

Advancement to the molecular level

"If it were not for the great variability among individuals, Medicine might be a Science, not an Art." This statement by the Canadian physician Sir William Osler (1849 – 1919) written in 1892 in his book *"The Principles and Practice of Medicine"* is as topical now as it was over a hundred years ago. For it remains true that medicines sometimes work as intended but sometimes do not, that one patient will tolerate a medical therapy but another will not, and that medicines may sometimes have serious side effects. These differences are due at least in part to our genes, the genetic material that makes each of us unique and that consequently makes each of us react differently to chemical compounds.

Modern biology can help us to understand the medical consequences of these differences, and in fact have already lead to the identification of many genetic factors that influence the action of medicines – whether this be by affecting the way in which the body deals with a product or by influencing the course of the disease concerned. A new scientific discipline – pharmacogenomics – deals specifically with the relationships between our genome and the effects of medicines.

At the same time, increasing attention is now being paid to the principal targets of pharmaceutical therapy, namely proteins. Here again, a new branch of science has appeared, namely proteomics, the study of the totality of, and the complex interrelationships between the proteins of an organism. Thus, as well as learning more about the genetic information that provides the blueprint for the production of proteins, science is building up an ever more detailed picture of bodily function and malfunction at the molecular level.

Acquisition of an understanding of the interplay between hereditary and nonhereditary factors in patients is an essential step on the way to better targeted, more personalised therapy. Applications of molecular biology are in fact now leading to the development of a new approach to diagnosis and therapy known as molecular medicine. Grouped around this term are a multiplicity of modern research techniques and disciplines. These include, in equal measure: pharmacogenomics, the search for new medicine targets, proteome research, the search for small but important genetic differences known as single nucleotide polymorphisms or SNPs, and new techniques such as polymerase chain reaction or PCR and DNA chips.

The change of paradigm

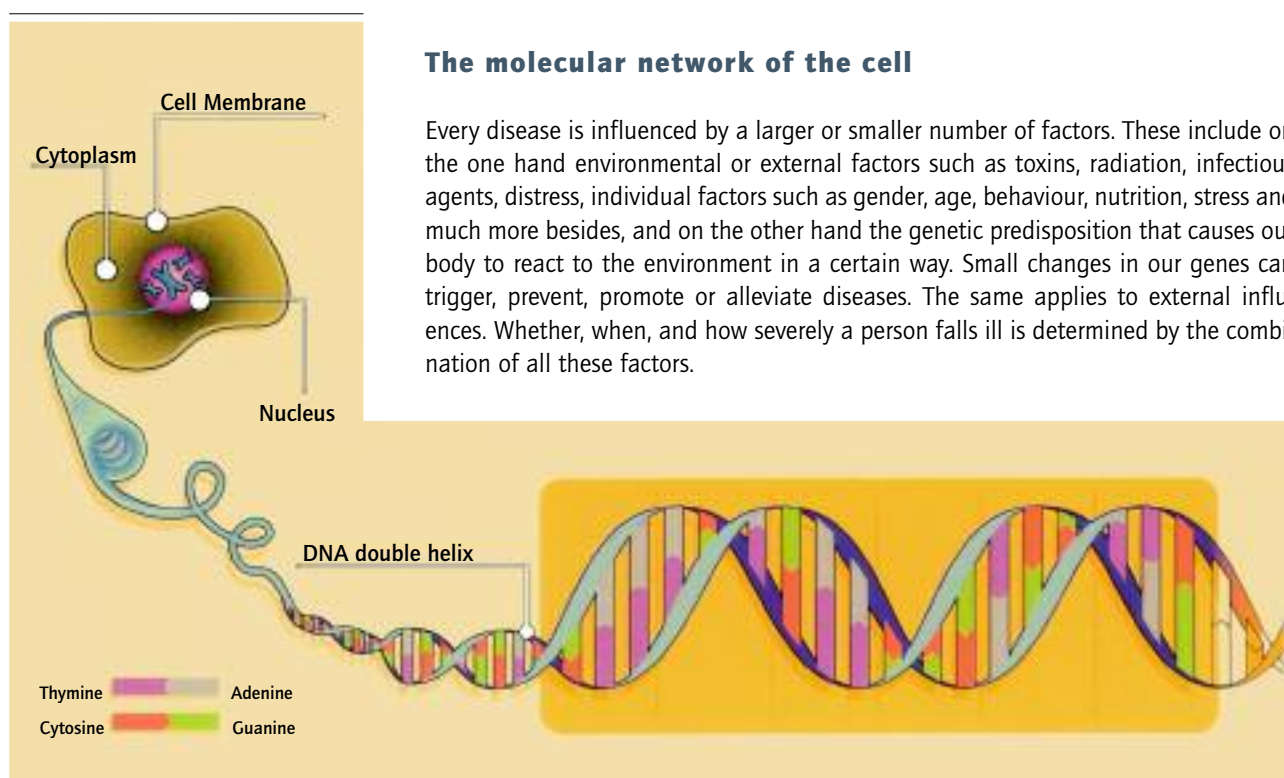
Today it is not possible to say exactly when the gradual revolution towards modern medicine started. Perhaps it was in the 18th century, at a time when cupping was still considered to be an effective remedy for headache, cancer and cholera. Even in those days every medical treatment was preceded by an examination. The diagnosis was generally made on the basis of a handful of symptoms and signs – the art of diagnosis had no more than that to offer. In the middle of the 18th century scientists such as the Italian anatomist Giovanni Battista Morgagni (1682 – 1771) for the first time set themselves the task of identifying the seat of a disease within the body of their patients. Whereas Morgagni continued to look into the "solid components" and more specifically the organs of the body, the French physician Marie-François Xavier Bichat



