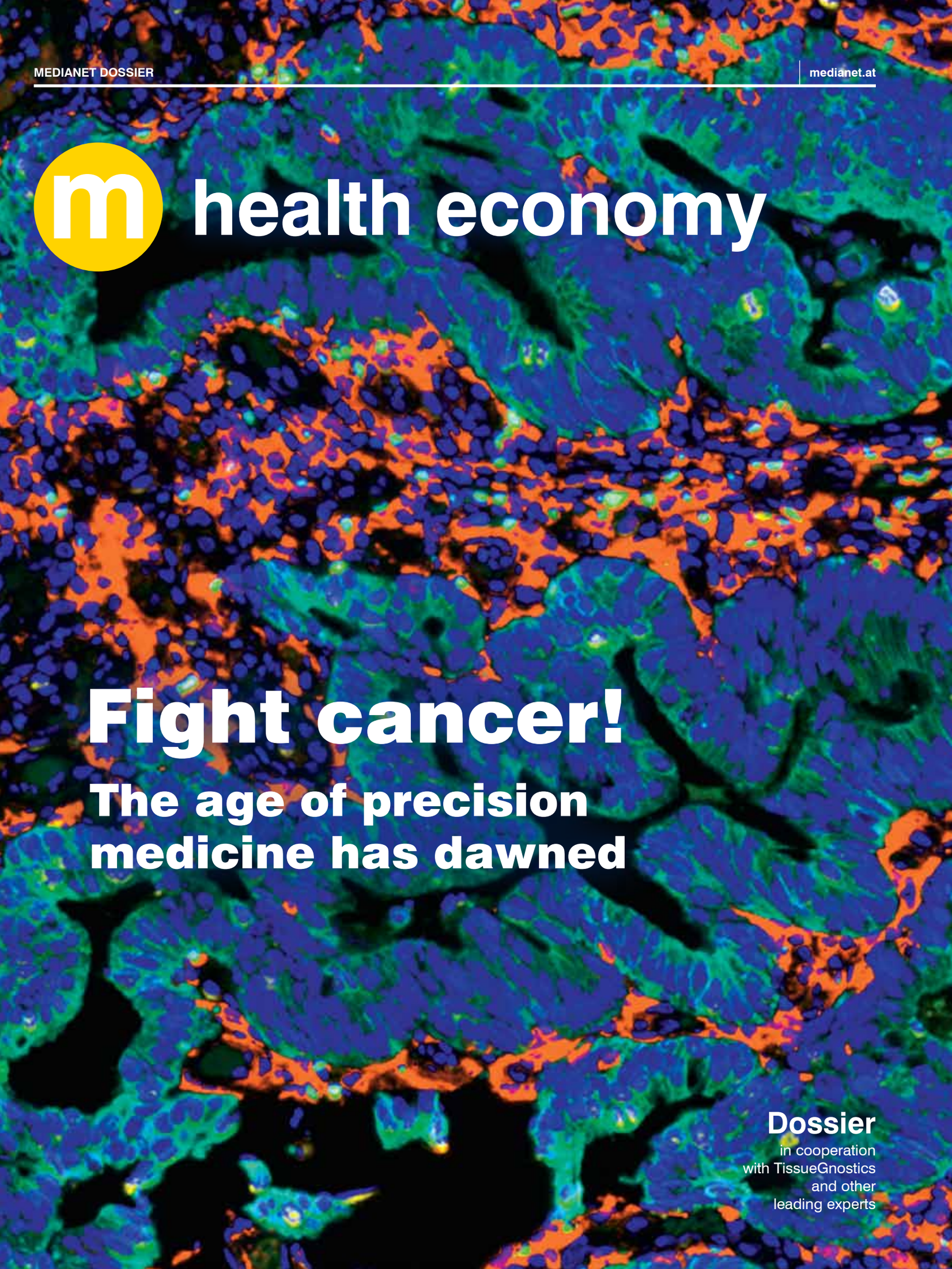

health economy

Fight cancer!

The age of precision medicine has dawned

Dossier
in cooperation
with TissueGnostics
and other
leading experts

The Editor
Oliver Jonke
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Editorial

Precision Medicine, Made in Austria

Dear Readers,
For 15 years now, the pioneering Austrian company TissueGnostics has been working successfully in the field of precision medicine with a variety of partners, including oncology centres around the world.

Big.
On average, all of us have an increasing life expectancy, and there is a global trend towards more prosperity. At the same time, the number of patients who have serious illnesses, such as cancer, is increasing significantly in the world's population. Overall, there are too few resources in the form of doctors, institutions and therapies for the efficient treatment of these diseases using traditional means. One of the biggest challenges of our time is to use research, continuously optimised diagnostic methods and therapies to improve every patient's prognosis, regardless of their socioeconomic status.

Data.
The ongoing digitisation of medicine has facilitated the collection and analysis of patient data to an extent that was never possible before. As the analysis of a variety of biomolecular measurement data becomes more and more accurate, it is possible to make more precise diagnoses; this is why we often talk about technology-driven medicine or precision medicine in this context. Dedicated scientists develop new techniques, mostly quantitative in nature, and they become milestones in the diagnosis and personalised treatment of cancer.

An outstanding example is the Viennese company TissueGnostics, founded in 2003, which is now active globally and has offices in the EU, USA and China. This dossier was commissioned by TissueGnostics and was compiled by TissueGnostics in cooperation with other leading research institutes.

Future.
Research and development in the field of precision medicine definitely pays off in every regard. Let's work to ensure that the best possible conditions are created for scientists, researchers and the companies created as a result! Let's make sure that there are as many qualified bioinformaticians as possible so that there can be more investigator-initiated trials on the one hand and, ultimately, so that we can help every patient more quickly and effectively in future. Let's use more efficient diagnostic and treatment methods to adapt our somewhat dated healthcare systems to patients' individual needs. Ideally however, we want to avoid creating perpetual patients …

Best regards
Oliver Jonke
Editor

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Precision Medicine

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A medical revolution

Individualised medicine will fundamentally change healthcare.

Guest commentary
••• *By Rupert Ecker*

VIENNA. An Airbus A380 is a highly complex and very valuable machine. Not only do four million individual parts need to be put together to enable it to fly, dozens of mechanical, hydraulic, electric and electronic subsystems also need to communicate with each other and work in a coordinated way.

