NOS-M
The Joint Committee of the
Nordic Medical Research Councils

Executive Summary of the NOS-M Workshop 2016
Nordic Common Strengths and Future Potential in the Field of Personalised Medicine

Date: November 23rd 2016.

Venue: Stockholm Waterfront Congress Centre, Stockholm.

INTRODUCTION

The Joint Committee of the Nordic Medical Research Councils (NOS-M) arranged a workshop on *Nordic common strengths and future potential in the field of personalised medicine* in Stockholm, Sweden, on November 23rd 2016. The workshop was the result of the recommendations in the 2014 NOS-M white paper on medical research[1]. The aim of the workshop was to discuss the potential of Nordic research cooperation targeting personalised medicine, including e.g. networking activities, academy-industry cooperation and joint research funding opportunities. The workshop attracted more than 70 participants, including representatives of Nordic research financing organisations, policymakers, and experts on personalised medicine (see appendix I for full list of participants). The workshop was chaired by Professor Jan-Ingvar Jönsson, Secretary General of Medicine and Health at the Swedish Research Council and Chair of NOS-M.

PROCEEDINGS OF THE WORKSHOP

In the first part of the workshop a number of presentations were given on the current state of personalised medicine in the Nordic countries and in Europe. The second part consisted of presentations on Nordic added value and future potential in personalised medicine including existing Nordic cooperation, each with the potential of moving the field forward. The final part of the workshop was a panel discussion on Nordic common strengths and the ways forward.

1.1 PERSONALISED MEDICINE IN THE NORDIC COUNTRIES AND IN EUROPE

1.1.1 Personalised medicine may radically improve health care within the next decade (Professor Mikael Benson, Linköping University)

A current key healthcare problem is the fact that up to 90 % of all medications are ineffective in 50 % of the patients. Only in the US the annual cost of ineffective medication has been estimated to around $ 350 billion. Personalised medicine aims to solve these problems by enabling early diagnosis and treatment, as well as individualised treatment. For many disease conditions, diagnosis and treatment is currently impeded by late appearance of symptoms and the involvement of several

[1] Nordic Potential in Medical Research – Cooperation for Success

genes. The emergence of -*omics and single cell technologies* has been of crucial importance for the diagnosis and treatment of multigenic disorders. By combining information from multiple sources, e.g. proteins, mRNA, DNA, environmental factors into network modules, one can understand disease mechanisms, find biomarkers and therapeutic agents, etc. However, there are a number of major ethical, societal and legal challenges that need to be tackled before this can be accomplished.

1.1.2 Reports on Personalised Medicine initiatives in the Nordic countries (*five speakers gave a short overview of the current state of personalised medicine in the respective Nordic country).*

Denmark (Professor Torben Falck Ørntoft, Aarhus University): a lot of activities have recently been undertaken in the field of personalised medicine. Political initiatives include a total of DK 5 million for a pre-analysis of the state of personalised medicine in Denmark and internationally. From a legislative perspective, a working group on ethics and legal issues has been assigned with representatives from ministries, agencies, patient organisations, ethical councils etc. One major challenge of this working group is to find a pragmatic way of interpreting the EU personal data act.

Finland (Dr. Jarmo Wahlfors, Academy of Finland): there are ongoing major reforms of the national social and health system and coordinated attempts are being made to better utilise social and health data in research. A health sector growth strategy roadmap for 2016–2018 was recently published[2]. There are currently 8 biobanks in Finland and the biobank act[3] from 2013 stipulates the legal framework for the operations of the biobanks. Another recent strategic initiative is the National Genome Strategy[4] in 2015 which sets key measures for ensuring that genomic data will be effectively used in healthcare and in the promotion of health and wellbeing in the future. The Finnish Government decided in April 2016 that a national genome centre and a national cancer centre will be set up in Finland.

Iceland (Professor Magnús Karl Magnússon, University of Iceland): more than half of the adult population has been genotyped and 25 000 whole genomes have been sequenced. Together with detailed genealogy data this enables imputation of the genotypes of the whole population to a varying degree of accuracy. A number of cancer risk genes have been mapped to the genotype data; e.g. it has been estimated that some 1,250 Icelandic women carry the Icelandic *BRCA2* deletion mutation associated with a 15-fold risk of ovarian or breast cancer. Whether the health care system need to proactively intervene in these cases is currently being discussed by the Ministry of Health.