(1771 – 1802) began to distinguish between the different tissues in organs. Both recognised that disturbances of function can be correctly treated only if they are correctly understood – and that an immeasurable and indefinable “*imbalance of humors*” (body liquids) was not adequate for that purpose.

This relentless search for causes is the driving force of the gradual revolution in medicine that has been taking place since Morgagni’s time: a shift away from symptom-based therapy towards causally based therapy. To this end doctors and researchers have been delving ever deeper into the human body. One of the most important steps up to that time was taken in 1858 by the Berlin pathologist Rudolf Virchow (1821 – 1902) whose work on cellular pathology drew attention to the cells of which all organs of the body are composed. Later, in the 20th century, increasing attention was paid to life processes within cells.

All these efforts and discoveries are ultimately directed towards a single goal, that of more precise therapy. The objectives are to identify the causes of a disease, to consider the possibilities for intervention and then to provide effective treatment. These objectives are more relevant now than ever before, and on the way towards them research is at present taking the next major step, that of replacing cellular pathology with molecular medicine. Genetics, genomics and proteomics are opening up totally new perspectives in diagnosis and therapy.



The molecular network of the cell

Every disease is influenced by a larger or smaller number of factors. These include on the one hand environmental or external factors such as toxins, radiation, infectious agents, distress, individual factors such as gender, age, behaviour, nutrition, stress and much more besides, and on the other hand the genetic predisposition that causes our body to react to the environment in a certain way. Small changes in our genes can trigger, prevent, promote or alleviate diseases. The same applies to external influences. Whether, when, and how severely a person falls ill is determined by the combination of all these factors.

DNA double helix

Proteins play a central role in mediating these effects. They read and make working copies of the genes; they carry out the instructions, while at the same time regulating the action of the genes; they receive signals from the environment, pass these on and incorporate them into the molecular network of the cell. It is precisely in this interplay of environment, genes and proteins (as well as a variety of other equally important substances that differ from case to case) that medicines exert their effect. They act directly on the molecules that make up our body – and in this sense are themselves an important environmental influence. The more we know about the actions of molecules in our body, the more effectively modern medicine will be able to intervene when these actions become disordered.