If a defect occurs in one of these systems, the aerospace engineers do not just start to exchange parts arbitrarily in the hope of repairing the defect. Instead, they follow up on the malfunction report by carrying out a detailed defect analysis. Their goal is to recognise and understand the exact cause of the defect as well as the mechanism which led to the breakdown – they want to be able to respond systematically and eliminate the cause of the problem. If, for example, a retaining pin breaks, the engineers will not only replace it, they will also try to understand why it broke in the first place. If we apply this analogy to biological systems – cells, tissue, organs and organisms – we have the basic idea behind personalised medicine.


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A paradigm shift
This buzzword is currently cropping up in many expert journals and in popular science media. Such sources even call it a revolution or a paradigm shift in the healthcare system which has the potential to fundamentally alter existing health services. However, the term is misleading because it implies that a doctor takes care of a particular person. It is more a case of individualised medicine or, even better, precision medicine.

The idea behind it is that people are different and can react to different medication in very dissimilar ways. In most cases, minor differences have a major impact on whether a therapy will work or not. So what do we do? For a doctor to try out different medications in a systematic manner to see which medication a patient responds to is not only purposeless, it is also unethical and expensive. Genetic analysis and analysis of molecular biomarkers can be very helpful and filter out which type of patient someone is.

Biomarkers are defined, measureable biological indicators which provide information on particular physiological processes. They include values such as body temperature or blood pressure, but also properties on a molecular-biological level, such as gene sequences, proteins and enzymes. We have known about many of them for a long time; research on other ones has only begun recently. In particular, research is focused on the effects of various markers. These biomarkers, in turn, provide the basis for the development of new medications. When these medications will become available later on, it will be possible to offer therapies tailored to individual patients. This can enable healthcare providers to reduce undesired effects and side effects, and may eliminate interactions with other medications. This saves money and, in particular, prevents the patient from suffering.

Debates on costs
In times when public spending on healthcare continues to decrease, this could mean that a revolution is coming. With such targeted, individualised therapies, it could even be possible to cure chronic illnesses. To turn this possibility into reality, however, requires true-cost pricing in the healthcare system; this is something that is lacking for the most part. When costs are reduced in an area in which it makes sense to do so, this still does not mean that funds will be allocated to therapy again, and other therapeutic fields will be downsized for that reason.

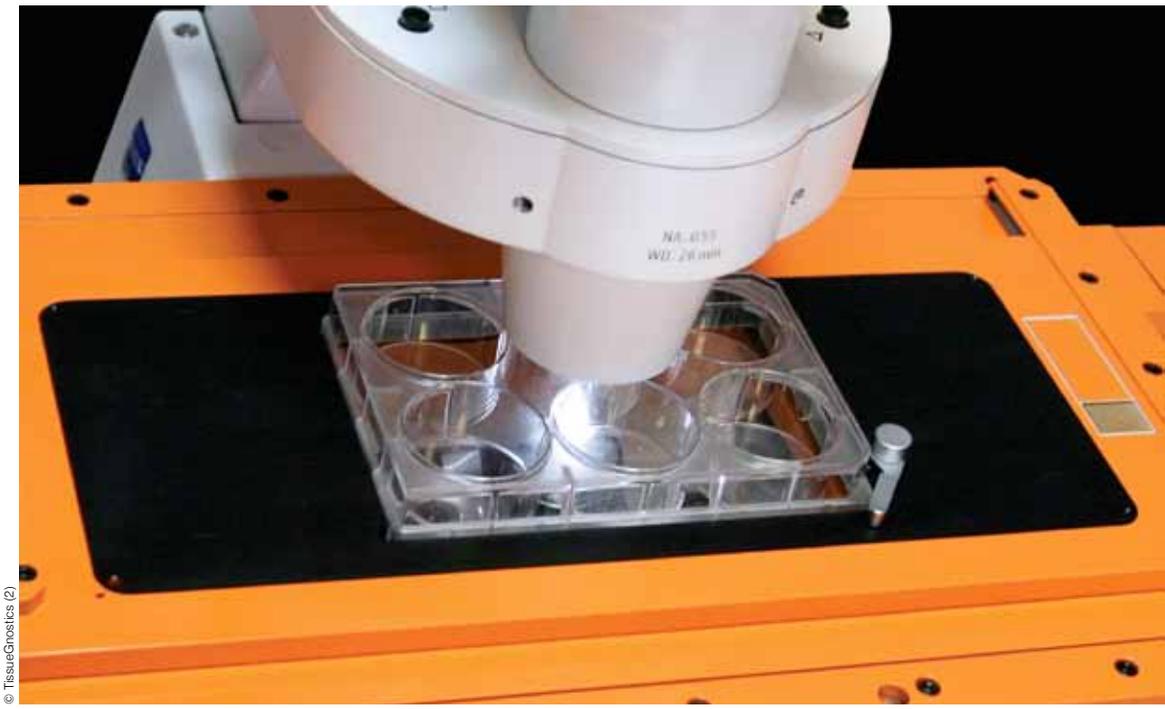
Will sci-fi become reality?
Future developments are not easy to predict. Fans of the science-fiction show "Star Trek" may be familiar with this scene: the doctor on the show has a "tricorder" and scans a patient, measuring every single health parameter and then diagnosing the disease within seconds. The American IT company Qualcomm announced a competition several years ago, offering a ten million dollar prize to the first technician who could develop a functional tricorder. In other words: the future has just begun.

> *"Genetic analysis and molecular biomarkers can help us figure out which medications are optimal for a patient. This saves money and prevents unnecessary suffering."*
>
> **Rupert Ecker**
> *CEO TissueGnostics*

CSI Cancer: how to find the appropriate therapy

A Viennese company strives to revolutionise healthcare diagnostics: a new technology analyses cells and helps to create targeted therapies.

••• *By Martin Rümmele*



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The computer screen slowly turns pale blue, the colour that represents the cancer cells in a tissue sample, interspersed with bits of brown. The brown indicates the immune cells which have been crippled by the tumour. The computer program developed by the Viennese company TissueGnostics makes it possible to *analyse* the following: where is the number of cancer cells particularly high in the sample? How many immune cells are in any given part? TissueGnostics has developed a process that automatically characterises tumour tissue and, in doing so, provides the basis for what is often referred to as the personalised medicine of the future.

