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CHAPTER 2

# Introduction

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## 2

## Introduction



## A la Carte Health Care Arrives

**M**aking a commitment to the future does not only involve keeping our eyes open to the new accessible technological situation that seduces and invades us and is so markedly altering the way we communicate, work and interact socially. Our lives may now be facing another crucial revolution by which they will not simply be changed, but improved, tended to and even extended in unforeseeable ways. Following the announcement in 2000 of the conclusion of the first draft of the human genome, personalized medicine is now standing at the door, visiting card in hand, and we are beginning to see to what extent the scientific and pharmacological advances resulting from a knowledge and understanding of the genetic structure of a specific individual will affect us.

We will certainly be faced by new techniques in customised medicine, geared towards more precise diagnoses, more reliable estimate of the risk of suffering certain pathologies and treatments which more closely match individualised – or segmented – genetic profiles. We are coming close to a scenario of medical prescription based on genotype<sup>1</sup> or genetic characteristics rather than on phenotype or observed features, and a new context in which traditional medicine, which primarily uses an analysis of symptoms and the experience of physicians, will be relegated to a second place.

As a result, the gigantic pharmaceutical industry is now facing its greatest revolution, now that it seems clear that the costly and complex method currently used for developing drugs, based on pharmaceuticals that are effective and safe for a broad majority of the population, is likely to be supplanted by the latest advances of new sciences such as pharmacogenomics and pharmacoproteomics. These sciences will make it possible to target pharmaceuticals at the right person or, rather at the right segment of population, and this will to a large extent help eliminate secondary effects, optimise response to treatment and, probably have a direct influence on the costs resulting from ineffective treatment.

However, this new horizon also presents a new diffuse and multifaceted scenario, in which current models of drug research, production and distribution will be changed; in which the future of public health systems, strongly dependent on the price, effectiveness and secondary effects of treatment, hangs in the balance; in which society faces potential changes in quality of life and life expectancy and the possible emergence of new ethical and moral conflicts; in which the business models of many industries will be affected to some extent or another.

1. There a glossary at the end of this document giving a description of some technical terms that appear in the text.

### A definition for personalized medicine

Personalized medicine (in the sense in which the term is used in this text) is a generic description of all the advances in disease diagnoses and treatments resulting from a knowledge and understanding of the genetic structure of a specific individual. In the specific literature, this concept is sometimes called genomic medicine, insofar as its development is based on discoveries relating to the sequencing of the human genome.

In general, we are not talking about individual preventative and/or curative treatments for each patient, but rather more segmented treatments applied to groups of people with common genetic characteristics. One exception to this rule are treatments with stem cells, which, for the purposes of this report, we have decided to include among the technologies making up personalized medicine, given their possible impact in a very near future.

Nonetheless, we have deliberately decided to exclude any research related to genetics which is currently the subject of great legal and moral controversy, and which is still at an embryonic stage, far from any reasonable practical application on human subjects. This includes cloning and genetic manipulation of organisms.

Before going on, I would like to stress that this chapter, like other parts of the document, includes certain scientific terms and assumes a very basic understanding of certain notions in the field of genetics. If you have any doubts, we recommend that you first read the appendix at the end of the document which explains what the genome is and what the project of genome sequencing has involved in rather more detail. We have also included a brief glossary of terms which you can turn to while reading this document.

### But, is personalized medicine something new?

The idea of personalising medicine is nothing new; to date it has existed in traditional medicine in the form of, for example, tailor-made master formulas created by pharmacists, transplants, individualised treatments, etc. The main difference with this new concept is that the personalisation of the treatment is based on the patient's genome rather than on symptoms, trial-and-error methods, and other systems.

Consequently, the challenge consists in using the genotype instead of the phenotype when treating a patient; of going from an analysis of symptoms, in which the doctor's opinion and experience were of basic importance, to an analysis based on people's genetic information.

