



**SAMS**  **Swiss Academy  
of Medical Sciences**

## **Report of the 2016 FEAM Spring Conference**

### **Precision Medicine and Personalized Health – New Dimensions**

Hosted by the Swiss Academy of Medical Sciences (SAMS) on 20<sup>th</sup> May 2016 at the Kursaal Berne, Switzerland

#### **Introduction**

The 2016 Spring conference of the Federation of European Academies of Medicine (FEAM) “Precision Medicine and Personalized Health – New Dimensions” attracted almost 100 senior representatives of the biomedical community from Switzerland and from across Europe. The aim of the conference was to facilitate cross-sectorial discussions in this field, to identify European research and policy opportunities and challenges, and to discuss potential future activities for FEAM and its Member Academies. The conference provided a very timely opportunity to hear leading experts address key issues on the development of national and international collaborative networks, consider the latest research findings in specific disorders, as well as review new dimensions in the assessment of the ethical and societal impact of this paradigm shift in medicine and healthcare.

The meeting was hosted by the Berne-based Swiss Academy of Medical Sciences (SAMS), the members of which, through their expert and advisory capacity, are committed to supporting the development of high-quality medicine based on ethical principles. SAMS supports early-career researchers and engages with academia and practice, as well as serving policy makers and the public. FEAM’s mission is to promote co-operation between national Academies of Medicine and Medical Sections of Academies of Science across Europe. FEAM, based in Brussels, provides its members with a platform to formulate their collective voice on all matters concerning human and animal medicine, biomedical research and European-focussed health issues.

The one-day conference was formally opened by Professor Peter Meier-Abt (President, SAMS), Professor Bernard Charpentier (President, FEAM and a Member of the French Academy of Medicine) and Dr Gregor Häfliger (representing the Swiss State Secretariat for Education, Research and Innovation). From a Swiss perspective the organisation of the conference was very timely in light of the national Personalized Medicine initiative (for which SFR 70million has been made available over the next 4 years) and which is being taken forwards under the leadership of the Swiss Academy.

Dr Elmar Nimmesgern (E2 Innovative and Personalized Medicine Unit, European Commission DG Research) described funding opportunities (for enabling and implementing personalized medicine) at a national and European level further. Connecting Europe for genomic health is a key priority for the European Commission. Speakers from more than 10 countries reviewed many recent developments in this complex field in a series of presentations that addressed such key issues as the establishment of national and international networks; the impact of

personalized medicine in the diagnosis and treatment of specific disorders and how ethical and societal challenges needed to be considered fully. The multi-factorial nature of the challenges facing the development of the technology was explored in a wide-ranging round-table discussion that concluded the meeting. Issues addressed in this final discussion included the future competence and skills-sets required by physicians as healthcare becomes more personalized and the technologies used more complex. Concern was raised over the future ability of researchers to be able to handle increasing large volumes of data (some of which may not even be interpretable). Questions were raised as to whether Society's trust in physicians will be maintained as ethical, regulatory and insurance-related issues associated with the anticipated increase in the monitoring and screening of patients take on more significance. One positive development from a commercial perspective was that personalized medicine was already overcoming some of the inefficiencies in the clinical trial process – leading to increased patient benefits.

A recurring theme throughout the conference was the anticipated future emphasis on disease prevention and prediction and how diagnostic tools and genomics will play a greater role. It was also recognised that the development of personalized medicine was happening at the same time as other aspects of healthcare were being re-organised, with both a shift from the hospital to the community, and a shift from treating disease to managing care. It was noted that future discussions on public health and the application of the new technologies of personalized medicine, would not be able to be separated from those on health economics.

## **Welcoming Comments**

Prof. Peter Meier-Abt (President of the Swiss Academy of Medical Sciences (SAMS) welcomed all delegates to the 2016 Spring Conference of FEAM, being hosted for the first time by SAMS.

The international conference on such a paradigm shift in medicine had been organised at a key time for there were many initiatives currently being progressed to ensure the effective implementation of Precision Medicine and Personalized Health. Seeking clarity on the definitions of these terms was important and there were many ongoing discussions on this matter as researchers and policy makers sought to distinguish between personalized medicine, stratified medicine, biomarker-based medicine, pharmacogenetics, etc.

Professor Meier-Abt argued that in fact all of these activities really meant the same thing – linking the genotype, molecular networks (with the impact of the environment and the epigenome) with the phenotype – leading to improvements in health (through better risk assessment and innovative new therapies). Much was already happening in the transformation of healthcare using big data. The importance of this field had been recognised by policy makers in the USA and Europe leading to the launch of well-funded prevention medicine initiatives, with the European Alliance for Personalized Medicine also playing a key role. Switzerland was also responding to the challenges and opportunities, with the establishment of the Swiss Personalized Health Network.

Professor Bernard Charpentier (FEAM President and Member French Academy of Medicine) thanked the SAMS for hosting and organising the FEAM Spring Conference on this important topic. He described the role of FEAM in promoting cooperation between national Academies of Medicine and Medical Sections of Academies of Sciences in Europe; to provide them with a platform to formulate their collective voice on matters concerning medicine, biomedical research, education and health. Through its network of 20 FEAM Academies, representing over 5,000 high level scientists, the Federation is in a position to provide independent EU-wide scientific advice and opinion on the European biomedical science base. FEAM, working with other Academy networks across Europe (ALLEA, Euro-case, EASAC, acatech and Academia Europea) was currently establishing a new EC-funded initiative (SAPEA) to contribute to the work of the Commission's Scientific Advice Mechanism (SAM) initiative.

FEAM was also seeking to work with other biomedical policy stakeholders across Europe, in the commercial, regulatory and patient representative sectors, to establish a safe-haven 'Biomedical Forum' for discussion on topics of mutual interest and concern. The topic of Precision Medicine was an important policy priority for FEAM and its Member Academies, and follows on from recent meetings held by the French Academy of Medical Sciences on 'Adolescent health in Europe' and "Developments in human genome editing" organised by the UK Academic of Medical Sciences and the French Academy.

In opening the conference, Professor Charpentier looked back at his career in medicine and how the lack of precision in diagnosis and treatment that he and other clinicians had to work with had changed completely with the new opportunities arising from precision medicine and personalized health technologies.

Dr Gregor Häfliger (Vice President, State Secretariat for Education, Research and Innovation) thanked Professor Meier-Abt and Professor Charpentier for organising the conference and spoke on how personalized medicine is creating new dimensions, both in terms of the massive amounts of highly precise data, but also the logistical and ethical issues being raised. He suggested that the regulatory and legal framework for clinical research would need to be adapted. Personalized medicine was also raising new challenges concerning its funding. In general, basic biomedical research carried out in academia has been publicly funded, while clinical research tends to be funded by the private sector e.g. by the pharmaceutical industry. However, personalized medicine may not always have immediate industrial relevance and as the number of patients affected by a specific disease may be small, it may take a long time to obtain solid data. It is to be hoped that academic clinical researchers will continue to collaborate with industry and generate successful Public Private Partnerships (PPPs) but it is anticipated that the amount of additional funding required in this field will be considerable.

Dr Häfliger pointed out how Switzerland is embracing these challenges. Over the last few years, infrastructures such as the Swiss Clinical Trial Organisation have been built up, increasingly with the involvement of Swiss National Science Foundation. Investigator-driven clinical trials will start to receive substantial funding later in 2016.

Over the next four years, 70 million Swiss Francs have been earmarked for a national Personalized Medicine initiative. The lead and major responsibility for this initiative will be with the Swiss Academy of Medical Sciences. Priority will be given to the strengthening bioinformatics and Biocomputing at Swiss universities and hospitals. For the Swiss Institute for Bioinformatics, which has been providing the world's scientific communities with databases such as Swissprot, it will be an immense challenge to manage the highly diverse medical data that will be generated by the translational research that will arise from this initiative.

The two ETH polytechnic universities under direct responsibility of the Federal Government will also be involved in this initiative, as will be the activities of the Swiss Biobanking Platform. These and other activities will eventually be fully integrated into the proposed 'Swiss Personalized Health Network'. Going forward there will be a need for effective coordination and sharing of best practice across Europe on issues concerning the regulatory framework for such clinical research.

## **SESSION 1: National and International Networks**

**Chairs:** Prof. Bernard Charpentier (FEAM President, French Academy of Medicine) & Prof. Peter Meier-Abt (President SAMS)

### **Connecting Europe for Genomic Health**

Dr Elmar Nimmegern (Deputy Head of Unit, DG Research & Innovation E2 Innovative and Personalized Medicine, European Commission) provided an overview of the EC's activities in

supporting personalized medicine. With such a wide-ranging topic it is important for there to be some agreement on what actually defined 'personalized medicine'. The definition currently used at EU level is: *"Personalized Medicine refers to a medical model using a characterisation of individuals phenotypes and genotypes (e.g. molecular profiling medical imaging, lifestyle data etc) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention"*.

As emphasised by such a definition, personalized medicine is more than just medicines *per se*, but with prediction and prevention being key elements. Diagnostic tools will play an increasingly more important role. At the same time, going forward there will be a shift from a focus on treating disease to that of managing care. Through personalized medicine, there will be a movement from the clinical definition of disease to the molecular definition of disease and the molecular definition of health.

Recognising that there is a need to look at the entire innovation ecosystem in the application of personalized medicine in clinical development, an EU-level toolbox has been established to address the key issues of funding, policy and regulation. A number of main challenges have been identified. These include:

- The need to break down barriers and develop a common language, something that is being addressed through capacity building, education and training, and the promotion of cross-disciplinarity
- The generation of knowledge and the development of the right tools. This is being addressed through the development of standards, clinical bioinformatics and the adoption of tools
- The translation of knowledge to medical applications – through the development of disease taxonomy, biomarker validation and clinical trials
- Understanding the value and economic aspects – this is being taken forward through healthcare pilot studies, HTA and comparative effectiveness research.

EU research funding has been in place since 2007, initially for enabling personalized medicine (via the 7th Framework Programme and the first Innovative Medicines Initiative (IMI)), and more recently through Horizon 2020 and IMI2 with a greater focus on implementation. The €3.2 billion made available through these programmes has been supplemented with additional support from the European Research Council (ERC), the COST programme and Eureka.

The EU rare diseases policy has been used as a testing ground for personalized medicine: e.g. the use of genetic and genome information in healthcare (raising issues concerning the quality of genetic testing, ethics and data sharing); clinical trials on small populations; and the development of clinical guidelines.