- Every newly discovered molecule that plays a role in the development of a disease constitutes a potential target for medicines. For example, in the past few decades researchers have discovered more and more oncogenes, i.e. cancer-promoting gene variants. Many anticancer agents act by restoring the correct function of the products of these genes.
- Knowledge of the structure, i.e. the three-dimensional form, of a target molecule makes it possible to decide in advance whether a given substance has any potential for use as a medication. Computer-based rational design of pharmaceuticals can greatly reduce the number of substances selected for further development.
- If the genetic preconditions for a disease are known, a patient's individual risk can be determined and appropriate preventive action taken. Sickle-cell anaemia is an example of this. In this condition, an inherited modification of a certain component of the gene for haemoglobin, the red blood pigment, results in production of an altered protein that changes shape when the oxygen supply is inadequate. Under these conditions the red blood cells assume the form of a sickle, clump together and block the blood vessels. Carriers of this trait therefore need to avoid great heights and changes in air pressure, among other things.
- More and more diseases will be amenable to intervention at the gene level. For example, genes can be turned on or off by medicines, and one day it may even be possible to replace genes completely by means of gene therapy. It is precisely in this latter field, however, that further intensive research is required. In many cases – e.g. severe hereditary diseases due to mutation of a single gene or a small number of genes – gene therapy, along with the stem cell therapy, offers the only hope of genuine cure.
- Medicines do not always have the same effects. The effect of a given pharmaceutical can be too strong, too weak or absent altogether in patients with the same symptoms. Moreover, adverse effects are always likely to occur. Human genes are at least partly responsible for these too; the discipline of pharmacogenetics investigates these relationships and attempts to foresee, and ultimately forestall, such problems.

Terms

Pharmacogenetics describes the influence of genes on the efficacy and side effects of medicines.

Pharmacogenomics studies interactions between medicines and the genome.

Pharmacokinetics investigates the uptake, conversion and breakdown of medicines in the body overtime. Environmental factors, diet and genetic predisposition all play a role.

Pharmacodynamics deals with the influence of genes on the interactions between medicines and their molecular targets.

A multiplicity of possible causes

Genetics, genomics and proteomics thus provide modern medicine with a variety of new ways of intervening in the development and progression of diseases. Nevertheless, intervention has not become easier, for the deeper medicine looks into life processes, the more complex are the things it sees. The humoral pathology of Hippocrates (~460-~370 BCE) distinguished between the four humors: blood, phlegm, yellow bile and black bile; Morgagni extended the search for the seat of diseases to a couple of dozen organs; Bichat concerned himself with a few hundred bodily tissues; Virchow directed attention to the body's cells, of which there are about 100 million; and each of these cells contains an enormous number of nucleic acids, proteins, sugars, fats and other organic and inorganic substances. And in addition to all this is the far less measurable influence of external factors.

Nevertheless, the effort is worthwhile. For in the past, methods of combating complex diseases were based largely on trial and error, precisely because such disorders are not caused by a simple agent or gene mutation, but rather arise as a result of a combination of external and internal, predisposing and protective, and variable or unchangeable influences. This is true of most of the major diseases that afflict people in industrialised countries, e.g. cancer, Alzheimer's disease, diabetes and cardio-

vascular disease. Every ray of light that genetic, genomics and proteomics cast on these factors that contribute to these diseases helps in the fight against them.

The central importance of genes

This is because disease-inducing environmental influences can generally be modified – whereas our genetic makeup generally cannot. Among the risk factors that contribute to the development of disease, our genetic predisposition is a constant. And this makes it all the more important for researchers to learn more about, and where possible to limit, its influence. In the 1980s scientists succeeded in identifying the genetic basis of a number of severe hereditary diseases brought about by a single defective gene. These include Huntington's chorea, cystic fibrosis (also known as mucoviscidosis) and haemophilia. More refined methods now allow scientists to investigate the genetic causes of more complex conditions in which various genes can exert positive or negative influences:



- **Monogenic diseases** such as Huntington's chorea, cystic fibrosis and haemophilia follow the classical (mendelian) laws of inheritance. The pattern of occurrence and non-occurrence of such diseases within affected families is determined by whether only one or both copies of the gene in question need to be altered for the disease to occur. In such cases the responsible genes are relatively easy to identify via studies comparing the genetic material of the parents and of other affected and unaffected members of a family.
- By contrast, the pattern of inheritance of **polygenic diseases**, which include type 2 diabetes and most types of cancer, is not so simple, since many genes

are involved. Most such diseases tend to occur with increased frequency in certain families, but not in such a way that the precise distribution of affected and unaffected individuals can be predicted. This requires larger studies to identify the various genes that influence the disease to a greater or lesser extent. This task is rendered even more difficult by the fact that in this case genes that predispose to the disease can overlap with genes that protect against it.

