a sequencer into his or her basement. Quality standards do not exist. I am calling for the mandatory accreditation of high-

throughput methods, uniform sequencing, data analysis and interpretation standards, as well as the acquisition and storage of clinical findings.

In general, you would have to put an end to requirement planning and planned economy. We need significantly more medical geneticists. At present, we have one specialist per 600,000 inhabitants. The reimbursement system would also have to be fundamentally changed. There should be more money to allow doctors to spend more time with an individual patient. Medically indicated diagnostic examinations would have to be reimbursed. This would save a lot of the money that is currently spent on unnecessary invasive diagnostic procedures and ineffective, hence unnecessary, therapies. And if he ever comes to visit us, I will say all this to Mr. Spahn directly (ed. note: German health minister).

According to experts, Germany's decentralised healthcare system makes it difficult to establish uniform quality standards. What do you feel about this?

I am very much in favour of centralising laboratories. I believe that this would actually make quality assurance easier. It is very simple as far as genetic testing in laboratories is concerned, as blood or saliva samples can easily be sent to test laboratories by post. CeGaT receives patient samples from all over the world because we are nationally and internationally accredited for the high-throughput methods that we use.

But I am also very much for decentralising patient care. It is not just about laboratory diagnostics, but also about taking care of patients and families by general practitioners, who, I'd like to add, provide an outstanding service. Unfortunately, GPs are not given the appreciation or reimbursement they deserve for their services. I believe that doctors who do not have a laboratory in their own practice should also be able to be adequately reimbursed.

Genetic data is sensitive data. How do you store this data?

We store everything "in-house" and work according to the Gene Diagnostics Law. Patient data obtained from genetic analyses are strictly protected and belong to the patient. Everyone has a right to genetic privacy, as well as the right to be able to share this data if he or she so wishes.

What will change for patients with genetic issues in the next decade?

The fact that we are entering the age of precision medicine will become more and more obvious. And precision medicine requires precision diagnostics. Only if we understand exactly what a patient's disease is will we be able to help him or her. Fast and cost-efficient genetic diagnoses will become a matter of course. Doctors will increasingly be dealing with issues related to how to find out the appropriate medication dosage or how to detect and treat diseases early. Genetics will play a key role for everyone.

Article

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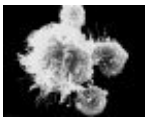

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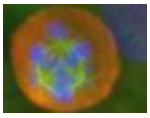

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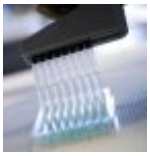

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