Dr Nimmesgern described some of the projects that are being funded in H2020. Two examples form the first H2020 calls are the 'Omics for prevention' programme and the 'Pilot projects' initiative. In the former, €22 million have been awarded to three projects for the development and assessment of a personalized/stratified health promotion programme, and €30 million have been made available to two pilot projects on new models of care, based on applying the concept of personalized medicine in existing healthcare environments.

Funding under the SME Instrument for the 'ADDIA' project has led to the development of a validated fast diagnostic biomarker kit for Alzheimer's disease. The PPP initiative IMI has led to the development of tools for cancer genomic medicine. The IMI QuIC-ConCepPT programme has developed standardised biomarkers for early-stage cancer drug development and advancing personalized cancer medicines research. The CANCER-ID programme has established standard protocols for blood-based biomarkers, paving the way for personalized medicine for different types of cancer.

Recognising that there is considerable funding available for research at the national level; the EC is seeking to enhance this work through support for coordination activities. Through the

International Consortium for Personalized Medicine (IC PerMed), participating countries have agreed to identify common strategic goals, to share tasks and costs, and to work to common research policies and standards, thus speeding up research. The IC PerMed collaboration is involving research funders and policy makers from EU Member States and beyond. The consortium will help establish Europe as a global leader in personalized medicine research, and will seek to provide evidence to demonstrate the benefit of personalized medicine to citizens and healthcare systems. A Roadmap is being developed based on the PerMed Scientific Research Agenda.

The Roadmap is based on five challenges and will include actionable research activities, the mapping of ongoing activities in this field (for proposed actions), and the proposed means of implementation. The Roadmap to be available before the end of 2016 will address:

- Developing awareness and empowerment
- Integrating big data and ICT solutions
- Translating basic research to clinical research and beyond
- Bringing innovation to market
- Shaping sustainable healthcare

The IC PerMed consortium was launched in Brussels on 1 June at the Personalized Medicine Conference [www.ec.europa.eu/permed2016](http://www.ec.europa.eu/permed2016)

Additional related policy activities taking place within the EU include:

- Joint action on Comprehensive Cancer Control
- Study on Big Data
- The work of the Expert group on Safest and Timely Access to Medicines for Patients
- Support to HTA cooperation at EU level
- Exchange of information on pricing and reimbursement

**(Presentation available at [Connecting Europe for Genomic Health](#) )**

#### Comments arising from Dr Nimmesgern's presentation

In response to a question concerning possible difficulties in data sharing between the private and public sectors in IMI projects, Dr Nimmesgern commented that IMI has allowed company data to be shared easily between project participants. Under Horizon 2020, all publications coming from funded projects need to be published in Open Science journals and as from calls under 2017 work programmes going forward, all data need to be made available (reasoned opt-out possible). The goal is to make the data available on the EU Science Cloud.

It was noted that the SME-biotech focussed ADDIA project to develop a blood diagnostic biomarker kit for Alzheimer's disease, was currently not part of the Human Brain Project, but efforts will be made to link them up.

Concern was raised over the need to ensure that effective data storage, curation and data quality systems are in place for EU-funded projects. Dr Nimmesgern suggested that this was an important task globally, and not just for European projects. There is, however, a data management plan in place in all EU grant agreements.

Reference was made to the importance of European Reference Networks developed (work led by DG Health and Food Safety). The Networks are more focussed on the provision of treatment and the provision of feedback to clinicians, and not directly related to research funding priorities. It is planned to link the European Reference Networks with the research and innovation actions and other activities in the rare disease field.

## **Big Data & Big Health: Personalized Medicine as a Paradigm Shift**

Prof. Lisette van Gemert-Pijnen (Center for eHealth & Wellbeing Research, University of Twente (NL)) spoke from a technological and social sciences perspective on the key role that big data were playing in the development of personalized medicine and healthcare.

Many changes were taking place in the development of 'bottom-up' medicine. The presentation addressed the key issues in the management of security and privacy over the use of big data. There was a need for those with "data wisdom" to make more sense of big data.

The key paradigm shifts affecting the growth of personalized healthcare were the digitisation of medicine (through the growth of and access to new healthcare technologies) the move to a more people-centred versus disease-centred approach (with a recognition that no one size fits all) and the explosive growth of data leading the 'wall of knowledge' being broken. The current data availability overload indicated that less than 5% of this information was currently being analysed.

Medicine was being blurred through changes to the health industry and the growing involvement of organisations such as Google. This new approach to medicine was more individualised (as opposed to population-based) making use of patient-generated, real-time and real world streamed data with the information owned by the rightful owner, and not the doctors and hospitals. The 'old medicine' had been more data-limited and having to make use of more expensive 'big-ticket' technologies.

The datification of the world is providing boundless data in terms of volume, velocity, variety and veracity, with advanced analytics allowing the leverage of data to provide new insights and add value.

The application of data is leading to digital-empowered citizens through, for example, the development of smart homes and communities. Older people are being able to remain in their homes through improvements to safety such as the application of sensors to prevent falls. Data generated by patients through 24-hour monitoring via smart watches is starting to allow meaningful real-time feedback, although there is still a lack of meaningful evidence.

Going forward there is a need for better prediction models making use of available data, and to learn from the mistakes of initiatives such as Google's 'flu trends' which had grossly over-estimated the prevalence of the illness. It was felt that the ability of computers such as IBM's Watson to make healthcare decisions is still a long way away.

The Centre for eHealth & Wellbeing Research at the University of Twente is currently looking into the value of available data, seeking the views of Big Data experts and healthcare workers. A key finding from these affinity group-based studies is the importance of empowerment. Issues concerning data sharing and data ownership had been raised in these discussions, together with concerns over accountability of use. The development of trust remained a priority. It is not clear who really benefits from the use of big data, or who will be liable when things went wrong. Accountability plays a key role in the development of trust – how is the field to be regulated and who has to prove what?

There is a need for 'data wisdom'. Many people will have the ability to generate lots of data, but few will have the knowledge to analyse it. The need for both enhanced data education to support critical and creative thinking as well as multidisciplinary data skills has been recognised.

In discussing the importance of evidence to support the application of big data in medicine, Professor van Gemert-Pijnen suggested that researchers currently might be more focussed on

searching for patterns rather than testing hypotheses. Reference was made to the publication in 2015 of the Foresight report on the evaluation of new technologies in healthcare.

Research into big data by the University of Twente is currently focussing on three key areas:

- Personalized Health care (tailoring technologies to support health and well-being)
- Persuasive coaching using big data (e.g. forensic psychiatry; early warning systems to prevent & control infections (HRMO))
- Value based healthcare (empowerment, trust, wisdom and evidence)

The development of wearable technology for home and work use is being carried out in collaboration with key stakeholders (e.g. technology companies). An example of this is the Twente TEACH telemonitoring system for chronic heart failure. Big data-based 'persuasive technology' is being developed to better measure, aggregate and make sense of behavioural, psychosocial, biometric and geodata to develop personalized coaching programmes for use in forensic psychiatry. The University is also collaborating with others to make use of big data in infection prevention. Digital surveillance techniques are being developed to track and trace infections (e.g. MRSA) and to develop a predictive model to prevent outbreaks.

Other work in predictive modelling is also taking place in the integration of geospatial data with epidemiological and clinical data to develop a smart surveillance system. It was noted that a MOOC in eHealth would be available in 2016 to learn more about eHealth: [www.futurelearn.com/courses/ehealth](http://www.futurelearn.com/courses/ehealth)

**(Presentation available at [Big Data & Big Health: Personalized Medicine as a Paradigm Shift](#) )**

#### Comments arising from Professor van Gemert-Pijnen's presentation

Professor van Gemert-Pijnen's presentation stimulated much discussion on the ownership of the data arising from personalized medicine (and other) healthcare studies. Issues of ownership were becoming more complex as people start to generate more data themselves from their personal smart watch-based devices. This also raised issues concerning the duties of patients, as well as their rights, in using such technology. It was suggested that issues concerning the 'democratisation' of smart data use, together with the ethical and policy challenges ahead, could be part of a future EU H2020 project call.

#### **From Population and Personalized Genomics to Personalized/Precision Medicine.**

Prof. Manolis Dermitzakis (Department of Genetic Medicine and Development, University of Geneva (CH)) discussed recent advances in key areas of the analysis of the genomics of gene expression and cellular phenotypes in human populations and multiple tissues. He described progress in projects such as the 1000 Genomics and Genotype-Tissue Expression (GTEx) initiative – and how this is assisting in the interpretation of human disease variants. He also presented results from a number of studies that provide mechanistic hypotheses for the genetic effects on complex disease, and how these, and other related developments are contributing to the delivery of personalized medicine.

The current revolution in medicine has come about through both the new advances in technology, but also a deep learning of human biology. It is acknowledged that the human today is very complex, but human genetic variation is actually quite limited, and in looking at disease there is not that much variation that is needed to be understood. It is actually the environment (behaviour, infections, external factors, etc) that varies a lot, and hence how it interacts with the genome. There is a need therefore to find the imprints of the environment and to see what impact this has on our health. To put the genome in the picture there is a need to look at genetic variation in detail. Much work has been done in the field through the International HapMap project and its cataloguing of 'common' genetic variations. A more

comprehensive view is being developed through the 1000 Genomes Project, which is cataloguing 'all' genetic variations. The International Genome Sample Resource (IGSR) has been established to ensure the ongoing usability of data generated by the project.

With reference to Genome-Wide Association Studies (GWAS) in Crohn's disease, and expression QTL (eQTL) analysis, gene expression as a key molecular phenotype was illustrated. Professor Dermitzakis demonstrated that whenever genetic association exists it is one-dimensional and causal. GWAS have identified hundreds of common DNA variants associated with multiple complex diseases and traits. Ninety per cent of GWAS single nucleotide polymorphisms (SNPs) are not in coding sequences and lie in non-coding regions (e.g. intergenic and introns). Many studies have shown trait-associated SNPs enriched for expression QTLs, but there are challenges in using such eQTLs to interpret disease associations. It is hard to identify what tissues are mediating the effect. Most human tissue types needed for such studies are hard to obtain, and large sample sizes are required for the necessary statistical analyses. There is a massive diversity amongst tissues.

The GTEx initiative, which started in 2007, is seen as a way forward. It was established to provide a database of gene expression, regulation and eQTLs from a wide range of non-diseased human tissues. A biobank of tissues and DNA/RNA samples has been collected from 900 post-mortem donors, enabling whole exome and genome sequencing, together with RNA sequencing of approximately 30 tissues per donor. From this resource, it has been possible to link eQTLs to GWAS. This has demonstrated that the expression level of a gene is not that important. The GTEx atlas has enabled a matrix of tissue activity of GWAS in multiple tissues to be developed allowing correlations to be made, such as for Type 2 diabetes tissue activity. The tissues in GTEx can also be used as a reference when working at the imputation of expression values in study cohorts.

