

The Human Factor



As the physician Hippocrates taught us, "It is more important to know what person the disease has than what disease the person has." Today, 2,400 years later, science is revisiting this tenet: our understanding of the genetic differences between individuals will soon provide a basis for personalized medicine. After all, around 30 to 80 percent of patients today derive no benefit from the medications they are receiving for a range of common conditions – some drugs and certain doses are actually hazardous for individual patients. There is no question that a paradigm shift toward specific, evidence-based and personalized medicine would be a great step forward.

Doctors are already able to choose specific drugs based on the patient's gene variants. The discovery that certain gene variants affect the way in which an individual responds to the components of a drug is itself an important addition to our knowledge. This has given rise to a new area of research: pharmacogenetics or pharmacogenomics, which aims to harmonize drugs and dosages with the patient's genetic profile. There are known genetic variants that affect the way patients respond to cholesterol-reducing drugs, anticoagulants, AIDS treatments, antidepressants and other common prescription drugs.

New diagnostic procedures also allow us to step up the fight against cancer. The basis lies in molecular genetic studies of the tumors themselves. A prime example of this form of personalized medicine is Herceptin – a therapeutic antibody used by doctors to treat a certain form of breast cancer. One of the defining features of these tumors is that large quantities of the protein HER2 are produced on the surface

of the tumor cells, stimulating cell growth. Herceptin can interrupt the protein function and thus also the growth of the tumor.

New diagnostic
procedures allow us
to step up the fight
against cancer

At the same time, it also activates the body's own immune cells in order to kill off the cancer cells.

The active ingredient is the product of research by Axel Ullrich, Director at the Max Planck Institute of Biochemistry in Martinsried. In the meantime, other approaches to the treatment of cancer are adopting his model, which combines molecular diagnostics and therapy.

The hope that decoding the human genome would lead directly to rapid progress in the field of medicine has, as yet, barely been fulfilled. The number of monogenetic diseases – those that derive from a defect in a single gene – is comparatively small, and the diseases themselves quite rare. Most widespread diseases are associated with multiple genetic mutations.

In addition, genetic regulation and a number of environmental factors play an important role in the way diseases manifest themselves. However, it is known that specific genetic variants increase the risk of contracting some chronic illnesses, such as coronary heart disease, diabetes and Alzheimer's. Corresponding studies may provide a basis on which to develop preven-

tive treatments for patients with a disposition toward certain diseases.

Still, if we are to derive a sustainable prognosis from an individual genome, there are other factors that science must be aware of. It is a matter of aligning the genomic data with the phenotype, that is, the various features of the organism concerned. Genomic and genetic testing procedures must be supplemented by technologies with the ability to create molecular fingerprints, such as transcriptome, proteome and metabolome analyses.

In practice, the new methods raise many questions – as in the case of individual genome sequencing, which, in less than two years, is likely to be available for only USD 1,000: Do companies adequately pro-

Politicians must initiate a public debate on the questions raised by personalized medicine

tect their clients' genetic data? Do they accept liability for false prognoses and misinterpretations? A legal framework for such tests is thus far lacking in Germany. There is also a lack of mandatory standards for the approval of predictive tests and, so far, no obligation to provide any details of the potential capabilities and limitations of the services offered.

Overall, the issue needs to be addressed by the legal system: there are questions of genetic privacy to resolve, such as a right to data protection and self-determination for

those who are genetically at risk. The ability of health and pension insurers, employers and other potentially interested parties to access such data must also be addressed.

Politicians must initiate a public debate on the questions raised by personalized medicine. Do we actually want to know about our genome and our molecular characteristics? Are we willing to disclose this information? Do we want a glimpse of our own medical future? Are we ready to adapt our lifestyle to our genome? Do we want to lead a biologically planned life? Are we even keen on the prospect of optimized human beings? All of these questions have to do with how we see ourselves. They touch on both legal and fundamental ethical aspects of our existence.

We must also ask how medicine itself should approach these new possibilities: these methods have found few specific applications in clinical practice to date. Their use on a broad scale will be determined by clinical success. If doctors are to correctly interpret diagnostic techniques based on molecular markers and initiate appropriate treatments, molecular genetics and systems biology must become part of medical training. In addition, in their conversations with patients, doctors must take a far more individualized approach and explain in detail their interpretation of molecular genetic diagnoses and the consequences.

In short, the human factor will play a greater role in personalized medicine – especially in matters of disease prevention, in which the personal responsibility of the individual plays a major role. Should there – dare there – be an “obligation to be healthy”? The social sciences could be helpful in this context.

It is also necessary to verify how effective the new methods are, and how they work in comparison with conventional treat-

Are we ready to adapt our lifestyle to our genome?

ments. Only then will doctors, patients and health insurers be in a position to decide how viable molecular medicine is in practice and whether it can lead to genuine improvements. Experts must ask themselves how much added value their approaches and methods of personalized medicine actually deliver for the patient and for society as a whole.

Medicine is experiencing a paradigm shift from healing the sick to predicting and preventing disease, but there is still a way to go. Hippocrates made another far-sighted recommendation: “Guide the healthy with care to preserve them from disease.”



Peter Gruss,
President of the Max Planck Society