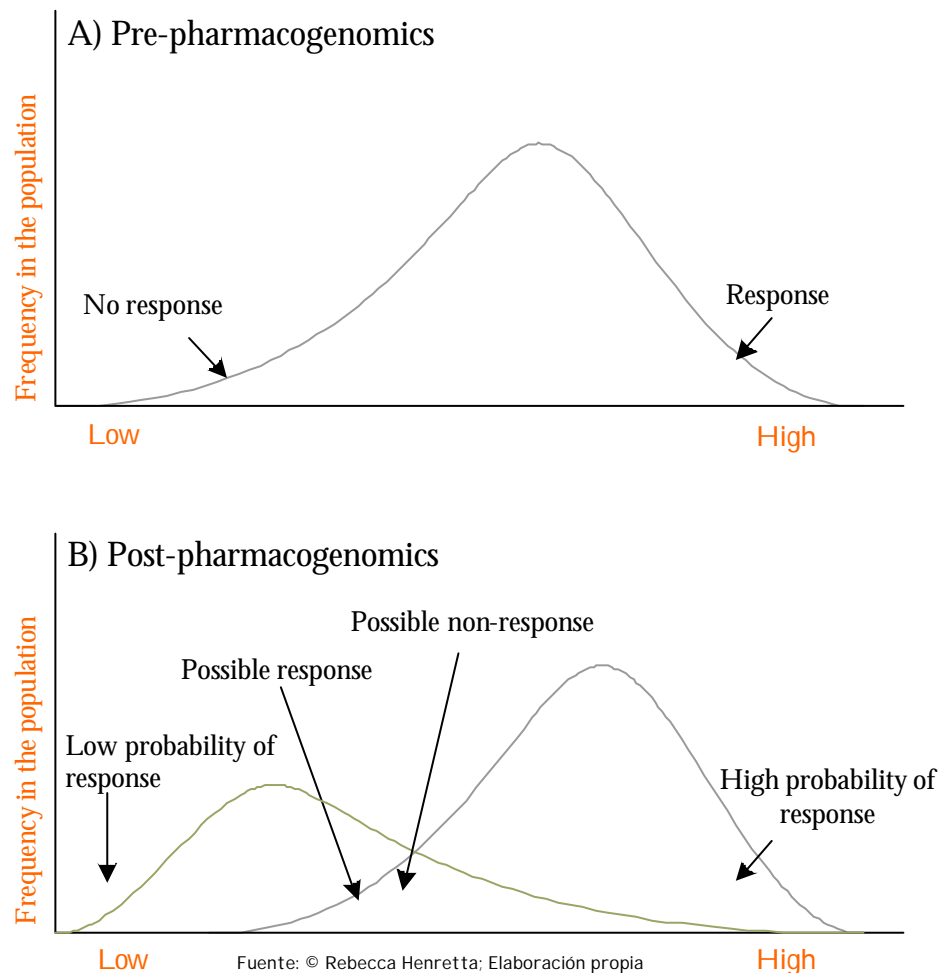
To date, most drugs have been developed using a "one drug for all" paradigm; in other words, they had to be safe and effective for a broad majority of the population. This has always led to a series of problems, mainly related to the high variability of response to treatment depending on each individual's genome:

- Reduced effectiveness of some drugs, resulting in effectiveness rates of less than 70% for such common conditions as epilepsy, high blood pressure and diabetes.
- High rate of secondary effects, with an estimated two million hospitalizations per year in the United States as a result.
- Difficulty of launching new drugs on the market as a result of the high variability of response among the general population.

In this context, as we have already said, the latest advances are leading to the emergence of new sciences that will decisively influence the process of developing and applying new drugs. We are referring to pharmacogenomics, which studies the way in which a person's genetic inheritance affects the organism's response to a pharmaceutical product, and pharmacoproteomics, which goes one step further and studies how pharmaceuticals influence the transformation of the genome into proteins. Understanding genetic functioning will therefore be the key to creating personalized drugs with greater levels of effectiveness and safety and will solve many of the problems associated with traditional medicine.



## Response to the drug before and after pharmacogenomics

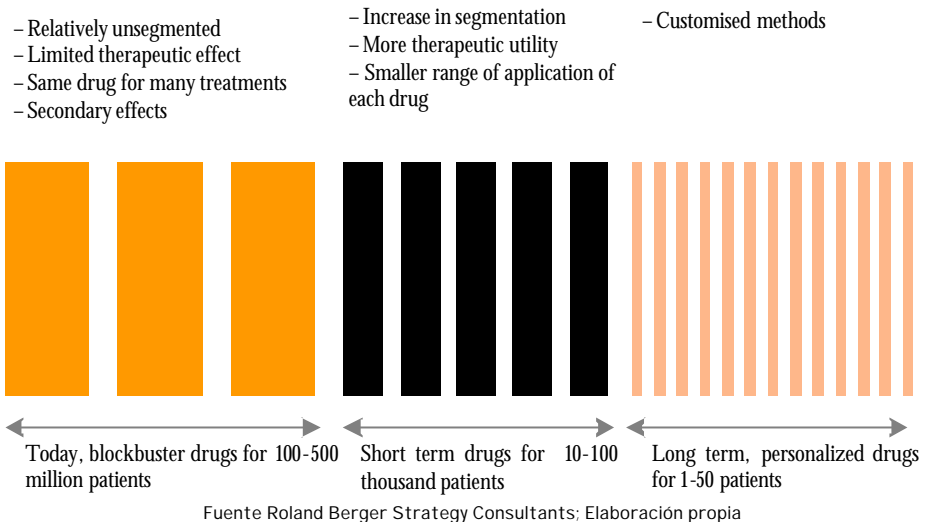


Specifically, as we can see from the illustration above, when faced with a medicine in our present pre-pharmacogenomics era (a), individuals are divided in two groups: those who do not respond to it and those who do, the latter being the majority. Pharmacogenomics (b) will enable us to break patients down into segments depending on their genetic profile. Thus, in the group of patients who respond to a drug, we will have individuals with a high probability of response to the drug and others with a low probability. Similarly, among patients who do not respond, there will be

some with greater a possibility of response and others with a more reduced probability of response.

