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-OMICS IN PERSONALISED MEDICINE

Workshop to explore the role of -omics
in the development of personalised
medicine

Organisers:



European Commission
Health Research Directorate

SUMMARY REPORT

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European Commission, DG Research - Brussels, 29-30 April 2010

Summary Report

Europe is facing multiple challenges in the health sector and in health research. In the health sector, ageing population, failures of blockbuster approaches, increasing costs of healthcare and concomitant cost containment for healthcare are just a few of the obstacles to face. In health research, there is a need to better understand the mechanisms of diseases, break barriers across disciplines, and translate research results into clinical practice.

Personalised medicine is an emerging field that promises to bring radical changes in healthcare. Personalised medicine may be defined as “a medical model using molecular profiling technologies for tailoring the right therapeutic strategy for the right person at the right time, and determine the predisposition to disease at the population level and to deliver timely and stratified prevention”.

The sequencing of the human genome together with the development and implementation of new high throughput technologies (so called “omics”) are enhancing our knowledge on human health and disease and have already, and will continue, to provide a sound foundation for personalised medicine.

The workshop “Omics in personalised medicine” that was held at the European Commission in Brussels on 29th and 30th of April, brought together experts from different fields: omics, epidemiology, pharmacology, experimental medicine and bioinformatics representing academia, industry, including SMEs, and regulatory and funding agencies. The aim of the workshop was to explore the role of omics technologies in making personalised medicine a reality in the delivery of treatment and prevention of ill-health, to build a 2020 vision, and to identify the research needs for its implementation and to define the role of EU-funded research therein.

The brainstorming during the workshop allowed the definition of short and long term visions, including the identification of bottlenecks that will need to be managed. The main conclusions of the workshop are described below.

2020 Visions & Bottlenecks

- *Systems level understanding of health and disease*

By 2020, a better molecular definition of “health” and “ill-health” will have been achieved and early markers that identify the transition between the two states will have been identified. This will be delivered by studying cellular and molecular mechanisms of both states and by studying the interplay between environmental factors to which the population is exposed and their genetic make-up. Classifying diseases at the genetic, molecular and cell functional levels will forge a stepwise change in a disease treatment and prevention that is already far advanced for some diseases, e.g. the stratified treatment of some cancers has delivered major health gains. The biggest challenge will be the discovery, evaluation and validation of bio-markers and -signatures for the common diseases.

BOTTLENECKS: The understanding of the genetic, molecular and cellular mechanisms underlying common diseases is currently limited. There is therefore a need to support studies on the mechanisms of diseases as this will lead to the rational discovery of omics-based markers and the development of more reliable pre-clinical disease models. Several omics platforms, particularly those for the analysis of nucleic acids, are ready for clinical application but others, such as proteomics, epigenomics, cell functional analysis, etc., require further development before they can contribute to large-scale clinical translational studies that aim to identify and validate bio-markers and -signatures. In addition, new omics

technologies need to be developed to become suitable for use in clinical studies that aim to discover bio-markers and –signatures.

- ***Personalised treatment and personalised prevention***

It is expected that the prescription of drugs and treatments tailored for the right patient at the right time will increase the efficiency of healthcare delivery and reduce healthcare costs. Applied healthcare studies will be required to obtain evidence for this assumption so that those who reimburse healthcare costs can incentivise the introduction of personalised drug prescription. Omics-based bio-markers and -signatures and the development of other non-invasive diagnostic methods will identify at risk groups supporting the implementation of risk-stratified health screening and timely prevention. This will ultimately lead to significant cost-savings at the societal level.

BOTTLENECKS: There is a need to foster economic return at all levels. Omics technologies reaching maturity should be tested in clinical practice. Prospective and, where necessary, randomised clinical studies will be needed to validate novel bio-markers and -signatures and these will benefit from an improved knowledge flow between industry and academia. High quality collections of biological samples procured in a standardised manner from relatively small age- and disease-stratified collections coupled to omics- and imaging-based phenotype information and of large population cohorts with core phenotype information are required for the purpose of identification and validation of bio-markers and -signatures respectively.

- ***Development of clinical bioinformatics***

Europe has a globally competitive infrastructure for bioinformatics that supports studies on the mechanisms of diseases. The integration of data-dense information from the different omics platforms at the individual and population levels is an essential step if society wants to reap the benefits of omics technologies for healthcare. The current European bioinformatics community needs to support the development of the new discipline of clinical bioinformatics, which will link omics experts with clinical teams and experts in quantitative sciences. Clinical bioinformatics will need sustained national as well as European support over the next decade.

