

From Biobanks for health to Biobank Norway

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ABSTRACT

Norwegian biobanks comprise a unique resource for researchers who want to investigate pathways to the development of common and complex diseases and improve prevention and treatment. Extensive efforts have been made in Norway during the last decade to facilitate the optimised use of human biological resources stored in the country's numerous biobanks. This paper describes the steps undertaken in the "Biobanks for Health" (BioHealth) project and the newly launched national biobank infrastructure "Biobank Norway" to lay the ground for the implementation of an infrastructure, tools and expertise that facilitate the maximised use of Norwegian biobanks and increase the ability of Norwegian researchers to participate in international research.

Norwegian population cohorts, biobanks and health registries are extraordinary resources for health research. The confluence of several factors, including an integrated system to identify all residents in Norway through personal identification numbers, a predominantly single payer public health care system serving the whole population, and a democracy with strong individual rights form an environment particularly favourable to the use of these resources in biomedical research. For instance, Norwegian researchers are able to follow each person from birth or immigration to emigration or death based on linked data in de-identified research files and can study health and the effects of environments and genes across the life course of generations of Norwegians. Other Nordic countries have similar research advantages, but as yet only a few other regions and countries in the world are in an equally advantageous position. However, Norwegian researchers are just beginning to exploit the opportunities their biobanks offer. This paper describes recent initiatives undertaken in Norway to facilitate and encourage the optimised use of data and samples that comprise Norwegian biobanks for health research. Particular focus is placed on the "Biobanks for health" (BioHealth) project (1) which created a coordinated platform for the largest Norwegian population-based health studies and biobanks, and was a precursor to the

newly financed "Biobank Norway" project (2) which aims to advance the work conducted in BioHealth through the implementation of a national biobank infrastructure.

BIOHEALTH: NETWORKING POPULATION-BASED STUDIES AND BIOBANKS

In 2002, the BioHealth project was launched as a consolidated national consortium of population-based health studies and biobanks. This consortium, financed by the Norwegian Functional Genomics Research Program (FUGE) of the Research Council of Norway, created a research network between the four main Norwegian Universities and the Norwegian Institute of Public Health. The overall objective of the project was to facilitate the use of biological samples and associated health data stored in Norwegian population-based biobanks to improve prevention and treatment of disease, based on discoveries of new genes associated to common and complex diseases and new information on the interaction between genes and environmental factors. Today, the BioHealth consortium holds biological samples from about 500 000 participants. These samples were collected through large Norwegian cohorts such as the Cohort of Norway (CONOR) (3) and the Norwegian mother and child cohort study (MoBa) (4). In addition, other studies such as e.g. the Janus biobank for cancer research (5), the Norwegian Women and Cancer cohort (6) with about 170 000 participants and the Norwegian twin registry (7) with about 30 000 participants were also invited to join the consortium.

The BioHealth project undertook several significant steps which dramatically changed the Norwegian research landscape. First, it strongly advanced the development in Norway of state-of-the-art biobanking facilities for automated sampling. BioHealth led the establishment of two large research biobanks; one at the Norwegian University of Science and Technology in Levanger (8) and one at the Norwegian Institute of

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Public Health in Oslo (9). Although the two biobanks were originally planned to serve local projects such as the North Trøndelag health survey (HUNT) and the MoBa study, they rapidly started to offer biobank services to outside researchers and institutions for the handling, storage and retrieval of human biological material. This occurred because, in addition to offering good biobanking facilities, these biobanks also developed standardised high quality procedures for quality assurance and management. These new facilities enabled Norwegian researchers to extract DNA from the majority of samples in CONOR and MoBa which could then be used in several large scale genetic studies performed at an international level. Second, BioHealth encouraged the co-ordination of efforts between the different partners in the project for the development of biobanking tools. For instance, while the University of Tromsø developed software for data storage and management (10), the University of Bergen prioritized the development of genetic analysis programs (11). At the same time, the University of Oslo worked at building a new deep sequencing platform for large-scale genetic analysis (12). Third, BioHealth worked intensively to facilitate linkages between epidemiological research data with other types of health data contained in Norwegian national health registries and clinical registries. There are currently 15 national health registries in Norway. These registries are extremely important because they offer comprehensive coverage of the population and provide primary sources of phenotypic information and socio-demographic data. In addition, 19 national clinical registries offer data describing the quality of care provided to patients. The Norwegian Ministry of Health and Care Services started a pilot project in 2008 to coordinate and modernize these registries in order to improve their utilization for research, health surveillance, prevention and to improve the quality of health care services (13).