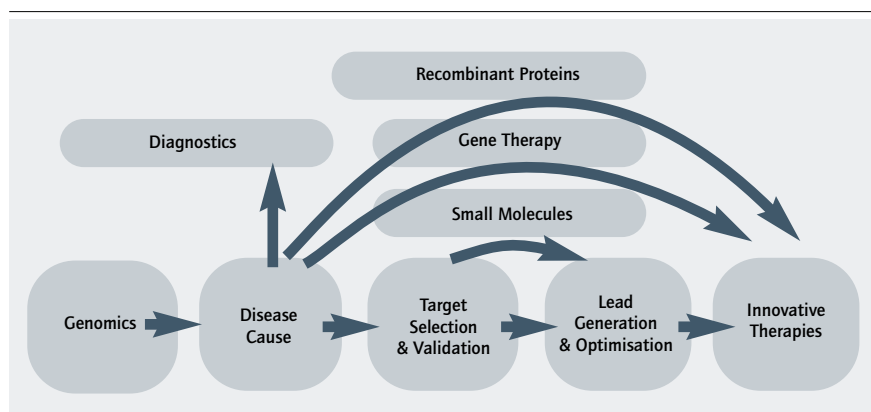
- Hopes have therefore been placed in the study of **single nucleotide polymorphisms** or SNPs for short, i.e. changes in single subunits of the genome. These variations, which are spread more or less randomly throughout the genome, are thought to determine our individual genetic differences to a large degree. The presence of such single nucleotide substitutions in important sections of a gene can have profound effects on the function of the corresponding gene product. An enzyme, for example, may be impaired, destroyed or improved – with corresponding implications for medicines which interact with that enzyme.

The finding of an increased frequency of certain SNPs in association with a disease indicates that genes concerned play an important role in the disease in question. Once such SNPs have been found, the associated genes have to be identified. Until a few years ago this meant tedious searching and sequencing. Today, however, this procedure can be bypassed. Thanks to the Human Genome Project, which sequenced the entire human genome, the relevant data are already available. The search for the identity and function of a gene is also straightforward, since researchers can conduct a computer search for available data or comparable genes. Even the associated gene products (usually proteins) and their functions can be pinpointed quickly in globally linked databases.

- It is not always easy to separate environmental influences from genetic influences, especially since the environment can influence the behaviour of our genes. Twin studies and adoption studies are helpful here. Monozygotic twins (identical, as they stem from one egg) brought up in different families have an identical genome but are subject to different environmental influences, while dizygotic twins (fraternal, as they grow from two eggs) brought up in the same family are subject to essentially identical environmental influences and have a similar, but not identical, genome. Finally, adopted children share essentially the same environment with, but are genetically different from, their stepbrothers and stepsisters.
- The genetic makeup also exerts a decisive influence on our predisposition to disease. Where genes that play a role in the development of a disease are known, an individual's risk of developing that disease can to some extent be determined by appropriate genetic tests. Knowledge of predisposition to a certain disease allows the individual to take appropriate precautions and to modify lifestyle accordingly – and if necessary to take preventive medicines. Early prevention is therefore one of the potential applications of molecular medicine. Given, however, that most pathologies result from the combined action of a large number of genetic and environmental factors and that predisposing and protective genes can overlap, such test can only ever indicate a greater or lesser probability that an individual will develop a disease.

Proteomics: seeing through the undergrowth

Every cell in the human body contains at least 100,000 different proteins, whereas the human genome contains only 30,000 to 40,000 genes. Moreover, the genome is the same in all cells, while every cell type contains a different set of proteins. These molecules form a vast and highly complex network: they construct and break down molecules; they transport, store and mobilise substances; they allow cells to communicate with each other; they give and receive orders; and they keep cells alive and can program cells to die. The structure of a protein determines its function. Thus, muscle proteins are fibrous, membrane channels are tubular and enzymes are mostly rounded with one or more depressions into which their substrate fits. It is precisely in this network that medicines act, and only now is science beginning to understand how, where, when and why they act. Proteomics is going to help to see through this molecular undergrowth.