BOTTLENECKS: Currently only a few European centres are able to deal with the large volume of omics data. At omics level, the challenges include storage, handling and integration of large volumes of data necessitating efforts on data standardisation and the introduction of innovative informatics solutions. Current medical coding systems are generally reimbursement-driven and are therefore of limited value for research studies. The development of a clinically more relevant medical coding system for research and the design and validation of algorithms and statistical methods for the analysis of multiple layers of omics data is required. Internet portals with “ready-for-use” applications to link clinical information with omics data, at the individual and population levels, are required to identify associations and for the purpose of data-mining. These applications, together with the training of a workforce for clinical bioinformatics, will support the introduction of personalised medicine across Europe.

- ***Personalised medicine available in all European countries***

Several European countries are at the forefront in the clinical application of omics technologies and have already delivered examples of omics-based personalised healthcare, e.g. for breast cancer. However, other European countries are lagging behind. In 2020 ideally all European countries should have local laboratory and clinical bioinformatics infrastructures to provide personalised healthcare.

BOTTLENECKS: Each European country will need to identify their specific and national bottlenecks for the uptake of personalised medicine. Collaboration and, particularly, training, at European level will aid member states to overcome their national bottlenecks.

- ***Multidisciplinary education and training***

An important part of Vision 2020 is the provision of multidisciplinary education and training at all levels and disciplines that is evidence-based. Physics, mathematics, statistics, machine learning, engineering, informatics and hands on training in omics technologies should be integrated in educational and career development programmes of the workforce for healthcare and related industries and the funders and regulators of the European healthcare systems.

BOTTLENECKS: Researchers, the clinical community and healthcare funders and regulators speak different languages. In order to adopt omics technologies into clinical practice, all groups need to be properly trained and receive advice on the design and execution of clinical studies that aim to deliver the evidence for the use of omics techniques in diagnosis, prevention and treatment.

Delivering on the Vision

Short/Medium term deliverables - before 2015

- ***Pharmacogenomics***

Pharmacogenomics may improve the efficacy of current drugs, increase the success rate in drug development and may reduce the incidence of serious adverse events of drugs. The lack of health economics evidence of the possible benefits of pharmacogenomics and the need for major system changes surrounding the prescription and delivery of drugs are barriers for the early uptake of genetic testing in routine drug prescription. An initial focus on serious adverse events should be considered, because they are rare and likely to have a strong genetic component and therefore genetic testing may be effective in reducing the prevalence of serious adverse events to commonly used drugs.

- ***Tackling rare inherited disorders***

A quick win in personalised medicine could be in the area of rare inherited disorders, of which most are life-threatening or seriously debilitating. Currently, 6000-8000 rare inherited disorders are known and the genetic basis of around half has been resolved. About a thousand are currently treatable and taken together all rare inherited disorders place a major burden on Europe's health care systems. Studying known monogenic disorders will improve our understanding of genetic and environmental modifiers of disease severity and provide an ideal for the discovery, evaluation and validation of novel bio-markers and -signatures for the prediction of severity that can be used for personalised therapies. The discovery of the genetic basis of the Mendelian forms of inherited disorders relevant to common diseases will result in novel insights into the molecular mechanisms of diseases and may identify novel drug targets for common diseases. Rapid and affordable testing for inherited disorders will reduce diagnostic delay, improve counselling and forge the modernisation of genetic diagnostic services across Europe. It was suggested that European research into unravelling the biological mechanisms of most rare diseases should be a research target for 2020.

Long term deliverables – before 2020

- ***Discovery, evaluation and validation***

We have arrived at a historical point in time at which for the first time all building blocks of life have been defined. It is predicted that the combination of this knowledge with omics platforms will lead to a better definition of health and ill-health at the genetic, molecular and cellular level. To bring novel bio-markers and -signatures to the bedside requires iterative cycles of omics platform development coupled with the discovery, evaluation and validation of novel markers and signatures. The discovery and evaluation phase are to be embedded in centres of clinical excellence that are specialised in disease-specific translational research. At these centres relatively small, age- and gender-stratified, collections of up to 1000 individuals, either patients with a specific disease or healthy controls, should be available for detailed clinical phenotyping including imaging, omics analysis, etc. The validation phase demands

access to large population cohorts so that the diagnostic sensitivity and specificity of bio-marker and -signatures can be defined in an age-, gender- and ethnicity-stratified manner and in the context of environmental exposures.