Turning to possible future developments in this field, Professor Dermitzakis emphasised the need for more understanding of human biology and how these studies could be implemented in medicine. There are currently a number of key components missing in the move from population and personal 'omics to personal biology. These include the need to interpret the non-coding genome, and an understanding of rare and private variants and environments, all of which were context dependence.

Professor Dermitzakis described the integrated nature of a 'learning human biology – implementing in medicine' approach in which new discoveries (drugs, biomarkers, knowledge of lifestyle effects etc) will influence future clinical trials. This will also help to understand more about how the genome and lifestyle choices will impact upon pharmacological interventions and disease manifestation, with this research leading on to new discoveries. In the future, each patient will become an individual research project. Much more investment in discovery research is going to be needed before direct medical applications will be forthcoming. This revolution in medicine is leading to a deeper understanding of the variability of the human body.

**(Presentation available at [The 1000 Genomes and Genotype-Tissue Expression \(GTEx\) Projects: New Results and Challenges](#) )**

### **From Biobanking to Precision Medicine**

Prof. Andres Metspalu (Estonian Genome Center, University of Tartu, Estonia) presented on the practical aspects of developing a gene bank in Estonia (population size approximately 1.3 million). He described the great potential that Estonia has to plan and implement personalized medicine solutions for the whole country. The Estonian Genome Center (EGC) is the research institute of the university, which also houses the Estonian Biobank. The longitudinal prospective and population-based biobank was established in 2000, and to-date more than 5% of the adult population (52,000 gene donors) has been recruited. The Government, under the terms of Estonia's biobanking legislation (the HGR Act) supports the Center financially. The main role

of the gene bank is to promote the development of genetic research, collect health and genetic information on the population, and to use the results of genetic research to improve public health. A detailed questionnaire completed by all donors has provided much data on health, diet, lifestyle, smoking and genealogy.

The population has been shown to be very close genetically. Estonians are generally supportive of the work of the Genome Center although almost 30% of the population have not heard of it as yet. When Estonia broke away from the USSR, it took the opportunity to introduce a completely new information system, and in the healthcare field, information is collected and collated relating to prescription data, patient information, and population statistics etc. All Estonian residents (aged above 15 years) must have an ID card, which enables secure digital authentication. Everybody in Estonia has their own National Patient Portal enabling medical data to be developed for over one million people. Information from the various national registries (population, cancer, TB, myocardial infarction etc), from the National Digital Health Record Data, etc, is fed into a central coding centre and a phenotype database. The Genome Center is able to monitor disease trajectory for all of the 50,000 subjects, linked to data from hospital clinical laboratories. With access to data from numerous sources (ADR diagnoses from electronic health records; drug prescription information from health insurance fund data; lifestyle information from the biobank questionnaire; and data on genome sequences etc), the Center is able to carry out pharmacogenomics studies. Subjects can be re-contacted for phenotyping allowing pharmacokinetic profiling to take place. The Center has also examined the incidence of coronary artery disease in individuals with a high genetic risk. This work has demonstrated the potential benefit (in terms of prevention of death) of targeting and treating those subjects with a high percentage of risk. Similar studies have been carried out in Type 2 diabetes where it was shown that the genetic risk score was the strongest predictor of the illness after BMI. (Läll *et al.* 2016).

Professor Metspalu described the importance of Clinical Decision Support Software (CDSS) in providing clinicians with the right knowledge at the most appropriate time. CDSS will become more important in this era of genomic medicine, for it has the potential to provide the necessary level of personalized guidance to providers at the point of care. He also postulated on the future of biobanking, suggesting that there was a need to merge the clinical and research cohorts, enabling better clinical information and research data to be generated.

The Estonian Government recently approved the establishment of a Personalized Medicine Pilot Program leading to the appointment of a senior ministerial role to promote E-Services and Innovation. Estonia has the potential to develop innovative personalized medicine solutions but many challenges remain. There needs to be greater awareness of the possibilities regarding personalized medicine, both within the general population and by the medical profession. The new technologies and data availability are leading to increased empowerment of patients who will need to consider the possibilities of managing their own health more. A number of ethical issues need to be addressed including the patient's right both to know and not to know information on their health, and how big data is to be used and protected. More needs to be known about the association between DNA variants and diseases. Finally, the need to keep the database of known risk variances updated will require a considerable ongoing workload. The high level of public trust and acceptance of the application of these technologies will make matters much easier.

**(Presentation available at [From Biobanking to Precision Medicine](#) )**

#### Comments arising from Professor Metspalu's presentation

It was acknowledged that the introduction of a personal ID card that could be used, not only as a donor card, but also to access individual patient portals, would be a major aspiration for most EU countries. Coverage was at 100% of the eligible population, and whilst there had been much discussion in Estonia on potential privacy issues, the people appeared to have fully embraced the system, with few concerns ever being raised.

Funding for the management of the Estonian Genome Center came from the Government (30%), from the EU and commercial companies (approx. 30%) and from local grants (30%).

### **Genomics-based Personalized Prevention**

Dr Hilary Burton (Director PHG Foundation, Cambridge (UK)) spoke on how the new genomic technologies may help solve many of the problems of healthcare, particularly relating to disease prevention.

The PHG Foundation, based in Cambridge, and a member of Cambridge University Health Partners, and the Cambridge Institute of Public Health (an independent think-tank/policy group) has been active since 1997 and has a specific interest in genomics and other emerging health technologies that can provide more accurate and effective personalized medicine.

Three key current challenges to healthcare are considered to be; demographic changes, greater patient expectation, together with the impact of new scientific and technological advances. Dr Burton said that the solutions to these challenges would be an increasing emphasis on prevention, patient empowerment and the radical re-organisation of healthcare, with a move from the hospital to the community. Genomics can play a major contribution to the understanding of disease risk. New biomarkers were helping to detect diseases earlier and well before the disease manifested itself.

It was noted that the traditional epidemiology and public health studies determinants of disease were environmental exposures (housing, water, infectious disease, and nutrition and chemical/physical agents) and social and behavioural factors such as poverty and lifestyle. Earlier work by the epidemiologist Geoffrey Rose on approaches tackling risk factors had distinguished those strategies aimed at populations which may bring large benefits to the community, but offers little to each participating individual, e.g. wearing seatbelts, to one that seeks to identify a minority with special problems who are at high risk (e.g. treating people with high blood pressure).

Personalized primary prevention recognises different types and levels of disease risk, and tailors the prevention according to the risk, making it more effective/cost-effective. Such an approach requires effective tests and interventions, avoiding those that are harmful. The same principles apply to genes and their interaction with the environment (e.g. via smoking, food, medicines, infectious agents, etc) and the differentiation between single gene disorders and multi-factorial disease.

Examples of personalized preventative interventions include the screening of new-born children (which can lead to dietary or drug intervention) and those for single gene disorders in adult life (e.g. breast cancer, cardiac arrhythmias, familial hypercholesterolaemia, etc.). New opportunities for screening were arising from whole genome sequencing initiatives.

Dr Burton referred to the multi-factorial roles that lifestyle and genes play in the development of diabetes. Obesity and a lack of exercise are important factors as are a genetic susceptibility (Type 1 or Type 2). The PHG Foundation has attempted to identify what influences the prevention of illness in other multi-factorial conditions such as coronary heart disease. Questions on diet and family history play a key role, but it is not clear whether knowledge of genetic involvement does help people to change their lifestyle. Much has been done on the interaction of genes with environmental factors such as food (as in coeliac disease, coronary artery disease); pollutants, medicines (e.g., CYP2D6 slow metabolisers); infectious agents and vaccines.

PHG has identified a number of key challenges in the development of personalized prevention. These include:

- Developing the evidence base. There are very long timescales involved when assessing disease prevention. Conventional epidemiological studies and randomised clinical trials have their limits in the provision of information on individual risks and their effect. The technologies involved are also constantly evolving.
- Integrating with other technologies. Genomics and an increasing number of new technologies are involved in data generation, data integration and data analysis.
- Empowerment of individuals for personalized prevention. As empowerment will lead to patients self-determining their own health and healthcare, and participating in shared decision-making, this will require a step-change in the response of health professionals, who are currently not well prepared for this. Understanding risks and genetics is complex and so there will be a need for more education, counselling and coaching.
- Ethics, legal and regulatory considerations. There will be numerous new regulatory complexities to consider in the future, including those related to the movement of health data across national boundaries, the rules covering the provision of genetic tests, etc
- The competence of health professionals. Very few medical specialists will escape the impact of genomics over the next few years, but most clinical specialties are not prepared for this. In the UK, the Royal College of Physicians has established an advisory group to look at future skills needs in genomic medicine, and has produced some educational material on this matter ([www.phgfoundation.org/education](http://www.phgfoundation.org/education)).
- Funding complementarity with public health programmes. This will require a cultural and educational shift for public health practitioners, but it is essential that complementarity be found between major public health programmes aimed at population determinants of health, and personalized prevention.

In conclusion, Dr Burton emphasised that prevention was an important aspect of the genomics personalisation agenda, but that this is not widely discussed. As she had described, to ensure effective implementation will require much more thinking on a range of issues, including the development of the evidence base.

**(Presentation available at [Genomics-based Personalized Prevention](#) )**

#### Comments arising from Dr Burton's presentation

Surprise was expressed that it had been shown that those individuals who are given information on their genome do not tend to change their lifestyle. Dr Burton noted that depending on the result of the test people do change their behaviour for a short time, do tend to worry about the implications of the outcome for a while, but then usually stop worrying and revert to their previous lifestyle.

Much interest was raised over the possibility of identifying the genetic influences affecting responses to vaccines. This was thought to be of particular relevance to those countries, e.g. France, where an increasing number of people are not getting themselves/their children vaccinated. Dr Burton suggested that although PHG was not looking into this at present she could see the possibility of identifying those people who may have an adverse effect or who may fail to respond. It was felt though that a much wider debate on the role of vaccination was needed. Some delegates argued that whilst the gaining of new data on the impact of genetics on variability of responses to treatment remained important, it would be wrong to focus on vaccines as they are working well.