Pharmacoproteomics will go even further and make it possible to establish segmentations based on the process of manufacturing proteins by the genome. As we can see in the figure below, this segmentation would lead to the appearance of numerous drugs targeted at ever smaller segments of the population, for whom it will improve the effectiveness and reduce the side effects as compared to drugs with a wider application.

### Progressive segmentation in the application of personalized drugs to the general population



In many cases, this segmentation would lead to the categorisation of new diseases, given that it will be possible to expand on the present symptom-based one once we have a greater knowledge of the way those diseases develop depending on variations in the genome of the patients. As a result, for example, we might move to a position of having three different types of diseases where we now only diagnose lung cancer.

All of these concepts also open new areas of work and applications in the field of preventative treatments, which could be designed according to the genetic code of the person and their propensity to suffer certain diseases.

In order to take advantages of the segmentation of treatments it will be vital to develop biomarkers, that is to say, any system based on genetic knowledge that makes it possible to obtain preliminary information on the most suitable treatment for a certain patient and disease.

## And why personalized medicine?

Obviously, in view of the Fundación de la Innovación Bankinter's commitment to detect and monitor emerging trends from a position of neutrality and independence, we could not ignore this situation and, thus the "Future Trends Forum" (FTF) project, seeks to offer, in this third meeting, its vision and conclusions of the economic and social impact of the imminent commencement of personalized medicine.

The FTF members freely propose, vote and, finally, decide on a theme which will then be debated in depth, with participation from leading specialists, at a meeting held every six months. At this fourth meeting it was decided to address the possible application of the sequencing of the human genome in the area of medicine and pharmacology, given that it is becoming increasingly clear that this is a scientific breakthrough with the potential for an even deeper and, above all, inevitable impact.

A series of factors has recently come together to create an ideal environment for personalized medicine to become a reality, rather than the stuff of science fiction. These aspects are:

- Molecular knowledge and understanding of the genome, as a result of the completion of the project of sequencing the human genome in 2000, which represented one of the greatest milestones in the history of science.
- Continued technological advances and greater data processing capacity, with a clear fall in the cost of processing the basic components of the genetic code (falling from 2 dollars to 1 cent in the last eight years), making it possible to consider the possibility of performing economically affordable tests to find the genome of specific individuals within a period of 1 to 2 years. As we shall see, the obtention of the genome with its more than three billion components has now become a problem of number crunching and it will continue to evolve apace with advances in computing.
- Greater knowledge of the way many diseases develop and their relationship with the genetic code for individuals.

### My Notes

## Other views of the development of personalized medicine

Finally, it is important to state that although the opinions set out in this document reflect the majority opinion on this subject, there are other views on the development of personalized medicine and its possible repercussions. These arguments and points of view are also reflected in this section, with a view to enriching the reader's background and placing him or her in a better position to take decisions in this regard.

The key aspect about which some people differ in their general perspective is the importance of the genome in the development of diseases. According to these other opinions, the person's circumstances (environmental conditions, lifestyles and social structures) is much more important than the genetic code when it comes to explaining the development of diseases, given that the surroundings interact with the genes and alter them continuously.

In their opinion, personalized medicine — as defined in this report—will not have a significant impact in improving the effectiveness of medical treatments and reducing their side effects. In contrast, it will have a significant impact on the cost of healthcare in the new paradigm.

The main conclusion that has been drawn is that, despite the fact that it is very necessary to improve our knowledge of diseases, where a knowledge of the genome will clearly make a positive contribution, it is also necessary to spend some of those resources on prevention and on campaigns to encourage people to change their lifestyles. These actions (such as, for example, campaigns in favour of a healthy diet, prevention of traffic accidents, etc.) might possibly have a greater effect than the benefits obtained from all the investment devoted to personalized medicine.

My notes

## FTF: A watchtower for changing trends

The "Future Trends Forum" has become the real showcase of Bankinter's "genetic code"—innovation and a commitment to the cutting edge developments. It is a forum in which opinion leaders, experts from different areas of knowledge and leading international scientists and intellectuals seek to anticipate advances in the near future, detecting social and economic trends and technological movements, analysing their possible effect on different areas and deciding which conclusions merit publication. This all uses a methodology whose central pillars are a multidisciplinary approach,



neutrality and globality, so that the public can be sure that the conclusions and the diversity of opinions deriving from these meetings on personalized medicine — and any other new development — are built on solid foundations of rigour, reliability and absolute credibility.

The pages below set out the analyses that FTF, together with ESADE Business School (which acted as a methodological consultant) has made of the possible impact of personalized medicine in areas such as the public healthcare system, the pharmaceutical and biotechnology industry, our own society and other sectors of influence. As well as the executive summary and this introduction, the document consists of a chapter establishing the right context for an understanding of personalized medicine from a technological, economic and business perspective, and a final chapter of conclusions setting out the FTF's vision of possible scenarios for the future and the most likely areas of impact.

This is another example of the Fundación de la Innovación Bankinter's commitment to increase social awareness of technology and research, and stimulate the creation of business opportunities based on the emerging trends that have been thus detected.

This project consolidates Bankinter's proactive attitude and its leading edge stance to society at large.