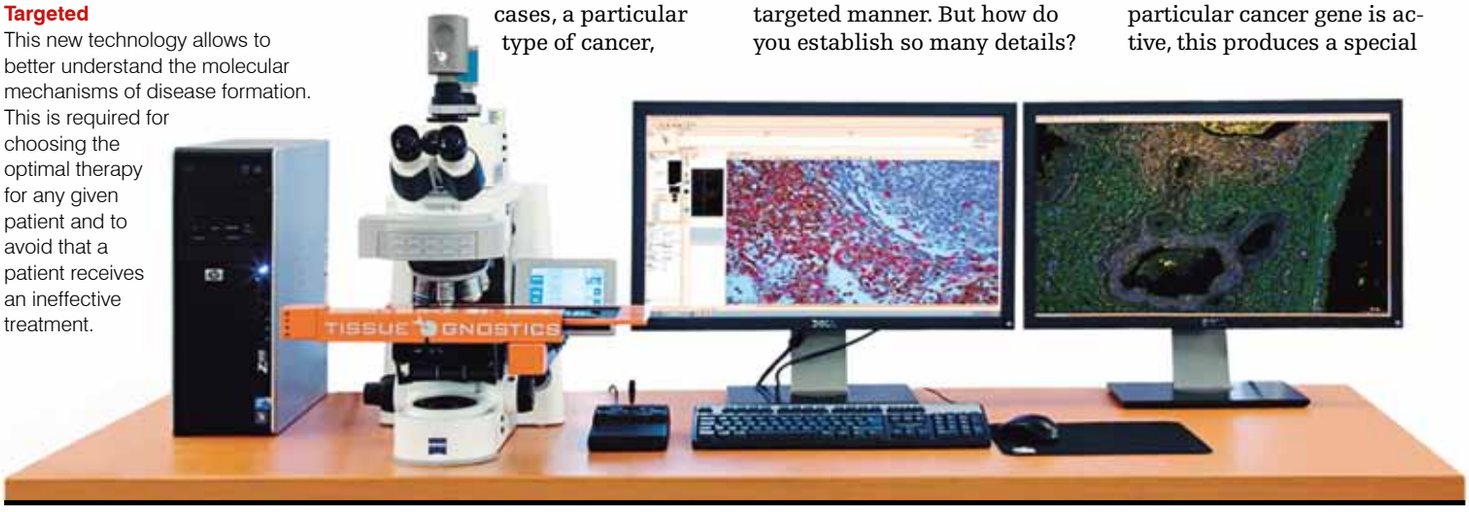
It sounds like a simple development when you present a simplified version of it: for us to be able to use targeted therapies in the first place, we have to do more than just diagnose a disease. We have to be even more precise, recognising what *type* of disease it is. In many cases, a particular type of cancer, for example, has its own specificities. When we are able to establish what these are with precision, we can also use the appropriate medication in a targeted manner. But how do you establish so many details?

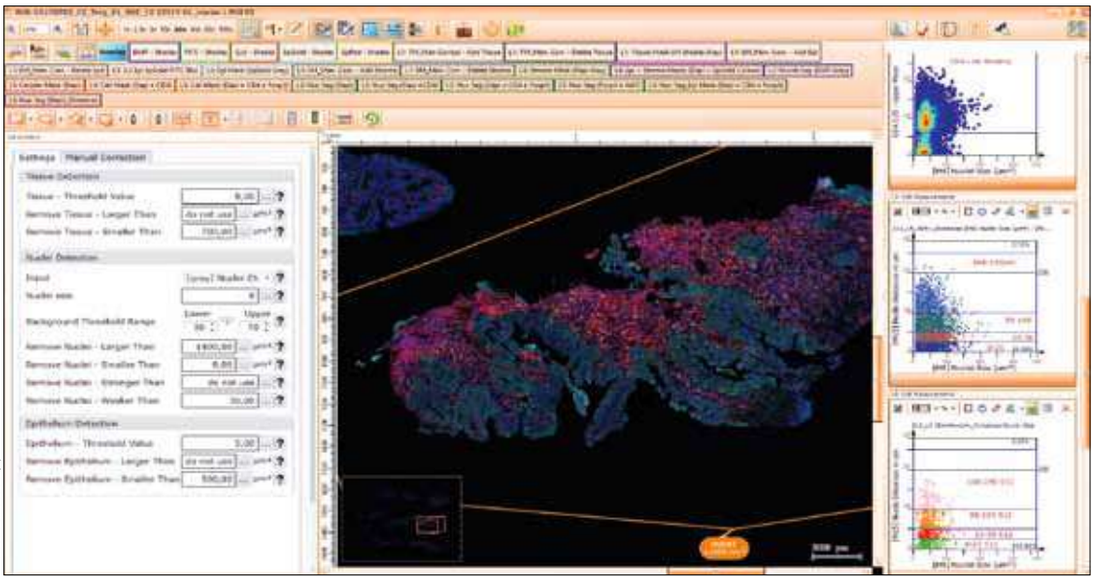
A complex diagnosis

"Pathologists nowadays use tissue samples not only to determine what type of cancer a patient has; if, for example, a particular cancer gene is active, this produces a special

Targeted

This new technology allows to better understand the molecular mechanisms of disease formation. This is required for choosing the optimal therapy for any given patient and to avoid that a patient receives an ineffective treatment.





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Analysis
TissueGnostics' award-winning software to analyse medical images creates the basis for the individualised medicine of the future, helping to organise millions of data points.

protein which appears on the surface of the cells. Only a few agents are able to interact with that protein and can thus attack the tumour," says Rupert Ecker, managing director of TissueGnostics. However, the diagnosis of these proteins is not easy. Mr Ecker, who has a doctorate in cell biology, would spend days on end conducting painstaking analyses of cells in tissue sections using a computer. At the time, he was writing his thesis whilst working in the research laboratory for urology at the Medical University of Vienna. It was very demanding work and, in particular, very error-prone, as the differences are often minimal. A pathologist identifies proteins using immunostaining. The greater the quantity of a particular protein that is present, the more antibodies will bind to it, which results in a stronger colour reaction. However, perception of a colour's intensity is very subjective. Furthermore, there are up to 30,000 different proteins.

Award-winning software
He thus set about developing software to automatically analyse microscope images – fast and with a high degree of precision. TissueGnostics was launched 15 years ago and rose like a rocket. Today, universities and research institutes from all over Europe, the USA and China utilise the company's software. Not only is it used in oncology, it is employed in neurology and dermatology for a long while now. Approximately 1000 scientific papers have already been published.

Because of their expertise in the fields of automated microscopy and tissue cytometry, TissueGnostics are being invited to participate in more and more research initiatives as an industry partner. The company supports research related to personalised medicine; so far it has been invited to four Marie Sklodowska Curie Innovative Training Networks, sponsored by the EU. These programmes are dedicated to developing various aspects and tenets of precision medicine, both translational and technical in nature *(see right)*.

"We work in close cooperation with universities and, in doing so, contribute to international cancer research."