Norway (Senior advisers Hege Wang and Kari Steig, Norwegian Directorate of Health): a Strategy for Personalised Medicine in Healthcare 2017–2021[5] was assigned by the Ministry of Health and Care Services. The focus of the strategy is on treatment and diagnostics, not on research. Key recommendations include development of expertise, a coordinated national development of the personalised medicine field, and development of ICT systems and registries. Storage and sharing of

[2] Innovating together: Growth Strategy for Health Sector Research and Innovation Activities: The Roadmap for 2016-2018. ISBN 978-952-327-142-5.
[3] http://www.finlex.fi/en/laki/kaannokset/2012/en20120688.pdf
[4] Improving health through the use of genomic data. Ministry of social affairs and health 2015:34. ISBN 978-952-00-3605-8.
[5] Summary of The Norwegian Strategy for Personalised Medicine in Healthcare 2017-2021. Helsedirektoratet. Publication number: IS-2146 E.

data are important questions, and sharing must be considered both for clinical purposes and research purposes.

Sweden (Professor Mikael Benson, Linköping University): there are many resources available for personalised medicine, but they are divided between different funders, underlying a need for national coordination including funding. Since health care is challenged by increasing costs, proof-of-concept studies including health economy are also needed. Current major initiatives include the national programme in protein research and biopharmaceutical drugs, with a total budget of SEK 320 million for 2016–2023. National resources include biobanks and registers, Bioinformatics Services to Swedish Life Science (BILS), Biobanking and Molecular Resource Infrastructure of Sweden (BBMRI), Science for Life Laboratory (SciLifeLab), and the national super computer in Linköping.

1.1.3 Report on European Personalised Medicine initiatives (Dr. Irene Norstedt, European Commission)

Research and innovation is a growing priority for the EU and Horizon 2020 is the major funding tool. The three pillars are personalised medicine, rare diseases and innovative medicines initiative. The International Consortium for Personalised Medicine, IC PerMed, was launched in June 2016. The consortium is a collaboration of research funders and policy makers from EU Member States and beyond, and the vision is to establish Europe as a global leader in personalised medicine research. A SRIA was published in June 2015[6] and the first action plan is to be published in late 2016. Also, EU Health research is funded by many different instruments, and many of these have a personalised medicine aspect.

1.2 Nordic Added Value and Future Potential in Personalised Medicine

1.2.1 Personalised medicine and the development of Life Science (Anders G. Lönnberg, Swedish Life Science Coordinator)

To retain welfare and growth, efforts need to be focused on the areas with highest yields, and there is no sector with higher added value than life science. Life science is therefore among the Swedish government´s top priorities. Although the sector is very dynamic, no long-term life science strategy has yet been developed and Sweden currently lacks a national agenda for personalised medicine. To retain welfare and growth, efforts need to be focused on the areas with highest yields, and there is no sector with higher added value than life science. So far, five priorities are suggested:

- Digitalisation.
- Reimbursement system (hospitals have to consider short-term budget).
- Meriting system (research/healthcare/industry).
- Government has to be clear in its priority. Too often, the healthcare system sees research as an obstacle.
- New knowhow.

1.2.2 Infrastructures for personalised medicine (Dr. Janna Saarela, Institute for Molecular Medicine Finland)

The Institute for Molecular Medicine Finland, FIMM, is located in the largest hospital campus in the country and it is part of the Nordic EMBL Partnership for Molecular Medicine. FIMM harbours a biobank infrastructure, as well as a technology centre enabling various aspects of molecular medicine research beyond genomics, e.g. metabolomics, imaging and clinical informatics. Personalised

[6] The PerMed SRIA: 'Shaping Europe's Vision for Personalised Medicine' (2015).

medicine is an important part of the translation of this novel technology into clinical practise. FIMM coordinates the Sequencing Initiative Suomi (SISu) search engine[7] which offers a way to search for data on sequence variants in Finns. A common Nordic database would be very useful because of accumulation of patients with rare diseases.

1.2.3 Nordic Commons for Register and Biobank Data (Professor Juni Palmgren, Karolinska Institute)

The total population of the Nordic countries is around 26 million. Nordic advantages include a high number of unique registers, cohorts and biobanks, allowing high quality epidemiology and clinical research, and a population that is generally very positive towards participating in research. However, the lack of a Nordic perspective for research data implies a risk of developing policy directives which are not aligned on the Nordic level. The challenges and obstacles for Nordic cooperation on data resources are illustrated in a report from 2012 by the Nordic Council of Ministers[8]. These challenges are presented from six perspectives: politically, organisationally, legally, financially, ethically and technically. *Nordic Commons* is a vision of a shared virtual space where scientists can work with the digital objects of biomedical research. A Nordic commons could rely on a clear legal and ethical framework for sharing data and tools across borders, transparency and an open access policy, and involvement of a broad range of Nordic key stakeholders. This will be associated with a number of possible financial, organisational, technical, legal, ethical and cultural obstacles, that need to be solved.