## **SESSION 2: Personalized Medicine in Specific Disorders**

**Chairs:** Prof. Françoise Meunier (FEAM Vice President, Belgian Academy of Medicine) & Prof. Martin Schwab (Vice President SAMS)

### **New Diagnostics in Personalized Cancer Medicine**

Prof. Michael Neumaier (Institute of Clinical Chemistry, University Heidelberg, Mannheim, Germany) provided an overview of recent developments in laboratory (companion) diagnostics in oncology.

The deeper understanding of pathobiochemical principles in the development and progression of malignant disease and deciphering the affected pathways are currently enabling the design of specific targeted therapies for an increasing number of tumour entities. It was noted that to make proper use of such therapies, comprehensive and detailed molecular analyses ('companion diagnostics') must be carried out first for patient stratification.

Diagnostic tests have always been personalized and focused on the individual, unlike the available therapies. In the past primary tumour tissues have always been analysed by a pathologist, with any follow-up and assessment of metastasized disease being carried out by imaging and then measurement of serum tumour markers. In the future it is anticipated that both primary diagnosis and follow-up will be carried out through liquid profiling e.g. through assessment of CTC and DTC, fcDNA and use of digital PCR etc. The increasing importance of companion diagnostics in helping to define the relevant therapy was emphasised. Over the last few years there had been numerous drugs approved by the FDA and EMA that had been associated with eligibility testing arising from the FDA's Drug-Diagnostic Co-Development Initiative. Many such examples included the treatment of metastatic breast cancer with Trastuzumab/Lapatinib and the measurement of over-expression/amplification of HER-2, and the use of Gefitinib and Erlotinib for non-small cell lung cancers, with mutated EGFR etc. Professor Neumaier described some of the studies being carried out in colorectal cancer and the increasing number of molecules being used as potential druggable targets.

The use of companion diagnostics and the measurement of key biomolecules in plasma are starting to lead to 'actionable health information' and the improvement of treatment response prediction. Studies on the measurement of free circulating DNA (fcDNA) in the plasma had been difficult as the amounts of circulating tumour DNA (ctDNA) was quite small ( $\approx 0.01$ -10% of total), as compared to the quite diverse (and much higher) levels of classic plasma proteins. To analyse such small measures, the vein, which acts as the 'exhaust pipe' of tumours is being used, with digital and emulsion PCR techniques being developed for such enhanced detection. Since 2010, there has been a proliferation of publications on the potential applicability of the monitoring of fcDNA and ctDNA. From these studies it has been shown that the concentrations of ctDNA varies between different tumour types and between tumour stages.

In describing studies on the use of BRAF-inhibitor therapy in malignant melanoma, Professor Neumaier illustrated that although patients did well in the early stages of treatment, by week 23 survival rates had dropped indicating the need for combination therapy in such cancers. The BEAMing (Breads Emulsion Amplification Magnetics) method technology, which can carry out very sensitive detection of cancer-related and other genes, has been used in recent trials on malignant melanoma. The use of BEAMing in the liquid profiling of melanoma follow-up studies has been able to detect tumour resistance to BRAF therapy at a much earlier stage.

Research into next generation sequencing is leading to significantly improved predicting in the use of molecular profiling of ctDNA for application in companion diagnostics. It was noted that in only a few years there had been key changes in molecular diagnostic strategies, as had been predicted by improvements to the performance of liquid profiling of ctDNA in peripheral blood. As recent as 2014 the taking of a tissue biopsy had been considered the first step prior to the

sampling of blood. The drawing of blood is now advocated as the first step (instead of tissue) and with cell-free DNA becoming the norm for longitudinal studies.

In conclusion, Professor Neumaier summarised how modern laboratory diagnostics in oncology are helping to detect the driver defects of tumours thus changing therapy regimens. They could detect minimal residual disease from blood samples, and will reduce the need for tissue sampling due to the availability of genetic footprints in the blood, measured by liquid profiling and biopsy.

**(Presentation available at [New Diagnostics in Personalized Cancer Medicine](#))**

## **Quantified Self Devices in Neurological Disorders**

Prof. Philippe Ryvlin (Department of Clinical Neuroscience, Centre Hospitalier Universitaire Vaudois, Lausanne) presented a clinician's perspective on the growth of the 'quantified-self' technologies and on their compatibility (or not) with precision medicine. The speed of scientific development in this field has been rapid, whereas the move towards regulatory oversight has been slower. In 2015, the Precision Medicine Initiative Working Group of the Advisory Committee to the NIH Director hosted a public workshop on the scientific methodological and practical consideration of including mobile and personal technologies into research programmes, indicating that progress was starting to be made in this field.

The concept of the quantified-self first arose in the late 1960s in the context of holistic approaches to health and the desire to see and monitor 'anything, anytime and anywhere'. Formal definitions were developed around 2007 through the collaboration of users and toolmakers with a shared interest in self-knowledge through self-tracking. This has led to the incorporation of technology (wearable sensors and computing) into data acquisition on aspects of people's daily lives in terms of inputs, states and performance. Quantified self-advancement has allowed individuals to quantify a very wide range of biometrics, and make data collection cheaper and easier. Numerous devices (mainly fixed) are now available for the monitoring of many different body systems including for the eyes, feet and even through underwear (where a carbon electrode can measure blood pressure and heart rate). Most quantified-self devices have however been developed for wearing on the wrist – via bracelets and wristwatches. The main sensors used in such wrist devices are either actimetry-based, used to measure skin conductance, or through pulse/EKG monitoring. None of these approaches was considered to be perfect as the results may be difficult to capture or interpret.

More recently small biosensor tattoos have been developed that can monitor electrolyte and metabolite levels in sweat. Professor Ryvlin emphasised the importance of the development of an appropriate biosensor if current neurological needs were to be addressed through such devices. Some work had been done in epilepsy and the development of devices that could detect imminent seizures. The monitoring of electrodermal activity could theoretically assist in the monitoring of some diseases, but few studies have been shown as yet to allow any specific prognoses. There are many neurological needs that in time could be addressed using quantified-self devices. At present, none of the devices provides any real advantages and are not reliable enough. The current needs include:

- Stroke: quicker acute management prevention/anticipation
- Epilepsy: seizure detection and management
- Alzheimer's disease: manage behavioural comorbidities, detection
- Parkinson's: optimise schedule and dosage of treatment
- Depression/bipolar: anticipate (and prevent) recurrence
- Anxiety: anticipate (and prevent) attacks.

It was noted that in Europe more than one in two people suffers from at least one illness of the nervous system, which represents a cost of €800 billions/year (5% of GDP). Many European health decision-makers, Professor Ryvlin suggested, are beginning to see that the new

quantified-self technologies might be the only short- and medium-term solutions to prevent the exponential cost of these diseases. However, although there were more than 165,000 mobile health applications available in 2016, with more than 1.7 billion downloads expected during 2017, only a few hundred of them have been approved as yet by the FDA, or even tested with results published in peer-reviewed journals. In the USA, almost half the population are thought to have at least one wearable device and further growth is anticipated. It will however take many more years for such new technologies to be able to fulfil current expectation of their usefulness.

In addition to the NIH initiative mentioned earlier, Professor Ryvlin pointed out that the EU has started to develop guidelines on the assessment of the reliability of mobile health applications. There will be a continued need for randomised clinical trials for the devices, but a different (and quicker) model to that used to assess pharmaceuticals is needed. To assist in this ongoing evaluation, the University of Lausanne is developing a new platform (Neurotech) for the evaluation of the impact of mHealth developments.

In summary, it was proposed that mobile health and wearable devices did offer high potential to reduce the burden of brain diseases. There is some synergy in their application with that for 'omics in precision medicine (gene-environment). The technology is not yet fully mature for most applications, but this was coming. A high level of evidence will be needed for their use.

#### Comments arising from Professor Ryvlin's presentation

Professor Ryvlin was asked to expand on his comments about the need for randomised clinical trials on mobile health devices, and on whether there was a need for other methods to assess the value and maturity of the technology. He considered that there was a need for these devices to be assessed for their quality, safety and efficacy as for all potential medical interventions.

The importance of investing in technology and new sensors to examine what was going on in the brain was acknowledged, but it is noted that the current approach was very invasive. A non-invasive approach was needed.

#### **Metabolomics and Personalized Medicine**

Prof. Oscar Yanes (CIBERDEM & Rovira i Virgili University, Tarragona (Spain)) presented on how a qualitative and quantitative analysis of metabolites (the functional output of cellular reactions) was contributing to personalized medicine. He described an untargeted metabolomics platform that provides a method for identifying cellular pathways that are perturbed during disease. He demonstrated the application of the technology in uncovering the metabolic derangements that determine the long-term health risks of hyperinsulinaemic androgen excess in prepubertal and pubertal girls.

The classical flow of information has been from the genome (genes) via the transcriptome (mRNA) to the proteome (proteins). This view has changed considerably with the greater understanding of the metabolome, which is now known to be larger and more complicated. At the same time, the microbiome (little of which is currently understood) and the external environment has an effect on the metabolome, which together will all have an effect on the regulation of gene expression.

Metabolites are used in clinical practice every day. Changes in metabolite concentration have served as the basis for the development of more than 180 different chemical or metabolite biomarker tests, for example; anaemia, gout, diabetes and atherosclerosis. The current wide range of metabolomics applications included the development of diagnostic and prognostic markers, drug toxicity assessment, measuring drug response and seeking mechanistic insights. Researchers active in the field of metabolomics will need to have cross-disciplinary expertise in electronic engineering and signal processing, analytical and organic chemistry, biostatistics and physics. A recent report by Samino *et al* (Scientific Reports, 2015) had demonstrated that

metabolomics was able to reveal impaired maturation of HDL particles in adolescents with hyperinsulinaemic androgen excess (HIAE). The HIAE in non-obese pre-pubertal and pubertal girls resulted in long-term health risks in adulthood, including anovulatory infertility, Type 2 diabetes and metabolic syndrome.

Professor Yanes described the work his department had carried out to find out what was the molecular evidence of these long-term health risks. LC-MS metabolomics studies of plasma from the HIAE girls revealed redox deregulation, including alteration of most intermediates of the gamma-glutamyl cycle involved in glutathione biosynthesis. Following the development of an NMR-based methodology to characterise lipoprotein subclasses, the alteration of the VLDL, LDL and HDL serum profiles in the adolescents with HIAE had been examined. There was a lower percentage of large HDL particles in the HIAE adolescents, compared to controls.