Rupert Ecker
CEO TissueGnostics

Support for research in the EU

Digital pathology
TissueGnostics was a partner at the "Academia and Industry Collaboration for Digital Pathology" (AIDPATH), an international project on the development of efficient and innovative products for digital pathology. AIDPATH was an IAAP Marie Curie Action European Union's FP7 Framework Programme that ran from 2013 to 2017.

Calcium sensing receptor
The CaSR Biomedicine European Training Network (ETN) is a project based in Vienna. Its research focuses solely on a single molecule, the CaSR (calcium sensing receptor), examining its role in several physiological processes and diseases. It is developing a unique, multidisciplinary and intersectoral training programme.

Breakfree from cancer
The European Training Network "ALKATRAS – Breakfree from cancer" is integrated into an internationally established research programme: the European Research Initiative on Anaplastic Lymphoma Kinase (ALK)-related malignancies. It is a network with 13 research partners.

Cell migration studies
InCeM is an international PhD programme offering young researchers the opportunity to improve their research and business skills and, by extension, their career opportunities. The programme's main focus is on research related to cell migration, a fundamental biological process that takes place everywhere in the human body.

Diagnostics of the future: it all begins with molecules

medianet editor Oliver Jonke in a round table discussion with leading experts and scientists from the field of precision medicine.

The discussion's participants all agree that the term "personalised medicine" is actually inaccurate. Every practicing GP offers "personalised medicine", just as every doctor who, for example, practises according to the principles of traditional Chinese medicine. "Doctors focus on the patients as people, talking to them and gathering information about them," says Renate Kain, the head of the Department of Pathology at the Medical University of Vienna.

However, this is not what personalised medicine is about, which is why the popular term is also misleading. According to Dr Kain, "Nowadays treatment involves incorporating vast quantities of data, comparative data and the corresponding

analyses." That is why personalised medicine has nothing to do with doctors' rapports with their patients, says Georg Stingl, emeritus professor at the Department of Dermatology of the Medical University of Vienna. Instead, he recommends using the terms used by scientists: "precision medicine", "stratified medicine" or "individualised medicine".

Differences between diseases

In principle – and this is where this type of treatment distinguishes itself from treatment focusing on patient rapport – it is medicine strongly driven by *technology,* viewing people or the disease being treated as a molecular whole, says Stingl. When we establish individualised differences, we can start treatment with a targeted therapy. A simple example, he says, is the fact that similar but distinct diseases can present the same symptoms. The difference only becomes apparent after a precise *analysis* has taken place. According to Dr Stingl, "Eczema – known as atopic dermatitis among experts – has about three significant types with the same clinical manifestation. But the *trigger* is different in each case. When we are able to identify these differences, we also know where we can begin treatment in the first place." The same is also true of many inflammatory diseases.

High costs

At the same time, the problematic side of this development, in which patients receive their own customised medication, becomes readily apparent. "That is a nightmare scenario, because we cannot afford it," says Dr Stingl. He stresses that he does not feel that it is necessary at all. What is important is that appropriate medications can be developed and administered accordingly in the first place. The experts agree that the advantage lies in the analysis of data and its use in the development of new medications.

The importance of these new concepts is evidenced by the increasing number of cancerous diseases. Unhealthy lifestyles, environmental factors and, in particular, demographic developments – the risk of mutations and tumours increases with age – are the reasons behind this development. This also explains why science and the pharmaceutical industry are

The participants

Renate Kain
Head of Department of Pathology, Medical University of Vienna

Bettina Zelger
Former Head of Department of Pathology, Medical University of Innsbruck

Helmut Klocker
Head of Urology Research, Medical University of Innsbruck

Georg Stingl
Former Head of Department of Dermatology, Medical University of Vienna

Richard Moriggl
Scientific Director Ludwig Boltzmann Institute for Cancer Research, Vienna

Rupert Ecker
CEO TissueGnostics

Moderator: Oliver Jonke
medianet Editor

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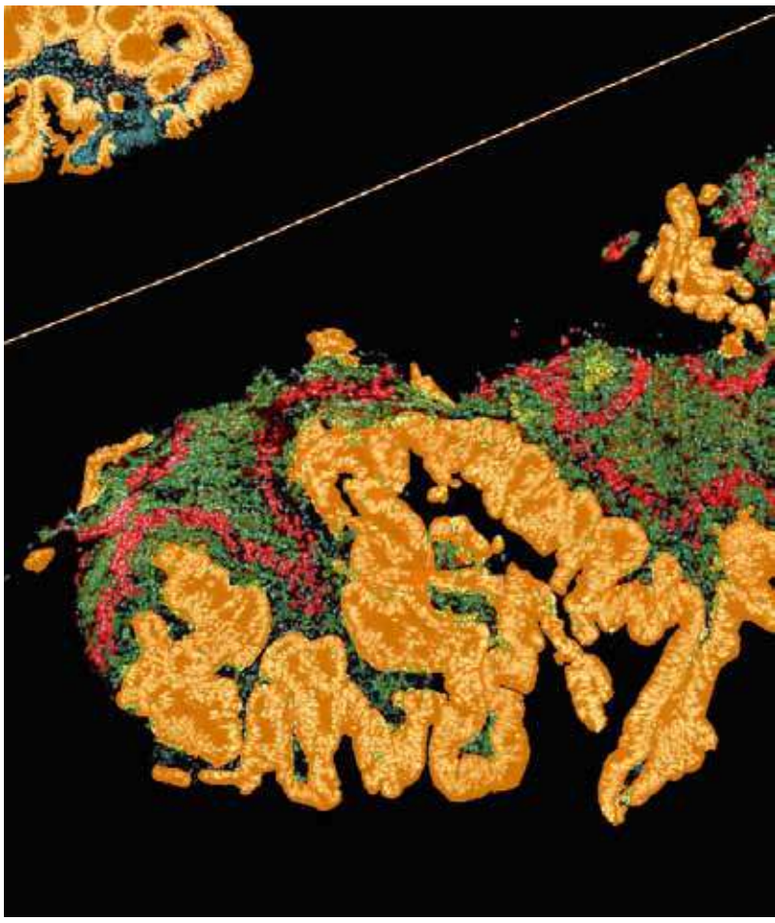
There are not nearly enough pathologists in Austria. We need more teams and centres to expand the field of individualised medicine. At the moment, however, there is a shortage of funds.