Genomics – a key driver to enhance innovation and productivity

Proteins bring about the vital processes that take place in an organism and are therefore the most important target for strategies – e.g. those based on the use of medicines – aimed at interfering with these processes. However, whereas a cell can only ever have one genome, a cell's proteome, that is to say the totality of its proteins, is highly variable. In theory, each cell's proteome is different at every point in time and

at every different site within the cell, since unlike its genetic material, a cell's proteins are being constantly produced, broken down, altered, moved around, bound and separated. Proteins play a central role in almost all the processes involved in the life of an organism or – viewed on a smaller scale – a cell:

- Structural proteins are responsible for the form and shape of cells. They form the structural framework of the cell and a large part of the outer envelope of the cell. Bodily structures such as tendons and hairs are made of protein. Structural proteins account for most of the protein in our body.
- Metabolic proteins, or enzymes, are responsible for the constant synthesis, rearrangement and breakdown of all the substances that are required by, or formed within, the body; they also provide the energy required for these processes. Even minor disturbances of the complex interplay between these proteins can result in serious diseases.
- Signalling proteins are responsible for communication within the body. These include hormones and intracellular messenger substances. Many medicines act by interfering with signalling pathways within the body.
- Regulatory proteins control the processes that take place within an organism, including correct transcription of DNA, the genetic material.

In addition, proteins perform a variety of other tasks, e.g. as antibodies in the immune system, oxygen transporters in the red blood cells and motors in muscle. Today the complex interplay between all the proteins of the human body is as fascinating as it is impenetrable.



