2017 COLLOQUIUM

**PRECISION MEDICINE AND TARGETED THERAPIES:
REALITIES AND PERSPECTIVES**

Definition and objectives of the colloquium: Towards incorporation of the new tools in medicine into current and future treatments

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Based on the introductory remarks by Professors Dominique Bellet and Jean-Paul Tillement, colloquium co-chairmen

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Knowledge of the molecular pathways of cancer, characterisation of pharmacological targets, pharmacogenetics, individualised adaptation of dosages, pharmacodynamic and pharmacokinetic monitoring of treatments, descriptive and functional imaging, disease prediction by genomic analysis of large population samples, biological tests to establish a disease prognosis or predict treatment response, artificial intelligence assistance in difficult diagnosis – these are the tools that have revolutionised the practice of medicine and made it more efficient.

The use of these new tools constitutes what has been called 'adapted therapy', 'personalised medicine' or 'individualised care'. As none of these designations is satisfactory, the authors have now agreed to use the expression 'precision medicine'.

The various presentations in this colloquium talk about 'innovation', translational research, personalised medicine and precision medicine. It is important to be attentive to semantics: what precise meanings do these terms cover?

The meaning of the term 'innovation' is widely debated. In reality, it simply boils down to distinguishing the idea and the invention from the innovation: an idea becomes an innovation only after it has been translated into a product or service that is useful to patients. The difference between idea, invention and innovation can be illustrated by the following numbers: on average, 3000 ideas will result in 300 patents (inventions) that will result in 125 projects that will lead to only 1.7 products (innovations).

The definition of translational research has also been long debated. In the end, it is accepted that this research aims to translate scientific theories and laboratory discoveries into concrete applications, thus into innovations. Translational research is unique in that it involves constant trips back and forth from the patient's bed to the bench. It therefore implies the existence of excellent relations between its various actors, clinicians, surgeons, pharmacologists and laboratory researchers.

The concept of precision medicine also raises some sticky semantic problems: it is common, even in the best journals, to see the terms 'personalised' and 'precision' medicine used interchangeably. This confusion can only dismay the clinicians and pharmacologists trained under Professor Pierre Godeau to whom we owe the origin of internal medicine: the patient is listened to, auscultated, examined, in order to treat him or her personally, individually, with the medicines best suited to personalise this 'art' that is medicine.

While the first mention of 'personalised' medicine dates back to 1971, according to a PubMed search, the term 'precision' medicine did not appear until 2012, therefore very recently, in particular because it calls on the fields of genomics, bioinformatics and artificial intelligence. It is these advances that led to a better

understanding of the molecular mechanisms of disease and the development of targeted therapies, precision diagnostics methods and algorithms to aid in rational decision-making.

This notion of rationality is central in precision medicine and indeed, the term 'rational' appears frequently in the literature devoted to the subject. Thus personalised medicine must be distinguished from precision medicine: we are faced with two different worlds, that of internal medicine, of personalised medicine, which belongs to 'art', and that, more rational, of 'precision' medicine. But it is clear that the second is at the service of the first and that both join forces to converge towards an optimisation of treatment.

Although the new form of medical practice is undeniably a step forward, the fact remains that it is still a tool which, far from replacing the practitioner, allows him or her to improve diagnosis and treatment. These new tools do not replace the practitioner's expertise, they facilitate it: medicine remains an art. To put it to use requires a definition of its scope, the methods to be employed, the medicines concerned and, ultimately, its performance in terms of quality, life expectancy and, of course, cost.

This colloquium aims to address these issues and to try to find answers, knowing that this topic is too broad to be treated exhaustively. Choices had to be made, obviously arbitrary, by selecting pharmacological, genetic, pharmacokinetic and immunological techniques that are general enough to be applicable to different pathologies. We also discuss some specific indications, of increasing difficulty, ranging from type 2 diabetes to renal transplantation. Finally, we plan for the future with the place of gene therapy and the use of stem cells. At the end of this colloquium, a review of precision medicine must be at the same time medical, scientific, economic and societal. Who can benefit from this new medicine? Can the state bear the cost? We hope that this colloquium, in which all speakers are widely recognised experts, will provide answers to the questions raised by the emergence of precision medicine and discussed in this introduction.

Our forebears have made French internal medicine a personalised medicine founded on in-depth knowledge of often complex pathologies, on active listening and auscultation of the patient, on a real empathy and, sometimes, on an intuition guided by clinical experience. A new world is opening up with precision medicine and artificial intelligence, both based on detailed analysis of many data, the so-called 'big data'. One may think that this will generate new and greater skills. But should not wisdom lead us to associate this with prudence and discernment in the permanent bedrock of what remains the very foundation of medicine: knowledge, listening, empathy, curiosity and intuition?

We know that many medical professions are going to evolve. Yet, that of the internist will surely remain (relatively) stable and probably mature. Specialists in artificial intelligence tell us that there are two reasons for this: (1) there will always be patients whose disease has an extremely unique presentation that can only be diagnosed by a detail that will most often elude artificial intelligence; (2) artificial intelligence and precision medicine will not replace personalised medicine because computers do not have empathy. There is a third reason, no less obvious: given the abundance of data that will be generated, they will have to be hierarchised in order to be taken into account, and for this, the role of the practitioner will remain irreplaceable.