Bettina Zelger



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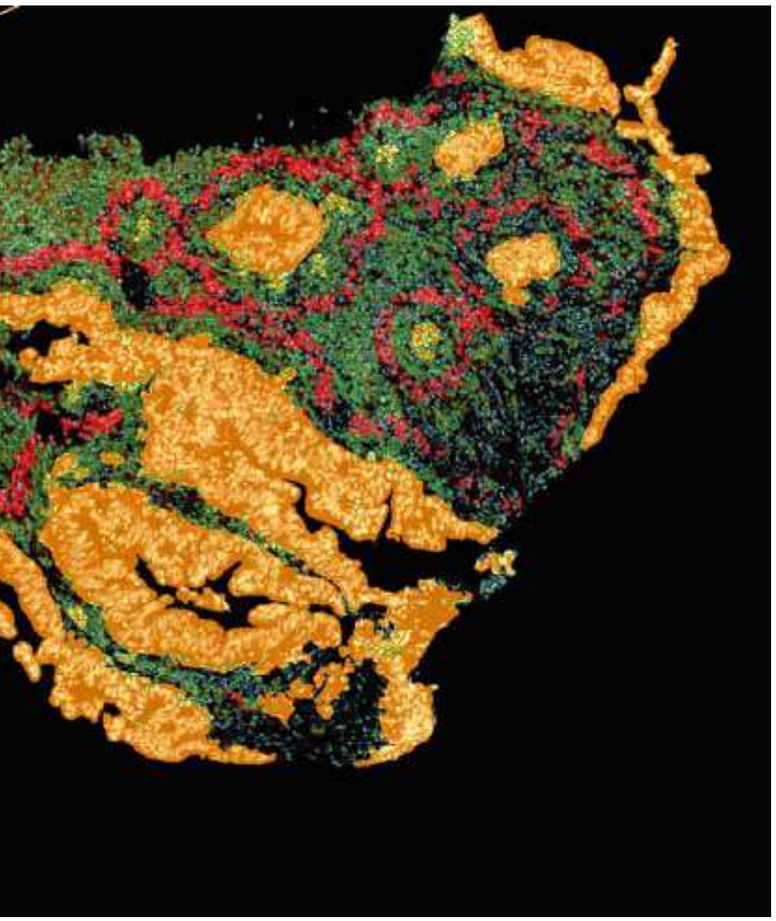
Individualised medicine helps us to figure out when we have to use an aggressive form of cancer treatment and when it might be better to leave a tumour untreated.

Helmut Klocker

intensifying their efforts to fight cancer. As Dr Kain notes, this has already been apparent for a number of years. "The developments that have been made in the past few years and what the pharmaceutical industry has been doing in this area is very significant. The therapeutic possibilities which have opened up are enormous. We have experienced quantum leaps in oncology, for example, in the past 15 years. We have seen things that were previously unimaginable." However, it is also apparent that costs are increasing significantly as a result.

Conversely, however, the *targeted* use of expensive therapies would entail savings potential, says Helmut Klocker, the head of the urology research laboratory at the Medical University of Innsbruck. "Our goal as researchers is to use therapies and, by extension, funding, as efficiently as possible. If I do not expect the patient to benefit in any way from a particular therapy, I should not use it at all. In extreme cases, such as a prostate carcinoma, you can also determine whether it is really necessary to use an aggressive form of cancer treatment, or perhaps to leave the tumour untreated because it is growing very slowly and is not dangerous."

Nevertheless, you should also question pharmaceutical companies' pricing policies in this context, as Richard Moriggl suggests. Dr Moriggl is a professor of Functional Cancer Genomics at the University of Veterinary Medicine, Vienna and the Medical University of Vienna. "Some products, such as those that increase survival rates, are very expensive. However, it could be the case that these products can be *produced* very cheaply. Sometimes it is because of time-consuming research, but this is not always the case." What is certain is that individualised medicine is transforming healthcare significantly, as Dr Kain is



The idea of every patient receiving individual medication is a nightmare scenario. That is something we cannot afford. Generally speaking, however, we do not need this. The matter at hand is the development of better medications.

Georg Stingl

convinced. It is also apparent that researchers and scientists everywhere are aware of this development – including in Austria. "This no longer applies exclusively to cancer treatment; it is true of *all* diseases. There are diseases where we still do not know how they progress, and there will be a great deal of progress here in the years to come."

A better framework

The medianet round table experts are calling for framework to be created which will make this possible. Although Austria is now becoming more active with regard to big data and the scientific use of data, there is no interrelationship with medical *research.* Consequently, there is also a lack of funding, as the experts critically note. "In Austria, there are not enough pathologists, for example. We need more teams and centres to expand the field of individualised medicine. At the moment, however, there is a shortage of funds," stresses Bettina Zelger, the former head of the Department of Pathology at the Medical University of Innsbruck. Furthermore, there are not enough experts being trained in Austria in bioinformatics, still a young profession. These experts are highly sought after, and at the moment they can have their pick of the best jobs around the world. The result: Austria is suffering a brain drain. Conversely, Austria does not have the means to keep talent here or to recruit it from abroad, as the participants agree.

No strategy

To tackle this issue, the experts are also calling for a national strategy. "Over the past ten years, Austria failed to train bioinformaticians," says Moriggl. Countries such as India, China and the USA are much more advanced in this regard and also have the resources to research and develop new products as a result. According

We provide researchers and doctors with tools so that they are better able to understand the fundamentals of cancer and other diseases at a molecular level and to develop specific therapies.

Rupert Ecker

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to Dr Moriggl, "Austria needs an international strategy which involves experts, and we have to raise awareness about the possibilities available here." Dr Stingl is even more critical: "I cannot think of any country whose *politicians* are as apathetic about the potential of science as in Austria. At the moment, we don't even have a ministry dedicated exclusively to science. We would need one to be able to show that scientific research is important to us."

All things considered, there is a lack of funding for research, both from the public sector as well as from private investors. With the exception of a few highlights, such as the Institute of Molecular Pathology funded by the pharmaceutical company Boehringer Ingelheim or the IMBA in Vienna, there are very few opportunities in Austria as compared to other countries. In the United States, for example, entire university faculties and centres dedicated to individualised medicine have received both public and private funding.

New possibilities

This is precisely what a country like Austria requires if it is to avoid missing out. TissueGnostics, for instance, is willing and able to help; according to CEO Rupert Ecker, the company is trying to provide scientists with new tools. "We are working on standardisation procedures and are also cooperating with international universities," says Ecker. This work includes, for example, discovering new biomarkers or signs of tumours which make it possible to predict whether a patient will respond to a therapy or not, for example. "At the same time, these biomarkers could also be target substances for new therapies." However, this also requires appropriate funding and grants. "We provide researchers and doctors with tools so that they are better able to understand the fundamentals of cancer and other diseases at a molecular level and to develop specific therapies," Ecker is convinced. He feels that his company is doing well in that regard.