It had previously been reported that methionine oxidation impaired reverse cholesterol transport by apolipoprotein A-1 leading to impaired maturation of HDL particles. The possibility of increased levels of free Metox in HIAE plasma reflecting greater oxidation of methionine residues in Apo-A1 of HDL particles was proposed. More recently, a number of publications had demonstrated that low sugar consumption was associated with increasing HDL levels in females during adolescence, and that excessive sugar intake in combination with hyperandrogenism causes oxidative stress. This work had led to the development of a proposed mechanism to explain the long-term health risks of hyperinsulinaemic androgen excess, in which a high glucose intake led to oxidative stress, causing lipoprotein modification (oxLDL and oxHDL) leading to hypertriglyceridemia, or impaired fasting glycaemia and impaired glucose tolerance. This in turn led to an increased risk of metabolic syndrome, diabetes and cardiovascular disease.

Professor Yanes also described some recent studies in drug responses in HIAE adolescents. It is known that in adolescents with PCOS, oral contraceptives can cause a reduction of hirsutism, acne and seborrhoea. They can lead to anovulation and pseudo-menses, and lead to weight gain. The use of metformin, AR-Blockade and low-dose pioglitazone in non-obese adolescents had been known to have many normalising effects, including on: hirsutism, insulinemia, lipidemia and IMT, adiponectin and body composition (more lean mass). Measuring the metabolic changes in HIAE adolescents after being given 18 months of low dose PioFluMet polytherapy had provided evidence of insulin levels being returned to (almost) control levels.

**(Presentation available at [Metabolomics and Personalized Medicine](#) )**

#### Comments arising from Professor Yanes' presentation and general discussion

With the increased sensitivity and speed of the equipment being used to measure biomarkers, Professor Yanes was asked about the likelihood of high throughput screening systems being developed in the near future. In response, it was suggested that what was important was the reliability and reproducibility of the biomarkers. This would influence their implementation into the clinic.

The challenge of implementing the use of possibly many thousands of metabolite-based biomarkers into the clinic was raised. It was acknowledged that much of the work in this field was still at the early discovery stage, but once such biomarkers were used routinely, they must be accurately quantified. It was noted that very little had been published on the evidence base for the validation of the techniques used in mobile biosensor devices. Very little raw data are available on how such devices function, nor has there been much independent analysis. It was suggested, however, that some of the diagnostic techniques currently being developed would enter clinical practice without being validated, where they will act as predictive models. An expectation of precision may not always be required. It was noted that the FDA had recently banned the promotion of some of the DNA tests offered by the company 23andMe, but that the same restrictions did not appear to be the case for many of the available mobile apps/devices.

It was suggested that the development of guidance in this field by the EU would lead to changes in practice over the next year or so.

### **SESSION 3: Personalized Medicine – New Dimensions and Ethical Issues**

**Chairs:** Prof. Maria do Ceu Machado (FEAM Vice President, Portuguese Academy of Medicine) & Prof. Christian Kind (President Central Ethics Committee of SAMS)

#### **The Ethics of Personalized Medicine**

In introducing this presentation, Prof. Effy Vayena (Health Ethics and Policy Lab, University of Zurich) sought to emphasise that ethics should not be seen as an obstacle to progress in the development of precision/personalized medicine. It would be a narrow concept to focus only on the constraints of ethics, and consideration should be given to how ethics can act as enablers.

The context in which the goals, processes and capabilities in the field of precision medicine are being progressed out has been shifting somewhat. The individual patient has become an enormous repository of information. Personalized medicine is now seen as the only way to define wellness and its progression to disease, rather than traditional medicine that defines disease and its progression to death. It was suggested that we were now at an inflexion point in the move from simple data collection to a greater understanding and integration of the information and its application to patients. A knowledge network is being established, built on developments in genomics, the microbiome, behavioural studies, clinical tests and participant-contributed data etc, but this now needed to focus on the needs of the individual participant. Numerous 'apps' have been developed allowing the collection of enormous amounts of health-related data (sleep patterns, heart tracking, glucose level, blood pressure etc) to be collected. Some, but not all, of these will prove to be useful.

Referring to a review by Weber *et al* (JAMA, 2011), Professor Vayena described the current 'tapestry' of potentially high-value information sources that may be linked to an individual for use in health care. A large data trail is being left behind by all of us, based on our medication use, social network information, credit card purchases and family tree searches, etc.

The development of the 'Big Data' ecosystem in biomedicine was beginning to lead to some new tensions. Some of these included:

- Data taxonomies – involving all data sources
- The development of 'black box' methodology and the uncertainty of why something is being measured
- The increasing porosity between the boundary of research vs. clinical activity (especially in genomics) and the impact this may have on the ethical framework in which studies are carried out
- The growing lack of distinction between the use of big data by public and private ventures
- The emergence of new 'actors' in the business of medicine and the uncertainty being caused by the involvement of for example, data companies such as Google in the use of National Health Service data
- The development of new partnerships

With all of these developments, it was suggested that it now needed to be asked whether existing ethical and regulatory frameworks were fit for purpose for precision medicine.

Professor Vayena pointed out that President Obama, in launching the US Precision Medicine Initiative earlier in 2016, had himself raised concerns over the possible misuse of his personal data, and its possible commercialisation in some way that he would not know about. He had also expressed the wish that a series of structures would be set up that would make him

confident that his data would be used appropriately. These concerns and the comments he had made on the ownership of information arising from tests on his genes were not new. Issues around autonomy, exploitation, trust, fair benefit-sharing, control and competing interests have been at the heart of the ethical debate on this matter for some time.

It was acknowledged that many of the ethical problems regarding data use are being solved through the current consent process. This remained a necessary part of the regulatory framework, but it was questioned whether it was still sufficient. There are now immense possibilities on how the data could be used, with many of them currently unknown. The scope of the 'digital trail' and the increased 'fuzziness' around the public-private interface suggested that more needed to be done. An illustration of this was the outcome of the genome data studies (on GWAS, MYL4, ABCB4 and SLC52A2) carried out in Iceland. Data now owned by the commercial organisation DeCode could be used to predict the DNA makeup of the whole island, which meant that the company is now able to tell all individuals information on their cancer risks, including those who had not given consent for their data to be used,.

Privacy is now an important issue, and organisations such as the World Privacy Forum were trying to help establish better security and legal systems to protect patients (in the context of the Precision Medicine Initiative). Trust in how genomic data is used is closely related to privacy. Looking to the future, Professor Vayena put forward some suggested solutions to the challenges that had been identified. A more innovative approach is needed on how context was obtained. There is a need for new privacy tools, including increased use of encryption, data tags and the development of differential privacy.

More importantly, there is a need for a better partnership with the patient, citizens and the public in general. Patients needed to be empowered more through access to better education and the right tools to help them make decisions. Issues of governance could be addressed through a better partnership with citizens and the importance of the right levels of accountability could be developed through the right relationship with the public.

**(Presentation available at [The Ethics of Personalized Medicine](#) )**

#### Comments arising from Professor Vayena's presentation

In the context of the activities of a South African company that was collecting information on activity, lifestyle, etc from many people to whom they had given smart watches, it was suggested that we were entering into a new field of discrimination. Many poorer people would not benefit from this work, as they would have no money to go to the gym, eat the right food, and less time to participate in such studies.

#### **Assessing the Human Gut Microbiota in Metabolic Diseases**

Prof. Jens Nielsen (Department of Biology and Biological Engineering, Chalmers University of Technology, Gothenburg (Sweden)) reported on recent studies based on the correlation of the composition of the human gut microbiome with a wide range of different diseases, including Type 2 diabetes, depression, malnutrition and cardiovascular disease.

The Systems and Synthetic Biology ([www.sysbio.se](http://www.sysbio.se)) Division at the Chalmers University of Technology has reconstructed a comprehensive genome-scale metabolic model (GEMs) for human metabolism (HMR2.0) used for the analysis of tissue specific metabolism. This is being combined with GEMs for the gut microbiome, enabling a complete description of human metabolism to be obtained. Using RNAseq from 32 tissue biopsies, GEMs have been generated for 32 tissues and organs with unique metabolic functions being identified for each tissue. Using this model, six sub networks have been identified, one of which is responsible for chondroitin sulphate and heparin sulphate. Analysing these substances in patients with metastatic ccRCC has led to the identification of a prognostic biomarker with strong predictive strength.

The human body contains 10 times more bacteria, archaea, fungi and other microorganisms than human cells. The make-up of this human microbiome changes with age. The gut microbiome can be analysed using metagenome analysis of total DNA extracted from faecal samples, leading to the generation of very large datasets. Using the 'Bioinformatics pipeline for MEtagenomic Data Utilisation and Analysis' (MEDUSA) provides relevant biological meaning. Following a recent meta-analysis study, a global gut microbiome gene catalogue has been prepared in which 11.7 million genes have been identified with nine million genes unique to a single study. However, despite this large diversity there was much overlap, with approximately 500,000 being core to all of the studies.

From extensive metadata studies, it was shown that symptomatic atherosclerosis is associated with an altered gut microbiome, and with particular bacterial species. Phytoene dehydrogenase was shown to be enriched in control groups.

The relevance of the microbiome has also been demonstrated in Type 2 diabetes (T2D). Using samples from one DNA study (a large Swedish study on the development of T2D in elderly women) it was demonstrated that there is a clear correlation of blood markers for diabetes with an abundance of various bacterial species. An understanding of this correlation could help in the treatment of T2D in the future.

These studies have started to lead to the development of a working model for microbiota, diet and host interactions, providing functional insight to the impact of the individual bacterial species involved. In the model, metagenomics will be able to identify associations and biomarkers, and will provide a catalogue of genes, and thus the generation of hypotheses. Modelling can then generate and test various hypotheses and provide detailed mechanistic understanding. All of this will be able to provide biomarkers and new interventions in the medical field, and will be used in the design of new medicines and probiotics for the healthcare and food sectors.

One such working model that has recently been developed is the MicroObese study in which it was illustrated that overweight subjects have a varied gut microbiome composition. The study sought to quantify diet-induced metabolic changes of the gut microbiome. Metagenomics analysis had revealed the prevalence of five dominant bacterial species. Those subjects in the study with a low bacterial diversity were not as effective in responding to dietary interventions (as measured by plasma amino acid levels) compared to those with a high bacterial diversity (a high gene count). The low bacterial diversity could therefore be used as a risk factor for other subjects.

Professor Nielsen's team has used GEMs to study the interactions between all key gut microbes, using metagenomics data from the USA (HMP) from Denmark (HIT) and from China and Sweden to identify key species abundance. One hundred and thirteen species have been identified to be of high abundance in all four studies. Further study on 107 of these species has indicated that competition, not cooperation, dominates metabolic interaction between gut microbes.