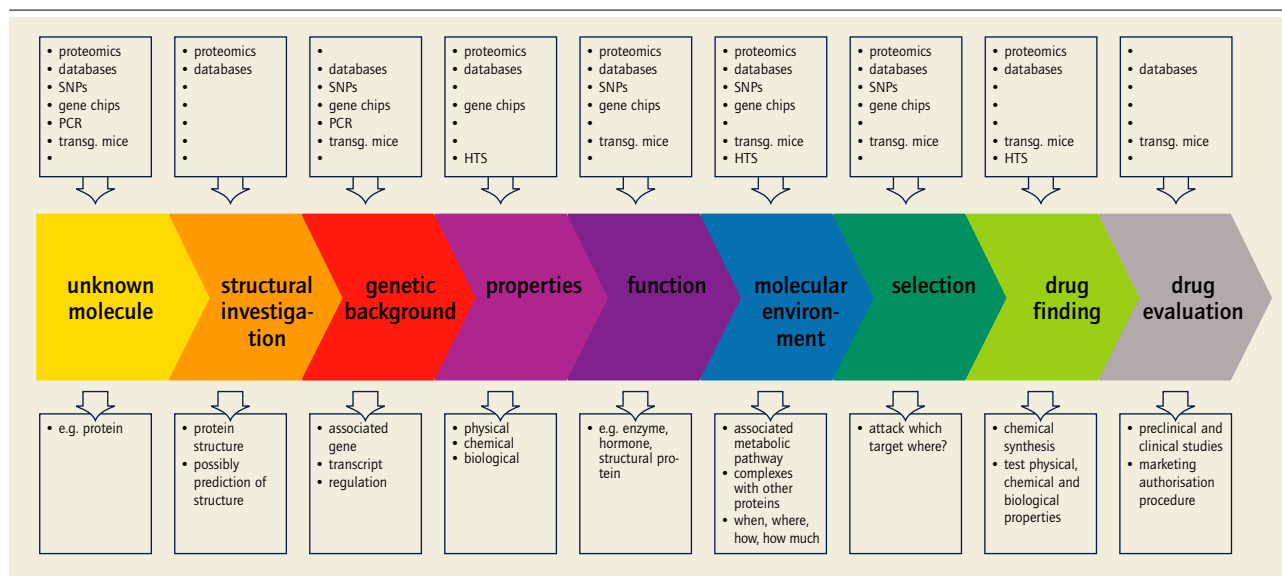
Targets for medicine

Because of the multiplicity of their functions and properties, proteins are by far the most important targets for medicines in the body. They play a role in the development and progression of almost all diseases. Since their correct function is directly related to their form, one of the fundamental requirements of a medicine is that it be able to distinguish between the correct and incorrect forms of a target molecule. Disease can also be caused by an excess or deficiency of a protein, or by its occurrence at the wrong time or in the wrong place. Since proteins, even when in the body, participate in a variety of chemical reactions and interactions, it is relatively easy to influence their actions by means of pharmaceuticals. Far more difficult a task is to specifically influence only a certain action of a certain protein. Almost all currently used medicines influence the molecular network of the human body at the level of proteins.

Other substances that occur in the body are also potential targets for medicine action:

- Sugars are found, among other places, on cell surfaces, where they serve as markers and permit mutual recognition. They can assume many different forms and are being intensively investigated at present.
- Fats not only form a large part of cell membranes, but also serve as hormones, antioxidants and much more besides. They are relatively small molecules that can assume very different forms.
- All metabolites, that is to say the starting substances, intermediate products and end-products of our metabolism, are theoretically susceptible to be influenced by pharmaceuticals.

With the exception of sugars, such molecules offer medicine only very non-specific targets for pharmaceutical action. Moreover, most of them are formed and broken down very rapidly in the human body and play only a minor role in metabolism as compared with proteins, in particular. Under some circumstances, however, it can be useful to bind a specific intermediate product of an undesirable metabolic pathway and thereby block production of the end-product of that pathway. Even the rapid turnover of such targets can be advantageous if, for example, the action of a medicine needs to be very rapid in onset and brief.



Modern target finding and evaluation is supported by a wide variety of methods. The techniques employed vary greatly in technical complexity and cost and often yield useful findings only when their results are considered together. Most techniques are used – in more or less modified forms – at various levels.

Prospects: more knowledge for medical science

Medical science is in the grip of change. Genomics, proteomics and other branches of molecular biology are generating a stream of new findings, and modern technology has introduced techniques of miniaturisation, automation and parallelism into research and development. And medical science is increasingly realising that apparently identical clinical pictures can have entirely different underlying causes requiring personalised treatment.

At the same time, the development of new medicines up to the stage of regulatory approval is becoming lengthier and more expensive. Traditional medicine research is growing riskier in economic terms, and it is becoming more difficult for it to contribute to genuinely significant innovations. On top of this, despite minor successes, the options available for treating many of the major common diseases remain unsatisfactory. A period of radical change is imminent.

Behind this upheaval is the recognition that no two illnesses are the same. It is now clear that with the exception of a handful of hereditary diseases and some severe infections, very few human diseases have a simple or even a single cause. And even in the exceptions just mentioned, which include, for example, cystic fibrosis and haemophilia as well as tuberculosis and AIDS, the severity of the symptoms varies so much from one patient to the next that a clinical picture of some complexity has to be assumed. After decades of genetic research and several years of genomic investigation, researchers know that a patient's genetic predisposition plays a significant role in the progression of almost all illnesses. In the case of infections, another factor can be the variable genetic makeup of the pathogens involved.

These findings are neither new nor surprising. And yet they confront medical science with a daunting problem. Until now the principle of “one disease – one treatment” has essentially held sway unchallenged. Though fine diagnostic distinctions have always been a driving force of medical progress, the sheer amount of newly acquired knowledge is now enormous. This calls for a rethink in many cases. The indications for existing medicines will become narrower, and the discovery of new compounds will be all the more crucial. And distinguishing between subtle variants of a disease instead of general clinical pictures will require a new molecular diagnostic approach.