> *In Austria, we need an international strategy which involves experts, and we have to raise awareness about the possibilities available here.*
>
> **Richard Moriggl**

> *What we have experienced here over the past few years has been incredible. We have experienced quantum leaps in oncology, for example, that were hitherto unimaginable.*
>
> **Renate Kain**

However, the experts maintain that individual countries will be facing an additional challenge – the large-scale *implementation* of findings and developments. "The question is how we will deliver it to patients. How do we organise hospitals? Where do we build the centres we need? Also, how will we be able to make it clear to the public in the first place that there is an incredible amount of potential and opportunity here, but that there will also possibly be upheavals in the system?" Dr Klocker asks. It would require a great deal of effort, nationally and internationally, because science is progressing at a rapid speed.

Important discussions

The experts who participated in the medianet round table have drawn the following conclusions: individualised medicine – or, more accurately, precision medicine – has what it takes to change the face of medical science completely and hence facilitate treatment for diseases that previously could not be cured. However, this will pose serious challenges to science, universities, healthcare systems and, by extension, society as a whole. Discussions about these challenges will have to take place as quickly as possible. Unfortunately, however, there is still a lack of awareness of these issues – among politicians and within society.

Knowledge is good for you

The more we know about patients' genetic parameters, the more effectively we can treat them.

••• *By Martin Rümmele*

NOTTINGHAM. Mohammad Ilyas is a molecular pathologist at the University of Nottingham in England and an expert in all things related to precision medicine. He sat down with us and explained how knowledge about a patient's genetic parameters can help in the selection of a therapy and hence improve the chances of recovery. "As a rule, medical treatment is based on statistical probabilities," he says. "So when a patient with disease B is treated using treatment A, this decision is based on several years of experience or on data from clinical studies which show that disease B is most likely to respond to treatment A. However, every doctor knows not all patients react in the same way and, indeed, in the case of some patients with disease B, treatment C will be more effective."

Individual therapy as a goal

The ultimate goal in medicine, Ilyas says is to help each patient *individually,* in a targeted manner, and not according to probability: personalised medicine. This point of view also entails viewing the patient from a holistic (diagnostic) perspective. Information from at least six different categories is necessary to offer truly personalised medicine. These are the "6 Ps of precision medicine":

- *Predisposition:* this information tells us about the risk of developing a disease; we gather this information from analysing a patient's DNA germline.
- *Pharmacogenetic:* this information tells us how a person will respond to a particular medication; we also gather it from analysing a patient's DNA germline.
- *Profile:* this information describes specific transformations that have arisen as a result of the disease. It is derived from a comprehensive analysis of the diseased tissue (including DNA, RNA and protein analyses).
- *Prognostic:* this information tells us about the disease's biology and how it is likely to progress. We collect this information from detailed analyses of the diseased tissue.
- *Predictive:* this information gives us an idea of the therapies which could be used to treat a specific disease. Again, this information comes from a comprehensive analysis of the diseased tissue.
- *Pharmacotherapeutic:* this information identifies the molecules specific to a disease, which could be targeted during treatment. A detailed analysis of the diseased tissue is the source of this information as well.

6 Ps

The genetics of cancer

For Mr Ilyas, the "6 Ps" of the genetics of cancer are as follows: predisposition, profile, prognosis, prediction, pharmacogenetics and pharmacotherapy.

© Mohammad Ilyas

The researcher

Mohammad Ilyas is a molecular pathologist at the University of Nottingham and a precision-medicine expert.

Tissue analysis

Pathology can be defined as "disease investigation" and includes, in practice, the analysis of diseased tissues so as to make a diagnosis. In its most basic form, pathology entails viewing the diseased tissue under a microscope. An experienced pathologist can tell which disease it is based on the image under the microscope. Over the past few years, however, advances in technology have significantly increased the amount of data which can be derived from tissue analyses, and some analyses have already become automated. In particular, techniques such as next-generation sequencing (NGS) make a very detailed analysis of DNA and RNA from healthy and diseased tissue possible. Developments in proteomics also make a very detailed analysis of proteins possible, and in much the same manner cytomics allows us to analyse tissue in an objective, automated way. Big data stemming from genomics, proteomics and cytomics can be analysed using the newest data mining methods, and new patterns which are clinically significant can be identified in the data. These methods include everything from novel algorithms that analyse digitised images of tissue based on artificial intelligence (AI) to sophisticated bioinformatic approaches to contextualised analysis of all data. These characteristic patterns can be categorised as one of the "6 Ps", which means that pathology has a very important role in the provision of data and can enable personalised medicine to become a reality.

Research around the globe is focusing on personalisation

This is not only true in Europe; researchers in Asia, Africa, South America and North America are working with biomarkers to answer individual questions.

••• *By Martin Rümmele*

Personalised medicine and precision medicine have essentially been around for a long time. Nowadays, we are expected to use the concepts of precision medicine as much as possible in research, says Beatrice Knudsen, Professor of Biomedical Sciences and Pathology at Cedars-Sinai Medical Center in Los Angeles, who was interviewed by **media**net. After talking to six global research centres, we have noticed that the topics of personalised medicine and precision medicine are at the top of everyone's agendas *(see the next page)*.

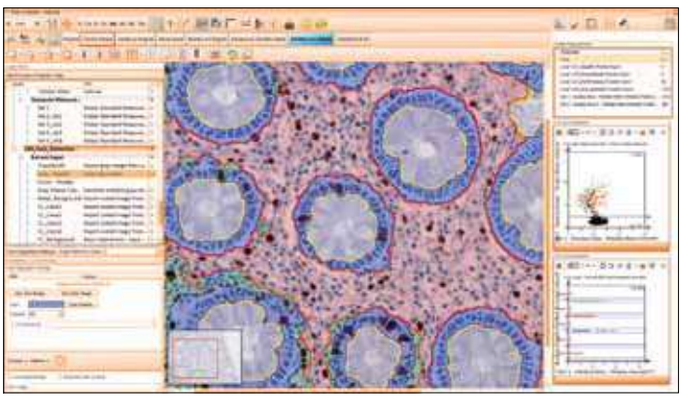
An essential feature

According to Thomas J. Diefenbach, the Co-director of the Ragon Institute Imaging Core of MGH, MIT and Harvard, incorporating genetic information into patient care is already an important aspect of clinical research and treatment in the Boston area. The Partners HealthCare Personalised Medicine centre, which has been available since 2001, offers assistance in terms of the use of genetic and genomic information, both in clinical practice and for medical training purposes. Financing for these types of programmes is already a part of American research clinics' operating budgets. "In 2016, the National Institute of Health (NIH) allocated millions of dollars towards the creation of four additional centres within the national network of Health Care Provider Organizations, which implement, the Precision Medicine Initiative (PMI) Cohort Program," says Diefenbach. Personalised medicine and precision medicine have already been integrated to a significant extent in Boston and surrounding areas.