Professor Nielsen's research team is currently collaborating with the Bill & Melinda Gates Foundation using their genome-scale metabolic models to find innovative solutions to the problem of malnutrition and child growth and development in Africa.

Looking to the future, over the next three to five years, Professor Nielsen believes that the research he described will lead to new therapies, particularly in the development of second-generation probiotics for the treatments of Type 2 diabetes, and combination drugs for cancer treatment. The use of gut metagenomics will play a key role in personalized medicine, in stratifying responder and non-responders to immuno-therapies in cancer treatment.

**(Presentation available at [Assessing the Human Gut Microbiota in Metabolic Diseases](#) )**

## **The Increasing Opportunities for using Health Data as a Tool for Clinical Research**

Prof. Dipak Kalra (The EuroRec Institute, London (UK) and the European Institute for Innovation through Health Data, Brussels) described how European public-private projects supported by the EU/industry-funded Innovative Medicines Initiative (IMI) had been contributing to improved patient recruitment into Phase III clinical trials. Secure remote querying of de-identified hospital electronic health record information was being developed via two IMI projects (EHR4CR- Electronic Health Records for Clinical Research, and EMIF- European Medical Information Framework.)

Professor Kalra opened his presentation by referring to the healthcare challenges facing society. There is a requirement for new, safer, more effective medicines in areas of changing medical need. With the pressure on healthcare budgets, there is a focus on best practice care and on the value of interventions. Although a large number of medicines are currently in development - to leverage new science, expand treatment options, improve quality of life and provide value for money - there remained a need to accelerate innovation in the life sciences. Identifying and recruiting suitable patients and trial sites are principal causes of clinical trial delays.

Only 18% of clinical studies in Europe (7% in the USA) complete subject enrolment in time. It is estimated that each day a drug is delayed from the market; the sponsors can lose up to \$8 million. It was now hoped that the growth in use of electronic health records (EHRs) in hospitals could help provide a solution to the patient recruitment challenge. The use of EHRs has moved to being more patient-centred, multi-disciplinary, structured and coded (allowing for improved semantic interoperability). More metadata was being collected, together with coding at a granular level. These developments had led to the formation of the IMI project EHR4CR, established to provide a platform for the trustworthy re-use of EHR data to support innovation in clinical research and healthcare operations. Thirty-five partners (10 of which were pharmaceutical companies) had participated in the five-year project, EU funding of which had recently come to end prior to its transition to a new sustainable platform. This platform can connect securely to the data within multiple hospital EHR systems and clinical data warehouses across Europe. It enables trial sponsors to predict the number of eligible patients for a candidate clinical trial protocol, assess its feasibility and locate the most relevant hospital sites. It also enables connected hospitals to efficiently identify and contact eligible patients for particular clinical trials. The commercial version of the platform 'In Site' has protection measures in place that ensures individual patient data never leaves the hospital.

A multi-stakeholder based 'Champion Programme' was established during 2015-16 to further validate and improve the technology, start building a network of participating hospitals, and to engage with the recently established European Institute for Innovation through Health Data (i-HD), set up to promote best practice and provide independent governance of the EU health data re-use ecosystem. Participating hospitals did need some time to ensure that their own internal assurance systems were in place, but they clearly saw the value of being involved. Participation was leading to better patient care, better quality data, enhanced reputation and an increased income from clinical trials.

The main goal of the other IMI EHR-focused project, EMIF, was to become a trusted European hub for healthcare data intelligence. As a gateway, EMIF supported the flow from data discovery to data access and data reuse. There was a large variety in the 'types' of data available to members of the EMIF consortium, including primary care, hospital, administrative, registries and biobank data. Data is available from more than 53 million subjects from eleven EU countries.

The targeting of therapies to the right patients was all about grouping patients to the target disease. Identifying clinically significant patient subgroups was a key element of any personalized healthcare strategy. This was helping to better understand disease diversity,

identify differences between patients, and identify the best drug target – all bringing clearly defined benefits for patients.

Following on from the work of the EHR4CR and EMIF projects a new neutral and not-for-profit organisation (the European Institute for Innovation through Health Data: i~HD) has been established to help grow trust across the EU in the use of EHR data, and to improve data interoperability. i~HD was helping in the response to a convergence of clinical research and healthcare needs, and in particular the need to remove the bottlenecks in accessing and combining health data from diverse sources across Europe. There is a need to optimise clinical research processes, enhance access to Real World Data, and improve the quality, safety and efficiency of care.

i~HD will seek to promote the adoption of healthcare standards and of data quality to enable more effective, safer and better-integrated healthcare. It will act as a connector between healthcare and clinical research standards. It will also promote to society the importance of using health data for research. Of equal, if not greater importance, will be its work in promoting the value to be gained from the use of health data. There is clear value to healthcare, to patients and society and to research, but this balance is currently poorly communicated to the average EU citizen.

**(Presentation available at [The Increasing Opportunities for using Health Data as a Tool for Clinical Research](#) )**

#### **SESSION 4: Perspectives for FEAM**

**Chair:** Prof. Dermot Kelleher (former FEAM President, University of British Columbia, Vancouver)

##### **Round-table discussion panellists:**

Prof. Maria do Ceu Machado (FEAM Vice President, Portuguese Academy of Medicine)

David Hans-U Haerry (European AIDS Treatment Group (EATG) and Positive Council Switzerland)

Prof. Peter Meier-Abt (President of SAMS)

Prof. Françoise Meunier (FEAM Vice President, Belgian Academy of Medicine)

Dr. Joachim Reischl (VP & Head of Policy, Portfolio and Externalisation in Personalized HealthCare and Biomarkers, AstraZeneca)

Prof. Effy Vayena (Health Ethics and Policy Lab, University of Zurich)

Prof. Andreas Wallnöfer (Head Personalized Health and Translational Medicine, University of Basel)

A wide range of issues was raised in the roundtable discussion, with contributions from the panellists and from the other delegates. Key topics addressed in this session included:

- Isn't precision medicine just good medicine?
- If every patient is to become a research subject and every physician an investigator what new skills sets will be needed in the future?
- How will the research community deal with the scale of data challenge with information now available on epigenomics, metabolomics, genomics and the phenome?
- What role will personalized medicine play in public health, and when will its implementation really begin?
- Personalized medicine is playing an important role in oncology, but how will it influence the pattern of decision-making in, for example, chemotherapy?

Some of the initial observations made by the panellists included:

- The essence of being human, and the desire to take risks (informed and uninformed) does not lend itself to the idea of being permanently monitored. There may be some future societal opposition to this, and to the growth of the associated technology. Every generation needs to redefine the basis of its civil liberties, and more dialogue will be required.
- There is now an expectation, within the general population, by the media, patients and by some clinicians that new discoveries in biomedicine (e.g. the possible identification of disease-related genes) will lead to immediate treatments. The provision of false hope to patients was thought to be harmful
- It was felt that precision medicine is what clinicians have always practiced; but what has changed is the availability of supportive technology
- It was suggested that special attention should be given to the challenges of involving young children in such personalized medicine studies. Not everybody should be a research subject, and there will be ethical issues in screening young subjects who may not want to be involved
- The increasing complexity of data arising from research studies is a matter of concern. Far too much of the data cannot be interpreted, and physicians do not know what to do with much of the data with which they are being presented.
- It was strongly suggested that there still is much inefficiency in the current clinical trial process, and more needed to be done on the validation of such studies. There is a need for more challenge between the commercial and academic sectors on how to get more value out of clinical trial data. The increased transparency of all clinical trials is helping here.
- Precision medicine was already changing how commercially sponsored clinical trials were being run. In the past companies may have had to run numerous such studies simultaneously, but precision medicine has greatly improved clinical trial design with a reduction in studies needed. Following many failures in the past in getting innovative new medicines through the pipeline, the pharmaceutical industry is increasingly following a precision medicine- based approach, leading to an increased success rate.
- It was felt that there is a need to look at data from a more holistic perspective, recognising that if data can be collected in a way that respects the patient it could be more valuable
- Patients may have more trust in their physicians in the handling of their healthcare data and tissue samples than is anticipated. The development of trust is an important factor, and patients do need to know that their data will be protected.
- It was suggested that there was still a significant lack of understanding in the general population on how precision medicine/personalized health is being developed and the potential benefit it may bring
- Noting that the governments of some countries were providing much financial support for research in this field, on the understanding that it would lead to clear health benefits, it was suggested that other research fields needed to be identified that could lead to public health benefits. Hepatitis C was considered one possible target for such studies. At the same time, the encouragement of patient participation in clinical testing was thought to be a concrete step that governments could take. There was agreement that any discussion on public health cannot be separated from a consideration of health economics.
- The economic benefits of focussing personalized healthcare more on the prevention of disease, than just on drug treatment was raised. The challenges of providing preventative interventions to people who were not yet sick were noted.
- The important issue of the quality, rather than quantity of available data was raised. At present it was felt that pharmacogenomics was not really being used properly to prevent drug side-effects

- It was understood that patients participating in precision medicine studies could face increased challenges in obtaining life insurance, depending on the outcome of the trial. This may be less of an issue in the EU compared to the USA
- Finally, it was strongly suggested that more needed to be done in addressing multiple morbidities, recognising that as patients get older they will face more illnesses and get numerous conditions.

