Science & Technology

FORESIGHT

from society to research

Background Document

"Theranostics for Personalised Medicine"

19-20 May, 2014 - Bologna

WG HEALTH

National Research Council of Italy

Theranostics for Personalized Medicine

– background document –

1. State-of-the-art

"One size does not fit all" best characterizes the fundamental problem with the drugs available in the market at present. Although numerous drugs are available for various diseases, they fail to act on the majority of the patients. The reason behind this is that our health is determined by many factors, among them: the genetics we inherit; our ethnicity, age and gender; our lifestyle; and our socioeconomic environment. These factors differ for everyone and change over our lifespan. Also unique to everyone is their experience with disease and how they respond to prescription drugs or other medical therapies.

In the past several years there has been a **revolution in human genetics** that is virtually having a very significant impact on all specialties of medicine. Several scientific advances are responsible for this revolution. One of them is the recognition that the genetic composition of an individual plays a significant role in his or her health and predisposition to common diseases such as heart disease and cancer.

A second scientific advance is the availability of the human genome sequence and the many high throughput technologies developed and advanced since the Human Genome Project. A third is the imminent ability to completely sequence the human genome in real time at very low cost. The new genomic era provides excellent opportunities to identify gene polymorphisms, genetic changes that are responsible for human disease, and to build an understanding of how such changes cause disease. In the clinical arena, it is now possible to utilize the emerging genetic and genomic knowledge to diagnose and treat patients. It is anticipated that such knowledge will revolutionize medical practice result in an advance in personalized medicine.

Personalized medicine is the tailoring of medical treatments to the individual characteristics of each patient, and the ability to classify individuals into subpopulations based on their susceptibility to a particular disease, and thus to try to shape steps that may help avoid or reduce the extent to which an individual will experience a disease, or their responses to a specific treatment.

In the meanwhile, **nanotechnology** has also provided many different medical solutions both for therapeutics and diagnostics. Nano-delivery of drugs, for example, allows us to address unmet medical needs in cancer and other diseases. In addition, many nano-features, such as new imaging agents or smart materials will be prerequisites for implementation of personalized medicine. Nanotechnology will have a significant impact on many different medical developments, as highlighted by the European Technology Platform on Nanomedicine:

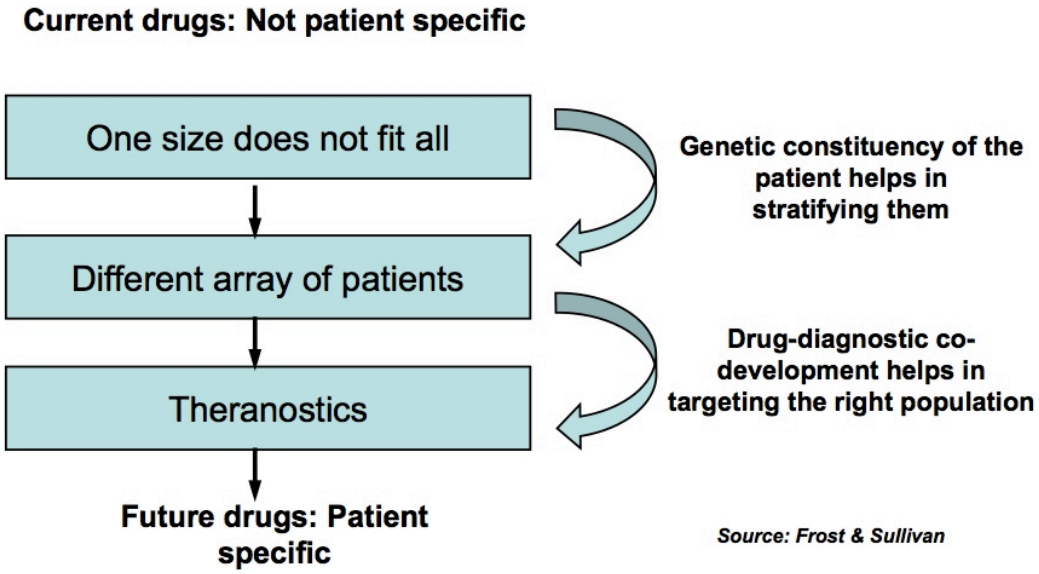
Challenges	Therapeutics	Diagnostics / Imaging	Regenerative Medicine
Cardio Vascular Diseases	▪ Implantable devices (nano surface modification) ▪ Targeted drug delivery into plaques	▪ Nanoparticles for theranostic approaches	▪ Intelligent bioactive materials ▪ Stem cell mobilisation and homing at site of injury
Neuro Degenerative Diseases	▪ Semi invasive nanodevices for drug delivery (for Parkinson) ▪ Nanoformulations for crossing the BBB	▪ Image guided implantation of advanced neurostimulators	▪ Site specific delivery of neuro active molecules ▪ Intelligent biomaterials controlling CNS regeneration
Diabetes	▪ Insulin measurement and delivery by nano enabled devices	▪ Encapsulation and monitoring of labelled islet transplants ▪ Whole body imaging of fat distribution with nanoparticles ▪ Implanted non-invasive continuous glucose monitoring	▪ Functionalization of 2D and 3D materials for time and spatial release of biochemical factors for artificial pancreas
Cancer	▪ New nano formulations for targeting agents to tumours ▪ RF-heatable Nanoparticles for thermal therapy ▪ Implantable devices for localised delivery of drugs ▪ New therapeutic tools with physical mode of action ▪ Monitoring of therapeutic efficacy	▪ Nanoparticle tracers and contrast agents for diagnosis (Magnetic Particle Imaging) ▪ Composite nano particles for monitoring of therapy ▪ Minimal invasive endoscope / catheter for diagnostics and therapy ▪ Nanostructured surfaces for biosensors	▪ Functionalised nanoparticles for targeted in vivo activation of hematopoietic stem cell production
Inflammation	▪ Soft nanomaterials for bone regeneration, Rheumathoid Arthritis and Crohn's disease ▪ Bacterial free nanomaterials to avoid infection by implanted materials	▪ Imaging of nanoparticle labelled white cells	▪ 3D Nanomaterials for stem cell immobilisation at site of injury ▪ Novel implant materials and surfaces to prevent implant infections

Source: www.etp-nanomedicine.eu

Other new technologies, such as wireless devices, 3D-bioprinting, medical smart textiles are increasingly customized and could help in establishing a more personalized model of care, and translate into improved cost-effectiveness.

Pharmacogenomics, the identification of "the genetic basis of variability in drug efficacy and safety" used to identify the preferred pharmacotherapy in cancer sufferers, as a standard of biotechnology in cancer biomarker research is being replaced by theranostics as the standard of biotechnology.

Theranostics represents the "fusion of therapeutics and diagnostics." Theranostics (a portmanteau of *therapeutics* and *diagnostics*) is a proposed process of diagnostic therapy for individual patients - to test them for possible reaction due to the administration of new medications and to tailor the related treatment on the basis of the test results. Combining diagnosis to identify the most efficacious pharmacological therapy and administered cure in the same process increases safety and effectiveness in the patient's overall treatment. This is a natural advancement in medical research, as theranostics focuses on "the integration of information from diverse biomarkers" rather than the single marker approach of Pharmacogenomics. Key applications of theranostics are also covered in the age-related disease areas, such as cancer, cardiovascular diseases and neurological disorders.