Financing in Brazil

Similar public subsidy programmes are also available in South America. For example, Brazil's public foundation "CNPq" invites tenders for research programmes on specific diseases; these programmes include research on regenerative medicine and the early recognition and treatment of diseases, says Henning Ulrich, a professor of Biochemistry at the University of São Paulo. His working group conducts research on regenerative medicine and neurodegenerative diseases. "In this case, we need precise histological recording and analyses of brain slices," he notes, also stressing that he uses the system developed by the Austrian company TissueGnostics. "In my opinion, the TissueGnostics systems are becoming more and more important for both basic and applied research. Furthermore, these systems should be in every pathology lab."

> *I think that TissueGnostics systems are becoming more and more important for both basic and applied research and should be in every pathology lab.*
>
> **Henning Ulrich**
> *University of São Paulo*



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HIV focus in Africa

In Africa, personalised medicine is used to develop new therapies for HIV/Aids, among other conditions. People react to the HIV virus differently, and we could learn from those who can keep the virus in check thanks to their genes, says Zaza Ndhlovu from the University of KwaZulu-Natal in South Africa. The South African government provides funding for health research in South Africa through the Medical Research Council (MRC), the South African equivalent of the NIH in the USA. "The MRC funds several different health research programmes, including those which focus on innovations in healthcare, thanks to strategic partnerships and grants which are administered by the Grants Innovation and Product Development (GIPD) unit." Public funding for genomics centres in Cape Town and in Durban also have the potential to promote the development of personalised medicine in South Africa.

Dr Ndhlovu says that this fits with the approach in traditional African medicine, where illnesses are viewed *holistically*. "According to traditional medicine, an illness is not only a physical disorder; rather, it is assumed to be the result of an imbalance between the patient's physical, spiritual, moral and social conditions. This is why traditional patient management is very personalised because everything depends on the patient's individual circumstances."

Makoto Yawata, a professor at the Yong Loo Lin School of Medicine at the National University of Singapore, also feels that cooperation between industry and public institutions is important: "I think it makes sense because every diagnostic

> *Precision medicine is also a hot topic in China and, like in Europe, it is considered to be very important.*
>
> **GuoGuang Ying**
> *Tianjin Medical University*

and therapeutic product essentially requires a commercialisation stage." As is the case in the United Stated and Japan, Singapore also needs platforms to collect detailed genetic, phenotypic and health-related information from patients so that it can optimise diagnostic and treatment options. "We will need to develop algorithms so that we can analyse massive data sets from every patient to make effective clinical decisions. Singapore, like the USA, is made up of many different ethnicities and hence has a great deal of human diversity. In terms of truly personalised medicine, it is a challenge for doctors here." Systems like the one developed by the Austrian company TissueGnostics could be useful in these cases.

TissueGnostics' system is also used by Professor Guoguang Ying at the Tianjin Key Laboratory of Cancer Prevention and Therapy: "TissueGnostics has developed the most effective system to date for tissue imaging and data analysis. It provides researchers and molecular therapists with useful tools for obtaining valuable molecular profile information. This information is important for diagnosing diseases and mechanisms." Molecular profiling is at the heart of precision medicine. In particular, it is embodied in genomic, proteomic and localisation information which is verified and collected through various techniques such as sequencing, chipping and immunohistochemical staining.

© TissueGnostics

Made in Austria
TissueGnostics systems are in demand at leading universities around the world, as the **media**net interviews in the Americas, Asia and Africa have shown.

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South Africa

Zaza Ndhlovu
University of KwaZulu-Natal

"The South African government recently began building the African Genomics Centre in Cape Town, which is dedicated to developing personalised medicine within the country. The centre will focus on research dedicated to quicker diagnoses and targeted therapy for conditions such as hypertension, cerebrovascular accidents, cardiovascular disease, diabetes and cancer. My research, which could lead to personalised medicine, consists of genetic and immunological studies on people who can keep the HIV virus in check for several years without medication; these people have several unique immune genes. Over the years we and other researchers were able to identify the molecular characteristics of these special killer cells. We found these cells in many other patients, but at much lower frequencies. Precision medicine is a very expensive undertaking and requires highly specialised equipment. Our biggest challenge when conducting innovative projects is limited funding opportunities. A company like TissueGnostics can help us here because their products make research cheaper."

Brazil

Henning Ulrich
University of São Paulo

"The University of São Paulo is the best university in the country and one of the top universities worldwide. The concept of personalised medicine is very important for us in medicine. The Hospital das Clínicas, which is part of the university, is the largest clinic in South America with approximately 11,000 beds. My working group's research at USP's Institute of Chemistry focuses on stem cells, neurodegeneration and regenerative medicine. Although we conduct basic research, our focus is on medical research. We use cell cultures and mice models to investigate the effectiveness of pharmacologically active substances on Parkinson's, Alzheimer's and other neurodegenerative diseases. Grants from the São Paulo Research Foundation are available for all forms of basic and applied research. Projects related to personalised medicine can be submitted under the categories of biological sciences and health sciences at any time."

Singapore

Makoto Yawata
Yong Loo Lin School of Medicine

"Precision medicine or, rather, personalised medicine is part of industrial and academic biomedical research in Singapore, and I feel the standards are on the same level as those in the USA and Japan. These two terms are often used as synonyms; however, I think the time has come for us to emphasise the differences between them. The way I see it, "precision medicine" refers to a biomarker or a symptom of the disease that can be used in a targeted manner for diagnosis and treatment. Sometimes a biomarker can be the goal for every patient, whereas quite a few other cases are associated with a greater risk. An example of "personalised medicine" is the two-in-one identification and use of biomarker variants when selecting and treating patients. The TissueGnostics system allows us to collect expression information as a continuous variable. This results in more precise analyses of the cancerous tissue sample's biology. What is more important is that this system makes it possible to evaluate how heterogeneous the levels of marker expression are. Basic research funding for development is provided by the Singaporean government, mostly through the Ministry of Education, the Ministry of Health, the Ministry of Trade and Industry and the Prime Minister's Office."