## **Appendix 1 AGENDA**

### **Welcome and Introductions**

Prof. Peter Meier-Abt (President, SAMS)  
Prof. Bernard Charpentier (FEAM President, French Academy of Medicine)  
Dr. Gregor Häfliger (Vice President, State Secretariat for Education, Research and Innovation)

### **SESSION 1: National and International Networks**

**Chairs:** Prof. Bernard Charpentier (FEAM President, French Academy of Medicine) & Prof. Peter Meier-Abt (President SAMS)

**Connecting Europe for Genomic Health** Dr Elmar Nimmesgern (Deputy Head of Unit, DG Research & Innovation E2 Innovative and Personalized Medicine, European Commission)

**Big Data & Big Health: Personalized Medicine as a Paradigm Shift** Prof. Lisette van Gemert-Pijnen (Center for eHealth & Wellbeing Research, University of Twente (NL))

**The 1000 Genomes and Genotype-Tissue Expression (GTEx) Projects: New Results and Challenges** Prof. Manolis Dermitzakis (Department of Genetic Medicine and Development, University of Geneva (CH))

**From Biobanking to Precision Medicine** Prof. Andres Metspalu (Estonian Genome Center, University of Tartu (EST))

**Genomics-based Personalized Prevention** Prof. Hilary Burton (Director PHG Foundation, Cambridge (UK))

### **SESSION 2: Personalized Medicine in Specific Disorders**

**Chairs:** Prof. Françoise Meunier (FEAM Vice President, Belgian Academy of Medicine) & Prof. Martin Schwab (Vice President SAMS)

**New Diagnostics in Personalized Cancer Medicine** Prof. Michael Neumaier (Institute of Clinical Chemistry, University Heidelberg, Mannheim (D))

**Quantified Self Devices in Neurological Disorders** Prof. Philippe Ryvlin (Department of Clinical Neuroscience, Centre Hospitalier Universitaire Vaudois, Lausanne (CH))

**Metabolomics and Personalized Medicine** Prof. Oscar Yanes (CIBERDEM & Rovira i Virgili University, Tarragona (E))

### **SESSION 3: Personalized Medicine – New Dimensions and Ethical Issues**

**Chairs:** Prof. Maria do Ceu Machado (FEAM Vice President, Portuguese Academy of Medicine) & Prof. Christian Kind (President Central Ethics Committee of SAMS)

**The Ethics of Personalized Medicine** Prof. Effy Vayena (Health Ethics and Policy Lab, University of Zurich (CH))

**Assessing the Human Gut Microbiota in Metabolic Diseases** Prof. Jens Nielsen  
(Department of Biology and Biological Engineering, Chalmers University of Technology, Gothenburg (S))

**The Increasing Opportunities for using Health Data as a Tool for Clinical Research** Prof. Dipak Kalra (The EuroRec Institute, London (UK))

#### **SESSION 4: Perspectives for FEAM**

**Chair:** Prof. Dermot Kelleher (former FEAM President, University of British Columbia, Vancouver)

#### **Round Table discussion participants**

Prof. Maria do Ceu Machado (FEAM Vice President, Portuguese Academy of Medicine)

David Haerry (European AIDS Treatment Group (EATG) and Positive Council Switzerland)

Prof. Peter Meier-Abt (President of SAMS)

Prof. Françoise Meunier (FEAM Vice President, Belgian Academy of Medicine)

Dr. Joachim Reischl (VP & Head of Policy, Portfolio and Externalisation in Personalized HealthCare and Biomarkers, AstraZeneca)

Prof. Effy Vayena (Health Ethics and Policy Lab, University of Zurich)

Prof. Andreas Wallnöfer (Head Personalized Health and Translational Medicine, University of Basel)

### Biographical details of main speakers

#### Session 1: National and International Networks

##### **Connecting Europe for Genomic Health**

###### **Dr Elmar Nimmesgern**

*Deputy Head of Unit, DG Research & Innovation, E2 Innovative and Personalized Medicine, European Commission*

Elmar Nimmesgern is the deputy Head of Unit, horizontal aspects of health research in the Commission's research and innovation DG. He has been with the European Commission since 2000, following different aspects of health research. Previously he worked 5 years in a biotech/pharmaceutical company in Cambridge/MA – USA. Elmar Nimmesgern is a biochemist by training and performed cell biology research at the University of Munich and at Memorial-Sloan-Kettering Cancer Center in New York.

##### **Big Data & Big Health: Personalized Medicine as a Paradigm Shift**

###### **Prof. Lisette van Gemert-Pijnen**

*Center for eHealth & Wellbeing Research, University of Twente (NL)*

Lisette van Gemert-Pijnen is a full professor at the University of Twente in Persuasive Health Technology. She has an appointment at the University Medical Center Groningen and University of Waterloo (Canada). Lisette founded and coordinates the first Center for eHealth & Wellbeing Research ([www.ehealthresearchcenter.nl](http://www.ehealthresearchcenter.nl)). Her research & tuition focuses on persuasive designs to increase trust, engagement and adherence to technologies, persuasive health technology lab ([www.cewr.nl](http://www.cewr.nl)).

Lisette collaborates with the University of Groningen (UMCG, medical department) and with Zorginstituut Nederland (National Health Care Institute) in ePublic Health research. In Persuasive Technology, she cooperates with Prof Dr H Oinas-Kukkonen, from Oulu University, Finland.

Lisette is a chief editor of the International Journal on Advances in Life Sciences and she belongs to the editorial board of Medical Informatics and Decision making. Lisette participates in the scientific board of eTelemed conferences ([www.iaria.org/conferences](http://www.iaria.org/conferences)) and the association for health informatics (NIHI) Canada ([www.nihi.ca](http://www.nihi.ca)). Lisette organized the first international conference on eHealth in the Netherlands ([www.medicine20congress.com](http://www.medicine20congress.com)), and she organizes the annually conferences "Supporting Health by Technology" ([www.healthbytech.com](http://www.healthbytech.com)).

In 2011, Lisette developed the CeHRes-Roadmap, a process guideline for development, implementation and evaluation of eHealth technologies ([www.cewr.nl](http://www.cewr.nl); papers). The roadmap is based on research in business modelling, persuasive technology and health psychology. The roadmap and its accompanied tools and instruments for development, implementation and evaluation have been used in several (inter)national eHealth projects. Lisette was editor of the first academic eHealth book for research and education, improving eHealth (2013), and contributed to several books in research methodology, dementia care and eHealth for professional education (target group applied universities).

##### **The 1000 Genomes and Genotype-Tissue Expression (GTEx)**

###### **Projects: New Results and Challenges**

###### **Prof. Manolis Dermitzakis**

*Department of Genetic Medicine and Development, University of Geneva (CH)*

Emmanouil (Manolis) Dermitzakis is currently a Professor of Genetics in the Department of Genetic Medicine and Development of the University of Geneva Medical School. He is a

member of the executive board of the Institute of Genetics and Genomics in Geneva (iGE3), a member of the Swiss Institute of Bioinformatics.

He obtained his B.Sc. in 1995 and M.Sc. in 1997 in Biology from the University of Crete (Greece) and his PhD in 2001 from the Pennsylvania State University in the USA, studying the evolutionary biology and population genetics of regulatory DNA in mammals and *Drosophila*. His post-doctoral work was at the University of Geneva Medical School, focusing on comparative genome analysis and the functional characterization of conserved non-genic elements. He, previously, was an Investigator and Senior Investigator at the Wellcome Trust Sanger Institute in Cambridge from 2004 to 2009. He was elected an EMBO member in 2014 and has also been named Highly Cited Researcher by ISI in 2014 and 2015. He served as the president of the Executive Board of the World Hellenic Biomedical Association (2014-2015).

His current research focuses on the genetic and molecular basis of human disease. He has authored and co-authored more than 150 papers in peer-reviewed journals and many of them in journals such as *Nature*, *Science* and *Nature Genetics*, his papers have been cited more than 35,000 times and his H-index is 68. His research is supported by the Louis-Jeantet Foundation, the Wellcome Trust, the Swiss National Science Foundation, the European Commission, the Juvenile Diabetes Foundation and the US National Institutes of Health (NIH). He is also the recipient of a European Research Council (ERC) grant. He has given invited talks and keynote lectures in >120 conferences in some of the most prestigious genetics meetings and is the organizer of multiple training courses including the Wellcome Trust HapMap course and co-founder and co-organizer of the Leena Peltonen School of Human Genomics. He has served as an analysis co-chair in the pilot phase of the ENCODE (ENCyclopedia Of Dna Elements) consortium and member of the analysis group of the Mouse Genome Sequencing Consortium and the International HapMap project. He had a leading analysis role in the extension of the HapMap (aka HapMap3 project) and is a member of the analysis group of the 1000 genomes project and a co-chair in the GTEx project. He has served in the Board of Reviewing Editors of *Science* (2006-2011) and *eLIFE* (2013-2015), and he was a Senior Editor in *PLoS Genetics*.

### **From Biobanking to Precision Medicine**

#### **Prof. Andres Metspalu**

*Estonian Genome Center, University of Tartu (EST)*

Andres Metspalu, M.D., PhD, Professor of Biotechnology and Director of the Estonian Genome Center of the University of Tartu. He was as postdoc (IREX fellow) at Columbia University and Yale University in 1981-1982. His main scientific interests are human genomics, genetics of complex diseases and population based biobanks and their applications in translational research and precision medicine. He has published more than 300 papers and chapters. His H-index is 59.

From 1986 -1992, he was at the Estonian Biocentre as a scientific director and head of the laboratory of gene expression at University of the Tartu. He worked at EMBL, Heidelberg (as a FEBS Fellow in 1985), at MPI Molecular Genetics in W-Berlin (as an EMBO Fellow in 1988). In 1993-1994, he was at Baylor College of Medicine, Houston, Texas. as a visiting faculty with Dr. T. Caskey and in 2000 at IARC, Lyon (France), as a recipient of the IARC International Visiting Senior Scientist Award. In 2012, he took a three-month sabbatical leave and was working at CIG Univ. of Lausanne. From 1996 to 2008 A. Metspalu was also the founder and head of the Molecular Diagnostic Center of the Tartu University Hospital. Metspalu is the past (2006) President of the European Society of the Human Genetics and president of the Estonian SHG. He is one of the founders and directors of the P3G Consortium of Biobanks and BBMRI -ERIC. In 2010, he was elected to the Estonian Academy of Sciences.

He supervised 20 Ph.D. theses. He has served and is serving in several national and international committees (ERC panel, P3G director, SAC in Science Europe), editorial boards (Clinical Genetics) and has received among other awards and honours the Order of the Estonian

Red Cross 3rd Class and L'Ordre des Palmes Academiques from the Republic of France. From 2010, he has Doctor Honoris Causa from Vilnius University.

## **Genomics-based Personalized Prevention**

### **Dr Hilary Burton**

*Director PHG Foundation, Cambridge (UK)*

Dr Hilary Burton is the Director and one of the founder members of the PHG Foundation and a Fellow of Hughes Hall, Cambridge. The PHG Foundation is a not for profit organisation with a special focus on how genomic and other technologies can provide more effective personalized healthcare and improve population health <http://www.phgfoundation.org/>. Qualified in medicine at Oxford University, Hilary subsequently trained in public health in the Eastern Region and worked as a consultant in Cambridge.

Since 1997 at the PHG Foundation Hilary has focused on the genomics context for population health, and, in particular, has led national work on the implementation of new technologies in mainstream UK health services. She has been closely involved in the implementation of genomics technologies for screening programmes in the contexts of carrier screening, antenatal or newborn screening and has worked with major European Commission research programmes looking at the potential for susceptibility testing for common cancers and cardiovascular disease.

Leading the PHG Foundation team has enabled a multidisciplinary approach to this work. Key themes at present for prevention include the importance of data collection and sharing, personal empowerment and consent, the education of health professionals and the resolution of many ethical, regulatory and social issues.