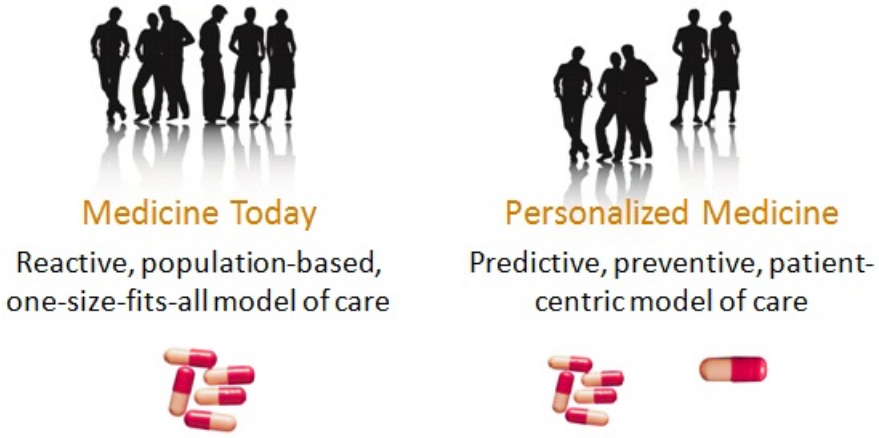


2. Challenges and barriers

We are at the dawn of a new age of tailored therapeutics, or personalized medicine. We are moving from the inefficient and experimental medicine of today towards the data-driven medicine of tomorrow. Personalized medicine is an innovative, efficient and patient-centered alternative to the one-size-fits-all medicine and it also promises to yield a maximum return on healthcare investment.

Recent biomedical research breakthroughs, including the sequencing of the human genome and a

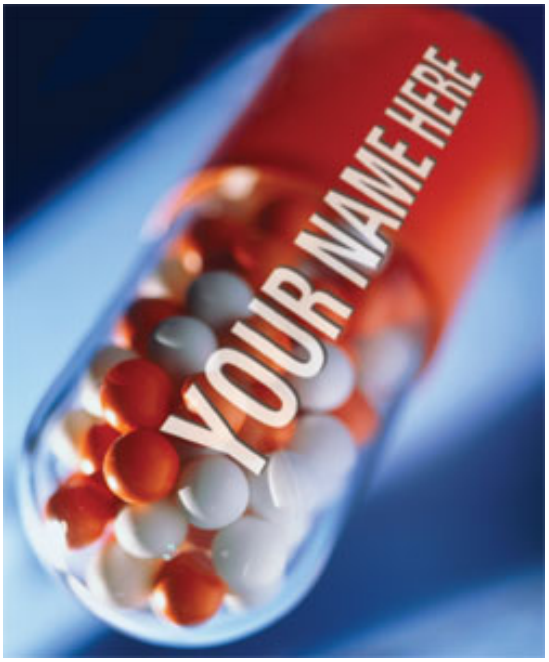
deeper understanding of the molecular underpinnings of disease, have the potential to transform the treatment of disease and the practice of medicine into Personalized medicine. By combining genomic and clinical information more accurate predictions can be made about a person's susceptibility of developing disease, the course of disease, and response to treatment allowing us to customize health management. The knowledge of the genetic basis of human disease is ushering a new era in drug development that is focused on targeted drug development. Genetic profiling of patients will help in defining individuals risk for clinical outcomes and their response to specific drugs. When your genetic information informs you of your increased risk for a disease and you make lifestyle changes to reduce that risk, personalized medicine has revealed itself. If you have a gene variation that influences how you process a medication and your physician prescribes dosing instructions accordingly, your medical care is now safer, well-timed, accurate, and more cost-effective for you and our healthcare system. Personalized medicine therefore has the potential to optimize targeted delivery and dosing of treatments so patients can receive the most benefit with the least amount of risk, cutting out the difficulties of the current trial-and-error process many patients endure to find the correct drug and dose to treat a condition. Hence, this new approach can help to reduce the risk of undesirable adverse reactions and at the same time, to make medicine more effective.



Personalized medicine has the potential to offer patients and their doctors several advantages, including:

- ✓ The ability to make better informed clinical decisions.
- ✓ A higher probability of improved health outcomes via better-targeted therapies.
- ✓ A lower probability of adverse reactions from medications and treatments.
- ✓ A focus on prevention and prediction of disease for earlier disease intervention.
- ✓ Reduced healthcare costs.