While BioHealth was actively working at developing co-ordinated biobanking facilities for Norwegian population-based studies, it interfaced regularly with other projects that concentrated on developing and harmonising biobanking activities internationally. This included the project "Promoting Harmonisation of Epidemiological Biobanks in Europe" (PHOEBE) (14) led by the Norwegian Institute of Public Health, the "Public Population Project in Genomics" (P³G) (15) hosted by the Research Institute of the McGill University Health Centre in Canada, the "European Network for Genetic and Genomic Epidemiology" (ENGAGE) (16) and the "Biobank Standardisation and Harmonisation for Research Excellence in the European Union" (BioSHaRE-EU) (17), both funded by the European Commission under the 7th Framework Programme, and the "Biobanking and Biomolecular Resources Research Infrastructure" (BBMRI) (18) project preparing the construction of a pan-European Biobanking Infrastructure for biomedical and biological research in Europe and worldwide.

BIOBANK NORWAY: MAXIMISING THE USE OF BIOBANKS

BioHealth was active for ten years and played a major role in elucidating the great research potentials to be harnessed from Norwegian population-based biobanks. During the project tenure researchers in BioHealth communicated regularly with national entities and funders and served on commissioned panels that forwarded recommendations for developing the Norwegian biobank platform (19). The importance of building a unified platform was recognized by the Ministry of Education and Research and the Ministry of Health and Care Services which requested further recommendations for the commercial use of Norwegian biobanks (20). Simultaneously, the work conducted under the preparatory phase of BBMRI (which ended in January 2011) was critical as national research councils and ministries across European countries started to encourage the funding and establishment of national biobank infrastructures – national hubs – which are envisioned to function as national units for a pan-European BBMRI. In 2010, the Research Council of Norway announced plans to fund the establishment of a national biobank infrastructure – "Biobank Norway" (2011-2013) – with 80 million NOK. The Norwegian University of Science and Technology and the Norwegian Institute of Public Health, both of whom were partners in BBMRI, were asked to take the lead in developing the national biobank infrastructure. Today, Biobank Norway is a national consortium representing all major population-based and clinic-based biobanks in Norway. It has expanded beyond the original BioHealth partners to also include the four regional health authorities that are responsible for specialist health care in the four regions of Norway. Biobank Norway aims to 1) become a national highly competitive infrastructure for health sciences, 2) maximize the use of biobanks as a basis for excellent research and innovation, nationally and internationally, and 3) provide internationally competitive biobanking services for basic, clinical, and epidemiological medical research.

The idea upon which Biobank Norway relies is simple. With proper management, current and future specimens stored in Norwegian biobanks will provide a unique source of research for many decades to come. This is illustrated, for example, by the ability to use archived and pre-processed genomic DNA and serum collected from healthy members of the Norwegian population who later develop a disease, for example a certain type of cancer identified by the Cancer Registry via registry linkage. This information may also be merged with a rich array of information on important environmental and life style factors such as smoking and physical activity that is available from the cohorts. Socio-economic status, place of residence, medication use, genealogy and additional phenotypic and clinical information may be obtained by linkage to regional

Table 1. Main activities of Biobank Norway work packages (2011-2013).

WP1 – Project management and coordination
<ul style="list-style-type: none"> • Development of strategic plans and a national governance structure for biobanks • Collaboration with national biobank initiatives in other Nordic Countries and internationally
WP2 – A Norwegian federation of population-based biobanks
<ul style="list-style-type: none"> • Identification of quality phenotype information from main Norwegian population-based biobanks and disease registries
WP3 – Clinical biobanks
<ul style="list-style-type: none"> • Acquisition of professional information management systems and tracking systems • Identification of existing biological material stored in hospitals • Identification of relevant international standards and guidelines, including ethical guidelines, for the annotation, storage and exchange of quality parameters and anonymous and de-identified personal data • Establishment of national standards for management of human biological material and related personal information
WP4 – Biomolecular resources
<ul style="list-style-type: none"> • Development of a streamlined system for easy access to analysis expertise and technologies • Identification of state-of-the-art technologies and corresponding service platforms of particular relevance to Biobank Norway, nationally and abroad • Establishment of an infrastructure of resource persons who can assist researchers within Biobank Norway in developing technologically sound research proposals involving molecular biology
WP5 – Databases/EUTRO
<ul style="list-style-type: none"> • Establishment of an IT platform and IT hubs that allow for national harmonisation of biobank databases
WP6 – Biocomputing
<ul style="list-style-type: none"> • Development of tools, including web-based programs, for the management, exchange and analysis of large amounts of genomic and other omic data
WP7 – Technological solutions
<ul style="list-style-type: none"> • Acquisition of technical solutions for automated sampling and storage at ultra-low temperatures • Establishment of two state-of-the-art large-scale biobank facilities as centers of excellence
WP8 – Ethical and social issues
<ul style="list-style-type: none"> • Identification of ethical, legal and social issues for bridging research biobanks and clinical biobanks into a national infrastructure • Development of tools to facilitate sound ethical harmonization between Norwegian and European biobanks and for public engagement
WP9 – Funding, financing and commercial activities
<ul style="list-style-type: none"> • Development of a basis for future funding of the Norwegian research biobanks