1.2.4 Risk screening and personalised therapy in cancer: a personalised medicine example (Professor Torben Falck Ørntoft)

Genomic medicine is the use of genomic information in the clinic to enable a more precise stratification of patients and citizens, for the purpose of surveillance, prevention, diagnosis and treatment. Sequencing can be used in a clinical context to identify inherited syndromes and diseases, to identify citizens with a high genetic risk of disease, to develop novel and more precise stratification of diseases based on cell biology, to choose appropriate treatment *etc*. GWAS can be used to identify risk SNPs for prostate cancer in individuals with elevated PSA levels. From an economical point of view, a lot of money can be saved by focusing on the high-risk groups. Sequencing can be used to select therapy based on mutations in cancer tissue. Solid tumours release DNA into the blood and sequencing may identify cancer from a blood sample. Molecular profiling can be used to choose the most appropriate treatment.

[7] http://sisuproject.fi/

[8] Reinforced Nordic collaboration on data resources – Challenges from six perspectives. TemaNord 2012:514. ISBN 978-92-893-2342-0

Panel discussion members, from left to right: Jan-Ingvar Jönsson (moderator), Anders G Lönnberg, Magnus Karl Magnusson, Mia Bengtström, Dag Erik Undlien, Troels Rasmussen, Irene Norstedt (Photo: Tor Martin Nilsen).

1.3 Panel Discussion – Way forward

The presentations were followed by a panel discussion on the Nordic common strengths and the way forward, moderated by Professor Jan-Ingvar Jönsson. The panel members were Mia Bengtström, Senior Adviser at Pharma Industry Finland; Magnus Karl Magnusson, Dean, Faculty of Medicine, University of Iceland; Irene Norstedt, Head of Unit Innovative and Personalised Medicine, EC; Troels Rasmussen, Special Adviser, Danish Agency for Science Technology and Innovation; Dag Erik Undlien, Professor, Department of Medical Genetics, Oslo University Hospital; and Anders G. Lönnberg, the Swedish government's national coordinator for life science. The panel was asked to address *the biggest needs and bottlenecks within personalised medicine*:

The importance of *political will* was raised, and the fact that the Nordic countries in many respects have very similar systems will probably entail fewer challenges at the Nordic level compared to e.g. at the EU level. Apart from the registries, the *governmentally funded healthcare* etc. in the Nordic countries are a great advantage, as there are much fewer obstacles than in countries with private actors. Besides, the mindset towards research among Nordic citizens is in general positive.

Cooperation on care of *rare diseases* was emphasised as one good starting point for personalised medicine in the Nordic countires, since several successful examples have been implemented in health care for decades. One of the most well known is neonatal screening. However, these examples are based on monogenic diseases, which affect a small portion of the population. Therefore, a key research challenge is implementation of personalised medicine in the diseases that are the main causes of ill health and death in the population, like cancer, inflammatory, cardio-vascular and metabolic diseases. There are already promising clinical examples of personalised medicine in cancer. Rapid technological advances, like genome-wide single cell analyses, and large-scale research efforts are likely to contribute to personalised medicine in cancer, and pave the way for clinical implementations in other common diseases.

One current bottleneck is data sharing and the related *legal* and *ethical* questions. Technical solutions and safeguards are often in place. Sharing data can avoid reinventing the wheel, but from a healthcare perspective, individual data is also necessary. Data sharing is especially relevant for rare diseases, where sample sizes are small. It was also pointed out that data sharing is not the only solution; interoperability of data is equally important as poor data management is a major issue at the moment. Another important issue is the question of *consent*. Ideally, each patient should be

asked for consent for research. It is however important for the patients to have an option of reservation as well. Sharing data should not be compulsory; rather, patients should be made aware of the importance of their contribution. Economic models as well as incentives for innovation and sustainability in health care costs are also relevant to consider. It is important to engage the healthcare providers. Rare diseases would be an appropriate way to begin due to the unique nature as monogenic diseases which is difficult to address in an individual country.

The workshop was closed by the Chair who summarised the discussions of the day and asked the participants to submit recommendations on the future path of personalised medicine in a Nordic context.

CONCLUSIONS

- Personalised medicine may lead to major improvement of health care, but there are a number of major ethical, societal and legal challenges that need to be tackled before this can be accomplished.
- Policy directives need to be aligned on the Nordic level.
- There are several Nordic advantages, including a number of unique registers, cohorts and biobanks, high quality epidemiology and clinical research, public-funded healthcare and a population that is generally very positive towards participating in research.
- Rare diseases and cancer are appropriate focus areas for Nordic cooperation.
- Overcoming the current obstacles related to data sharing is highly important, especially for rare diseases, where sample sizes are usually small. Computational resources and skills are crucial.
- It is important to have a common definition of personalised medicine. In the US, *precision medicine* is very much focused on genomics, whereas personalised medicine in Europe is more holistic.
- Personalised medicine is about making healthcare smarter and better by using multiple information sources about the person, his/her environment and lifestyle focusing on prediction and prevention shifting from treating disease to managing health. To achieve this it is necessary to work together across disciplines, organisations and countries.

ANNEXES

1.4 LIST OF PARTICIPANTS