No two treatments are the same

The recognition that diseases can have entirely different causes despite producing the same symptoms is not new. What is new is the molecular biological understanding that now makes it possible to examine the genetic differences between individual patients and the effects of these differences on treatment. In other words, no two



treatments are the same. A medicine might be right for one patient but wrong for another, even though both patients have the same illness, because medicines can vary in their efficacy and tolerability in different individuals. The field of pharmacogenetics has been investigating the reasons underlying this phenomenon for over a hundred years now, but only recently have molecular genetic techniques made it possible to apply these insights to clinical medicine. Pharmacogenetics is now threatening to upset the second half of the dogma of “one disease – one treatment”. In future the choice of the right treatment will depend not just on the disease diagnosed, but also on the way in which each patient's body deals with the medicines in question. To make this kind of choice possible, two closely related factors need to be taken into account:

- **Genetic factors:** pharmacogenetics is concerned with the relationship between the gene variations and the body's response to medicines. Genetic differences can cause medicines to be absorbed, metabolised or excreted too rapidly or too slowly. Or they can prevent sufficient active compound from reaching the target site. Or they can give rise to adverse or even dangerous side effects. Ruling out such genetically caused uncertainties relating to the efficacy and safety of medicines will be one of the major challenges facing pharmaceutical researchers in the coming decades.

SNPs assume particular importance whenever they are associated with the effectiveness or tolerability of medicines. For example, the cytochrome P450 proteins are of great importance in the elimination of medicines from the body. Many of the P450 proteins occur in a number of variants (based on SNPs) and some of these variants have clearly altered functions. At least two dozen different SNPs are known to exist within the *cyp2c19* gene (a member of the P450 family) some of which have considerable influence on the function encoded by the gene. Thus, some individuals break down a medicine which is used to treat stomach ulcers four times faster than others, with the result that standard doses of this normally very potent medicine bring scarcely any benefit in these patients.

Another example of pharmacogenetically important SNPs is the gene for the beta2-adrenergic receptor. Activation of this receptor in the lungs relaxes the smooth mus-

cles of the airways. Some anti-asthma medicines therefore aim to activate this receptor. The presence of a certain SNP in the gene for this receptor can greatly reduce the effectiveness of some anti-asthma medicines.

- **Environmental factors:** external factors are at least as important as genetic factors in determining the efficacy and safety of medicines. Prominent among these factors is diet. Elements of the diet can interact with pharmaceuticals, accelerating or preventing their uptake and affecting their excretion and utilisation. The same applies to interactions between different medications, which can enhance or reduce each other's effects and exacerbate each other's side effects. External stress factors such as physical and mental fitness, environmental toxins, radiation, temperature and so forth can also influence the efficacy and safety of medicines. In practice, the environmental influences to which a patient is exposed cannot be exhaustively determined; also, they vary over time – though this means that they can be influenced. This is not true of gene variants. It is therefore all the more imperative to recognise how environmental factors influence the way the body interacts with medicines.

The personalisation of medicine

If future therapies are to be based on genetic factors, medicine will inevitably become more personalised. However, the term "personal" in this context does not mean that at some time in the future patients will have their own tailor-made therapy. Rather, it means that a far broader range of therapeutic options will be offered from which doctors can select the one most suited to their individual patients. Of course, such choices are already available, at least for some diseases, however the number of such choices will increase and so too – hopefully – will the success of therapy. As an inevitable consequence of this development, the target groups for medicines will become smaller. The indications for new chemical entities or biologicals will be determined not only by the molecular causes of the disease being treated, but also by the pharmacogenetics profile of the individual patients. This is unexplored territory in pharmacology.

In future, therefore, patients will be able to expect that a medicine that is prescribed for them is more likely to be truly suited to them than at present. The effects of almost all currently used medicines can vary to a greater or lesser extent, and in extreme cases there is total lack of efficacy. The safety of many currently used medicines is similarly unsatisfactory. The incidence of severe side effects needs to be reduced, since even the occasional occurrence of such side effects can be acceptable only if the disease concerned is relatively rare and unresearched and therapeutic options and experience are correspondingly limited.

Doctors' responsibilities will grow accordingly. They will have to deal with entirely new diagnostic resources, a considerable expanded range of therapies and – as is already evident from the growth of the Internet – far better informed and more self-confident patients.

Consequence: integrated healthcare

This means that the demands made on medical science will increase. One innovation gives rise to another. Personalised therapies require individual diagnoses. Molecular diagnoses call for differentiated therapy. And both aspects, diagnosis and therapy, depend on rapidly expanding technological possibilities. In fact, a synthesis is taking place at the moment: research and development, diagnosis and therapy, information and prevention are evolving together. The key to successful healthcare lies in integrated medicine.