Disease-specific centres of clinical excellence need to be identified and links with omics experts and centres need to be established. SMEs may lack funding for the final phase of platform development and experience problems with access to biological samples of well characterised individuals in good health and ill-health. The reproducibility of the results of omics platforms is to a great extent determined by the pre-analytical phase of sample handling and knowledge and standards of best practice for sample procurement and processing must therefore be developed.

- ***Gene-lifestyle interaction***

Reliable gene-lifestyle interaction studies will yield important evidence for the shaping of personalised healthcare. Studies need statistical power with adequate environmental exposures and lifestyle heterogeneity to obtain reliable evidence on the interplay between nurture and nature.

Europe has a historic strength in large epidemiological studies but technology development and implementation is needed to better ascertain environmental exposure and dietary heterogeneity. There is a lack of information about the quality and quantity of biological samples of existing European cohorts and about the completeness and consistency of phenotype data. This type of information is required to arrive at informed decisions whether to invest in Europe's historic cohorts or to establish new ones. Enrolment and follow-up in large epidemiological studies will be more cost-effective if embedded in existing healthcare delivery systems and collaboration between existing and new cohorts across Europe is to be encouraged.

Role of EU-funded research

- ***Early proof-of-concept projects***

Proof-of-concept projects that demonstrate the feasibility to bring early returns from the omics revolution to the healthcare industry should be considered. Primary focus could be on rare inherited disorders, and this should include severe adverse effects of a selected number of commonly used drugs.

- ***Fostering small but ambitious projects***

Exploratory and high-risk projects that aim to develop novel omics technologies for application in the clinical arena for the discovery of bio-markers or –signatures are to be encouraged. This would stimulate a productive competitive environment.

- ***An ambitious investment to kick-start Clinical Bioinformatics***

EU funding should be encouraged for the establishment of the critical connectivity between the clinical community, the omics experts and those with expertise in the quantitative sciences. Funding should stimulate initially the development and validation of novel algorithms to explore the complex signatures that are obtained from the omics platforms, including the clinical interpretation of the sequence of the entire genome, the epigenome and the RNA and protein landscapes of cells and other biological relevant samples. Once validated the use of the algorithms in healthcare research can be achieved by a hub and spoke model for clinical bioinformatics, which will provide the means to deliver informatics functionality and education at the local level.

- ***Maximising the opportunities for clinical outcomes from omics research through better interaction with national health care systems***

The ultimate impact of omics technologies on improving the delivery of personalised medicine will depend on demonstrating its cost-effective utility in daily practice. The cost of generating large scale

prospective bio banks/trials with high quality outcome data is enormous. The EU should work with national health and research funding agencies to determine whether there are mechanisms to integrate omics-based outcomes research into existing service delivery models. The advantages of such an approach not only include reduced cost but also more generalisable findings. Three types of bio bank initiatives should be supported and/or strengthened:

- gender- and age-stratified collections of hundreds of healthy individuals with deep clinical phenotype information and an extensive repertoire of biological samples that have been analysed with a comprehensive set of omics techniques;
- gender- and age-stratified, disease-specific collections of hundreds of patients with deep clinical phenotype information and an extensive repertoire of biological samples that have been analysed with a comprehensive set of omics techniques;
- large population-based epidemiological collection, existing or new ones, with a core set of phenotype information on health status and lifestyle, which includes environmental exposures and diet.

- ***Coordination and fostering of multidisciplinary training***

The successful integration of omics-based personalised medicine into clinical practice does not only require the demonstration of its clinical utility and cost-effectiveness but also the development of processes so that the relevant information is available to the correct health practitioner at the appropriate time. This is particularly important as the routine availability of whole genome sequences becomes a reality. In conjunction with education, research in clinical bioinformatics needs to be undertaken as to how such vast data can be appropriately presented. In addition and to further advance personalised medicine the European Commission should promote evidence-based multidisciplinary training of omics researchers, clinician-scientists, quantitative scientists, clinical care and pharma & biotech teams and healthcare policy makers with the aim to introduce validated and cost-effective omics technologies, including clinical bioinformatics and statistics, into Europe's healthcare systems.