China

GuoGuang Ying
Tianjin Key Laboratory of Cancer Prevention and Therapy

"Personalised medicine is not really a new concept for patient care. Chinese medicine is based precisely on an individual philosophy and uses prescriptions tailored to each individual patient. In China, we have a specialised approach to medical treatment that combines traditional and modern medicines to diagnose and treat diseases. I feel that precision medicine is a concept which defines how we will treat diseases in future, and it has to be defined differently, as it has to be concentrated on the molecular level and be based on molecular mechanisms which are brought about primarily through basic research in biomedicine. That is why, from a technical perspective, precision medicine cannot be used without the most modern diagnostic techniques. We need them to obtain 3D or even multidimensional depictions of every patient's state of health, and also so that we can administer appropriate, personalised treatment."

USA

Thomas J. Diefenbach
Ragon Institute of MGH, MIT and Harvard, Boston

"Boston probably has the highest concentration of biomedical research centres and hospitals in the world. The number of clinical studies is breath-taking. The Ragon Institute of MGH, MIT and Harvard's mission is to bring the most brilliant minds together, with a focus on the development of an AIDS vaccine. The immune response differs greatly from patient to patient. Our research group is collecting blood samples from patients all over the world in order to understand why some people are naturally able to suppress the HIV virus with their viral load under a certain detectable level. As only one in 300 people infected with HIV has this ability, it is essential for us to understand rare cellular phenotypes. The TissueGnostics system is an indispensable tool for our clinical research when it comes to answering key questions related to the progression of AIDS and how to find rare cells in tissue. A large part of this research concerns biopsy analysis. The ability to quickly quantify cell populations using several immunological markers in lymphatic tissue or tissue from the site of infection helps us better understand the relationships between these cells in an immunological context."

USA

Beatrice Knudsen
Cedars-Sinai Medical Center, Los Angeles

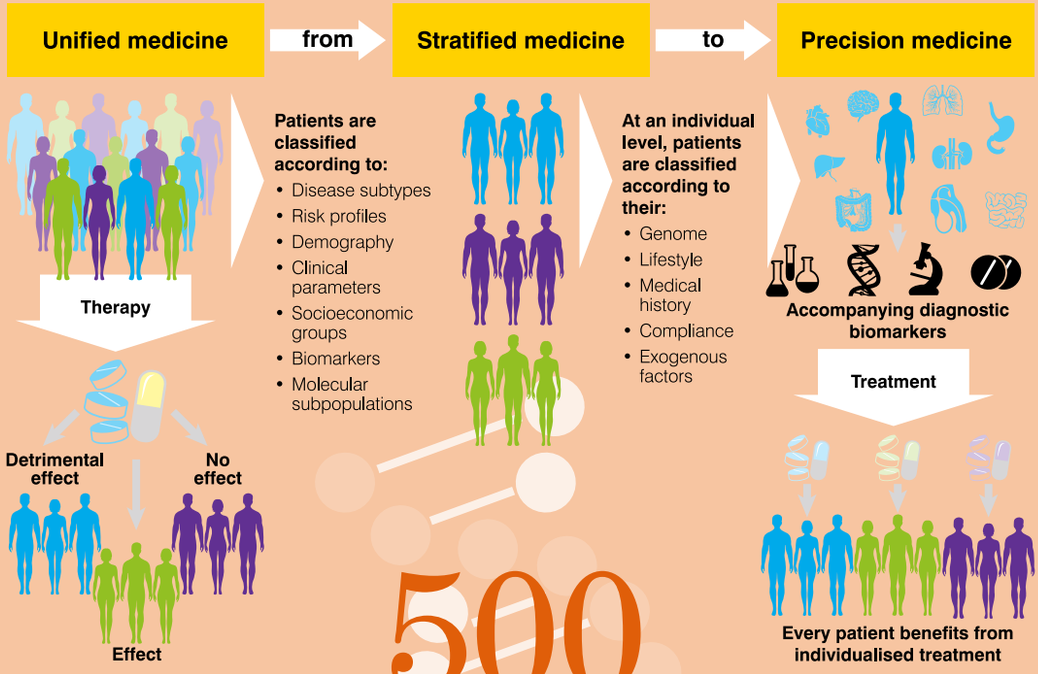
"Personalised medicine is our main goal here at Cedars-Sinai. To achieve this goal, there are several clinical studies which test how effective the medications that can successfully treat certain types of cancer actually are. Like in many other universities, our research focus is on activating the body's immune system against cancer. My group looks directly at marking various immune cells in tissue, observing them and measuring them. We use the analysis software every day and for every project. The tissue is scanned, and the digital images are then ready to analyse. We only use TissueGnostics analysis software. Sometimes we also have to do a bit of programming ourselves, but we are currently attempting to develop an app together which does not require any knowledge of programming. The analysis software has several options which are very helpful for us. For example, we are currently looking at macrophages in tissue. The software has an option that allows us to identify macrophages, which is something that similar systems do not have. Learning to use it is simple, and you can learn how to use it quickly. In addition to its software, TissueGnostics also has fantastic customer service."

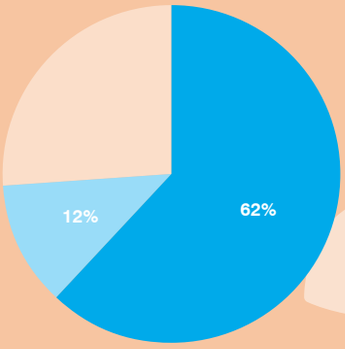
The steps of precision medicine

Not everyone responds to drug therapies in the same way. The next step in future is to develop the right products for various groups of patients.

New assistance

In many fields, such as cancer treatment, conventional therapies can only go so far. Experts believe that personalised medicine – or to be more exact, precision medicine – could harbour new breakthroughs. However, this requires exact analyses of patients' tissue and biomarkers in order to find the right therapies for them.





- they are already active
- they are planning it/ intend to do so

62%

At the moment, 62% of the relevant companies involved in biomarker research and translational research are active; an additional 12% are in the planning stage or intend to become active.

56%

… of the organisations which do not have an official "personalised medicine initiative" feel that this sort of initiative would provide them with a competitive advantage.

500

Single nucleotide polymorphisms

SNPs are positions in the genome in which a population's DNA differs from that of other humans by a single base pair. These positions can be found in approximately every 500th to 1000th base pair, distributed across the genome.

Areas of application for precision medicine

The number of deaths around the world in 2016, with the specific cause of death that differs according to risk factors such as air pollution, nutrition and other lifestyle factors

Cause of Death	Number of Deaths
Cardiovascular disease	17.65 million
Cancer	8.93 million
Respiratory disease	3.54 million
Diabetes	3.19 million
Dementia	2.38 million
Liver disease	1.26 million
Tuberculosis	1.21 million
HIV/AIDS	1.03 million
Malaria	0.72 million

Source: Institute for Health Metrics and Evaluation

Sources: Frost & Sullivan, Genomeweb