If the new possibilities of medical science really are to bring about progress, they must mesh smoothly. The concept of diagnosis will need to be extended beyond symptoms and clinical findings to include the molecular underpinnings of diseases and their treatment. Also to be considered is the hitherto relatively undeveloped field of prevention, which in most cases is still limited to fresh air and a healthy diet. Testing, i.e. diagnosis, of genetic predisposition will play a far greater role here in future. It will also make it possible to provide patients with more specific counselling – such as already available, for example, in relation to high serum cholesterol levels.



Treatment follows seamlessly. The earlier a disorder is discovered, the easier it is to treat – a long-recognised fact that can take on new relevance in connection with the possibilities of early molecular diagnosis. This is especially true when specific diagnosis is matched by a corresponding range of personalised therapies. Progress will be achieved only if both sides move forward together.

Consequence: upheaval in the pharmaceutical industry

For the pharmaceutical industry, these developments impose the need for a continuous rethink. A new order will prevail in the healthcare market, where the changes are already in full swing. New strategies, alliances and competitions are emerging:

- **Integration of diagnosis and treatment:** The more finely differences between individuals are distinguished and considered, the more difficult it is to separate these two poles. Close cooperation is required here: medicines whose prescription depends upon pharmacogenomics considerations will be prescribable only if a corresponding means of testing is available. Thus, a specific genetic variation first has to be identified in the patient so that a medication geared to this variation can be sensibly used. And because the development of diagnostic tests and therapy are to some extent interdependent, expertise in both areas needs to be gathered together either within a single company or else by means of close alliances between companies. The traditional boundaries between diagnostics and therapy will therefore largely disappear.
- **Greater development risk:** The fact that the available options for treating most of the major common diseases are still unsatisfactory means one thing above all: pharmaceutical companies will have to take the risks associated with the development of new medicines with new mechanisms of action. Certainly, the future will continue to hold the occasional surprise, as when a well-established compound is found to possess previously unsuspected beneficial properties. But for the most part, medical progress will depend on the exploration of new avenues – particularly via new target molecules, which are already the most hotly contested objects in medical research. Above all, new diagnoses, new targets and new medicine groups mean considerably stepped-up research and development efforts with an undiminished risk of failure. Nevertheless, the effort may well be worthwhile.
- **Smaller target groups:** The advent of more personalised medical care inevitably means that a new medicine can only be sensibly used in a limited number of patients. This limits sales possibilities. However, the development of such medicines also has advantages, as they are more effective thanks to their targeted activity. This should reduce the risk of failure in later stages of development while increasing acceptance among patients and thereby reducing the number of patients who stop treatment. The actual investment-to-yield ratio can be very attractive.

- **Increased demands:** New opportunities bring new responsibilities. In the not-too-distant future, pharmacogenetics data will certainly form part of the data required by health and medicine regulatory authorities. In addition, after a period of adjustment, patients are likely to become more demanding in terms of the efficacy and safety of the medications they take.

Internationally active healthcare companies will not escape this trend. On the contrary, active participation in this process of change is fundamental to their survival, whereby the term “change” does not imply a revolution, but rather a systematic evolution towards more informative investigations and more effective and safer medicines. The fact that many years of laborious and detailed research work are required before personalised diagnostic tests and medicines can be developed is evidence enough of the evolutionary nature of this change.

Also in many cases a distinction will have to be made between what is feasible and what is reasonable, desirable and economically sound. For instance, the size of a patient group above which the development of medicines specifically for it becomes economically viable still cannot be predicted – at least, not until new forms of cooperation between society and industry, such as “orphan disease” programmes for particularly rare diseases, have been set up.

Nevertheless, progress is opening up far-reaching new opportunities for medicine at the scientific and technical level. Personalised diagnosis and treatment promise to be substantially more effective with substantially fewer side effects. At the same time they can tackle the causes of diseases whose treatment has until now been only symptomatic and often inadequate. Notwithstanding all the commercial and ethical imponderables, in a certain sense the new possibilities also impose a moral obligation to apply the new findings of molecular medicine for the practical benefit of patients.

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