and national registries. Analysis of tissue specimens from clinical biobanks will in addition constitute a useful source of information. Thanks to this new ability to combine data from different sources, Norwegian and international researchers will in the future be able to discover biomarkers for disease and trait prediction as well as for prognosis in a much greater extent than today.

The ambitious objectives of Biobank Norway require a co-ordinated action among the partners in the project. Biobank Norway is structured into nine work packages (WP), ensuring a comprehensive and competent research network which covers a range of biobank related activities. Key activities of these work packages are outlined in Table 1 and span the critical elements and technological solutions that must be addressed and coordinated across population-based and clinical biobanks in order to develop a national infrastructure. To ensure that the Norwegian biobank infrastructure will be ethically robust and will comply with international standards, a work package is dedica-

ted to mapping the ethical, legal and social challenges in the project and to develop tools to facilitate sound ethical harmonization between Norwegian and European biobanks as well as strategies for public engagement. Finally, a separate work package works at developing sustainability mechanisms to secure the future funding of the Norwegian research biobanks.

Three specific features of Biobank Norway deserve particular attention. First, while the BioHealth project primarily focused on population-based health studies and biobanks, Biobank Norway has expanded its scope to include both population-based biobanks and clinical biobanks. A long-range goal will be to bridge procedures for the access of data and samples derived from both types of biobanks. Second, Biobank Norway aims at enabling interoperability between different types of biobanks and registries not only at a national level but also at an international level. This will require a high level of interaction between Biobank Norway and other projects in other countries and regions of Europe. Third, Biobank Norway aims to explore routes for a

potential commercialization of biobanking services for basic, clinical, and epidemiological medical research. These novel features imply a number of new challenges related to e.g. the scope of consent and the acceptance for international use of biobank resources among the general public that will be worth discussing with experts within the international biobanking community (21). These discussions are already taking place. For instance, Biobank Norway works closely with the Nordic BBMRI (22) which was recently established to encourage the exchange of experiences across borders and harmonise biobanking processes at a Nordic level. The Nordic countries share a number of advantages due to similarities in administration of national person numbers and health registries and studies. Consequently, Nordic biobanks share many characteristics and experiences that give the Nordic countries the opportunity to influence the development of best practices for biobanking at a European level. Common research projects are also being developed under the auspices of the Nordic BBMRI such as a Nordic research project on colorectal cancer (23). Biobank Norway, together with 14 other European countries, also participates in the ongoing effort to establish BBMRI as a legal entity under the European Research Infrastructure Consortium (ERIC) programme (18).

CONCLUSION

In the first decade of this century, the BioHealth project strongly strengthened and helped to consolidate national collaborations between Norwegian population-

based studies, biobanks and health registries. Increased competence in genetic epidemiology, bioinformatics, statistical genetics, data management, high-throughput analytic approaches, automated technical solutions and ethical guidance has placed Norwegian epidemiology and biobanks in the international front line of biobank research. Biobank Norway is taking this work forward at a rapid pace. One year after the project started, several clinical biobanks are already using the national biobank infrastructure for handling and storage of their biological samples and cross-biobank collaboration is taking place. Centralisation of biobank services at the regional level is also becoming more commonplace (24). Norwegian biobanks are increasingly contributing to a number of cutting-edge international research projects within e.g. lung cancer, type 2 diabetes, atrial fibrillation and schizophrenia and new projects are under planning (25-38). Biobank Norway will, in the coming years, continue to work for higher sample quality, improved health biobanks and registries, better research and optimized integration with our international biobank partners.

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