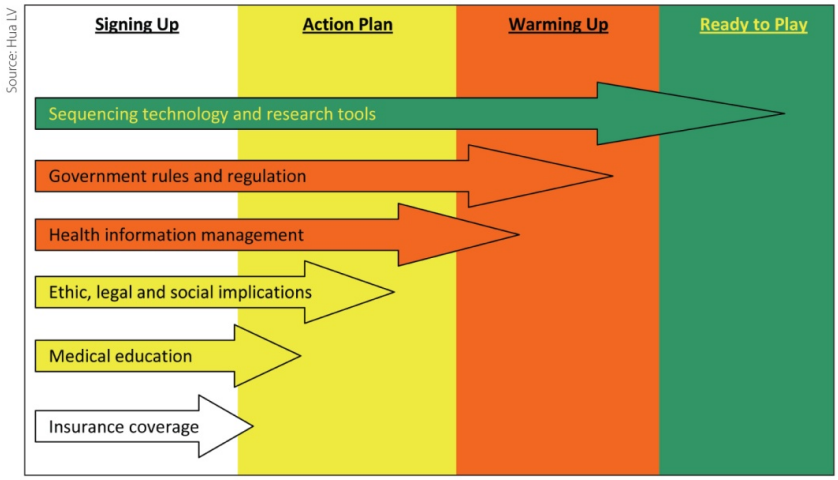
Theranostics would be a key part of personalized medicine and require considerable advances in predictive medicine. Theranostics could help us to accelerate the path towards personalized medicine by stratifying the patients according to the biomarkers they possess, thereby prescribing the most appropriate drug. Theranostics would also rely on pharmacogenomics, drug discovery using genetics, molecular biology and microarray chips technology. It uses molecular assays to determine the optimum dose of drugs for a patient, paving the way for personalized medicine.



The move towards personalized medicine is an evolutionary process. Although some personalized medicine treatments are already available on the European market, its full potential is yet to be tapped and there is still a long way to go to turn personalized medicine into a widespread approach to treating illness.

- Factors such as cost and regulatory timelines are the key hurdles that need to be addressed at the moment.
- For personalized medicine to be a fully functioning reality at the clinical level, certain features are essential: an electronic medical record, personalized genomic data available for clinical use, physician access to electronic decision support tools, a personalized health plan, personalized treatments, and personal clinical information available for research use.
- Realizing the promise of personalized medicine requires a sustained commitment to advancing our understanding of the structure and function of our genomes, including our microbiome, the underlying genetic and environmental bases of human disease, and human genomic variations and the ways in which these variations influence disease or responses to therapy. This research also requires a pathway to translate such findings to real world medical products and practices.
- Much of the **applied regulatory science** for evaluating the strategies and outcomes for personalized medicine - such as standards for whole genome sequencing, fully qualified biomarkers (measurable characteristics in patients), and innovative clinical trial designs and

statistics - are still underdeveloped. Novel infrastructure modifications are necessary to support the development of these more personalized targeted therapies, most immediately through investments in regulatory science, clarification of Regulatory Agencies' policies, a reorganization of leadership, and engagement of physicians, patients, and their advocacy groups.



This diagram portrays the stage of readiness of the important players for implementation of personalized medicine, according to the Personalized Medicine Coalition.

Ensuring patients' access to safe, quality treatment lies at the very heart of European policies, and personalized medicine is part of plans for the future of European healthcare. The European Community is currently improving the legal framework for clinical trials and medical devices, which will benefit personalized medicine. Once adopted, the new Regulation on Clinical Trials will facilitate multi-national trials. This is critical for the testing of personalized medicine, which often requires cross-border clinical trials to meet the necessary target population. The proposed Regulation on Medical devices will reinforce the current regime for in vitro diagnostics in order to ensure an appropriate level of safety and performances specific to those tests. Finally, the EU network on Health Technology Assessment enables Member States to exchange information on scientific developments and achievements, thereby reducing duplication of efforts.

The Personalized Medicine Revolution Is Almost Here!

Open questions for the foresight exercise:

1) **How can we move beyond the "one-drug-one-diagnostic" paradigm?**
2) **How can we move to patient-centric therapy?**
3) **What is the potential for point-of-care and home-diagnostic solutions?**
4) **Are clinicians ready to adopt novel technologies?**
5) **What problems might personalized medicine face in terms of social acceptance?**
6) **How will insurance companies and regulators cope with the advent of personalized medicine and what impact will this have on society?**