Throughout her time at the PHG Foundation Hilary has been closely involved in genomics policy work in the UK. In 2011/2, she sat on the UK Government Human Genomics Strategy Group and is currently a member of the UK Genetic Testing Network Clinical and Scientific Advisory Group, Joint Committee on Genomic Medicine of the Medical Royal Colleges, the Council of the British Society for Genetic Medicine and the Health Education England Genetics Advisory Board. She is also a founder member of a European group on public health genomics, led from the Università Cattolica del Sacro Cuore in Rome.

## **Session 2: Personalized Medicine in Specific Disorders**

### **New Diagnostics in Personalized Cancer Medicine**

#### **Prof. Michael Neumaier**

*Institute of Clinical Chemistry, University Heidelberg, Mannheim (D)*

Michael Neumaier is a Clinical Chemist and Laboratory Physician working as a university professor at the University of Heidelberg. In 2002, he was appointed director of the Institute for Clinical Chemistry at the University Hospital Mannheim and also holds the chair for Clinical Chemistry at the University of Heidelberg, Germany. He has been engaged in quality assessment and management systems for laboratory diagnostics since many years.

Since 1998, he has been setting-up and organizing molecular EQA programs in Germany and Europe with more than 350 laboratories participating biannually in nucleic acids isolation, genotyping and sequencing exercises. Since 2000, he acts, by appointment of the German Chamber of Physicians, as a director of the national EQA system for medical laboratories organized and run by the Reference Institute for Bioanalytics (RfB) in Bonn, Germany. Since 2009, he has been Chairman of the section for Molecular Diagnostics of the Germany Society for Clinical Chemistry and Laboratory Medicine (DGKL). In 2011, he was appointed Chairman of the Scientific Board of the RfB, of which he has been a member for many years.

Currently, he acts as the Vice-President of the DGKL in preparation for the presidential term starting in 2014. His main scientific interests are colorectal tumorigenesis, pathobiochemistry of malignant disease and the development of methods for the molecular diagnostics of cancer. His interest also includes assessment of biomolecular quality in complex clinical bio-specimens.

### **Quantified Self Devices in Neurological Disorders**

#### **Prof. Philippe Ryvlin**

*Department of Clinical Neuroscience, Centre Hospitalier Universitaire Vaudois, Lausanne (CH)*

Philippe Ryvlin is Professor of Neurology and Chair of the Department of Clinical Neurosciences at the University Hospital of Lausanne (CHUV), Switzerland, and Director of the Epilepsy Institute (IDEE) in Lyon, France. He is President of the European Epilepsy Monitoring Association (EEMA), co-Chair of the Epilepsy Advocacy Europe Joint Task Force, founder of the European Network for Epilepsy Research (ENER), and coordinator of the European pilot network of reference centres in refractory epilepsy and epilepsy surgery recently granted by the European Union (E-PILEPSY). He is the author or co-author of over 200 PubMed referenced papers on topics primarily related to epilepsy surgery, anti-epileptic treatments and Sudden Unexpected Death in Epilepsy (SUDEP). At CHUV, Philippe Ryvlin has developed NeuroTech, a clinical research infrastructure dedicated to the evaluation of novel technologies in patients with neurological disorders, with emphasis on mobile and connected devices as well as assisting robots.

### **Metabolomics and Personalized Medicine**

#### **Prof. Oscar Yanes**

*CIBERDEM & Rovira i Virgili University, Tarragona (E)*

Oscar Yanes received his B.A. and Ph.D. degrees in biochemistry from the Autonomous University of Barcelona (Spain). In 2007 he joined The Scripps Center for Metabolomics and Mass Spectrometry (La Jolla, California) headed by Dr. Gary Siuzdak. Since January 2011 he is the scientific co-ordinator of the Metabolomics Platform of the Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM) and Assistant Professor at the Universitat Rovira i Virgili (Tarragona, Spain), where he also leads the Yanes Lab group ([www.yaneslab.com](http://www.yaneslab.com)).

He has long experience in developing new technologies, methods and applications in mass spectrometry-based metabolomics. His lab now focuses on understanding metabolic dysregulations in disease through integrating mass spectrometry and NMR-based metabolomics with other 'omic technologies such as transcriptomics and proteomics.

### **Session 3: Personalized Medicine – New Dimensions and Ethical Issues**

#### **The Ethics of Personalized Medicine**

##### **Prof. Effy Vayena Health**

*Ethics and Policy Lab, University of Zurich (CH)*

Effy Vayena, Ph.D., studied Medical History and Bioethics at the University of Minnesota (USA) and completed her habilitation in Bioethics and Health Policy at the University of Zurich. From 2000- 2007 she worked at the World Health Organization (WHO), focusing on ethical and policy issues relating to reproductive health, and assisted reproduction as well as on health research ethics. She remains at consultant to WHO and is visiting faculty at the Harvard [Center for Bioethics](#), Harvard Medical School. In 2015–2016, she is Fellow at the [Berkman Center for Internet and Society](#) at Harvard Law School. In 2015, she was named a Swiss National Science Foundation (SNSF) Professor of Health Policy and leads the newly-established [Health Ethics and Policy Lab](#) in the Department of Public Health at the EBPI, University of Zurich.

Her current research focus is on ethical and policy questions in personalized medicine and digital health. At the intersection of multiple fields, she relies on normative analyses and

empirical methods to explore how values such as freedom of choice, participation and privacy are affected by recent developments in personalized medicine and in digital health. She is particularly interested in the issues of ethical oversight of research uses of big data, ethical uses of big data for global health, as well as the ethics of citizen science. Using the ethics lens in innovative ways, her work aims to provide concrete policy recommendations and frameworks that facilitate the use of new technologies for a better and more just health.

### **Assessing the Human Gut Microbiota in Metabolic Diseases**

**Prof. Jens Nielsen**

*Department of Biology and Biological Engineering, Chalmers University of Technology, Gothenburg (S)*

Jens Nielsen has an MSc degree in Chemical Engineering and a PhD degree (1989) in Biochemical Engineering from the Danish Technical University (DTU), and after that established his independent research group and was appointed full Professor there in 1998. He was Fulbright visiting professor at MIT in 1995-1996. At DTU, he founded and directed the Center for Microbial Biotechnology. In 2008, he was recruited as Professor and Director to Chalmers University of Technology, Sweden, where he is currently directing a research group of more than 50 people. At Chalmers, he established the Area of Advance Life Science Engineering, a cross-departmental strategic research initiative and was founding Head of the Department of Biology and Biological Engineering, which now encompass more than 170 people. Jens Nielsen has published so far more than 550 papers that have been cited more than 18,000 times (current H-factor 65), co-authored more than 40 books and he is inventor of more than 50 patents. He has founded several companies that have raised more than M25EUR in venture capital. He has received numerous Danish and international awards including the Nature Mentor Award, and is member of several academies, including the National Academy of Engineering in USA, the Royal Swedish Academy of Science, the Royal Danish Academy of Science and Letters, the Royal Swedish Academy of Engineering Sciences and the American Academy of Microbiology. He is a founding president of the International Metabolic Engineering Society.

### **The Increasing Opportunities for Using Health Data as a Tool for Clinical Research**

**Prof. Dipak Kalra**

*The EuroRec Institute, London (UK)*

Dipak Kalra, PhD, FRCGP, FBCS, is President of The European Institute for Innovation through Health Data (i~HD). He plays a leading international role in research and development of EHR architectures and systems, including approaches to harmonise clinical meaning and protect privacy, and had led the development of key international standards on EHR interoperability. Dipak leads the Managing Entity (EuroRec) for a €16 million Innovative Medicines Initiative (IMI) on the re-use of electronic health record information for clinical research, EHR4CR, alongside ten global pharmaceutical companies. EuroRec is also a partner in another IMI project, EMIF, on the development of a European clinical research platform federating multiple population health and cohort studies. Dipak also leads an EU Network of Excellence on semantic interoperability, and is a partner in other EU projects on the sustainability of interoperability assets and the transatlantic sharing patient summaries. Dipak is Clinical Professor of Health Informatics at University College London, United Kingdom, a Director of the openEHR Foundation, and a member of standards bodies including CEN, ISO and HL7-UK.

## Appendix 3

### SAMS – Swiss Academy of Medical Sciences

The Swiss Academy of Medical Sciences (SAMS) was founded in 1943 and it currently comprises 232 members. The academy is committed to high-quality medicine based on ethical principles. It supports early-career researchers and engages with academia and practice. With its expert and advisory activities, the SAMS also serves policymakers and the public.

#### Core activity: Promoting research

The SAMS is an institution of research promotion recognised and financially supported by the federal government. It promotes high-quality research, supports early-career scientists and also focuses on less well-established fields of research.

#### Core activity: Ethics

The Central Ethics Committee of the SAMS identifies and discusses emerging ethical issues and challenges in medicine. To provide guidance for medical practice or biomedical research, it prepares guidelines and position papers and supports their implementation. The guidelines are incorporated into the Code of Conduct of the Swiss Medical Association (FMH) and thus become binding for all FMH members.

#### The SAMS as a think tank

In its capacity as a think tank, the SAMS aims to stimulate reflection on challenging questions in medicine and to shape reasonable developments. In this context, it often collaborates closely with the Swiss Academies of Arts and Sciences. The SAMS regularly organises and supports scientific conferences on key topics and forward-looking projects.

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### FEAM – Federation of European Academies of Medicine

FEAM's mission is to promote cooperation between national Academies of Medicine and Medical Sections of Academies of Sciences in Europe; to provide them with a platform to formulate their collective voice on matters concerning human and animal medicine, biomedical research, education, and health with a European dimension; and to extend to the European authorities the advisory role that they exercise in their own countries on those matters.

To underpin European biomedical policy with the best scientific advice drawn from across Europe, through the FEAM network of Academies representing over 5000 high level scientists from the whole biomedical spectrum. To improve the health, safety and wealth of European citizens through research by promoting a nurturing, creative and sustainable environment for medical research and training in Europe. FEAM's strength lies in its member Academies that give it the authority to provide an EU-wide scientific opinion on the European medical science base and evidence to underpin European bio-medical policy. The 20 FEAM Academies represent the following EU Member States: Austria, Belgium, Croatia, Czech Republic, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Portugal, the Netherlands, Romania, Spain, Switzerland and the United Kingdom. Observers include the European Academies Advisory Council (EASAC – the European network of Academies of Sciences) and the Inter Academy Medical Panel (IAMP – the global network of Academies of Medicine).

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