

**The International Evaluation of the  
Genetic and Genealogical Strategy of Biobank Research  
Umeå University, February 25-26, 2010**

**Evaluation Report by  
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***Introduction***

In September 2009 the Medical Biobank together with the Demographic Database (DDB) invited the Review Panel to conduct an independent Evaluation of a proposed programme for collaboration between these two institutions at Umeå University. The members of the Review Panel (Appendix 1) were asked to evaluate the collaboration in its entirety, and where appropriate to assess individual projects within the collaboration. The background to the Evaluation was that:

1. DDB had received major financial support for its activities from the Swedish Research Council for the period 2005-2010, with interaction between DDB and geneticists expected to be a key component of its development strategy;
2. Major support has been provided for the establishment for a Regional Biobank and a national Swedish Biobank, with possible future extension to other Nordic countries;
3. A number of collaborative projects between the Umeå Medical Biobank and DDB were under consideration but, more importantly, a new unified and comprehensive mode of collaboration was envisaged.

This Evaluation Report has been prepared by the Review Panel and is based on the material provided by Göran Hallmans from the Medical Biobank and Anders Brändström from DDB prior to the site visit, presentations by individual project leaders during the site visit, free and open access to members of the Medical Biobank and DDB who participated in the Evaluation, and to members of the Steering Committees of the Medical Biobank (see Appendices 2 and 3 for the list of participants and Agenda of the site visit respectively). The Report summarizes our observations, details our evaluation of the potential of the combined resource, and lists recommendations for future actions that could contribute to an even more extensive utilization and liberalisation of the full potential in the collaboration between the Medical Biobank and DDB.

The Evaluation comprises the following elements:

1. Description of the format of the evaluation;
2. Description of the resources and scientific ideas;

3. Organisational and “political” recommendations that could strengthen the initiative;
4. Specific recommendations related to projects, programs, promotion/branding and educational activities;
5. A brief summary with concluding remarks on the uniqueness of the resource, and key recommendations that could contribute to the release of the potential within the resource.

Each of the recommendations relate to the overall evaluation of the initiative. While the presentation of individual projects was very helpful in illustrating the relative strengths and weaknesses of the combined resource, the Review Panel considered that evaluation of specific projects would not only require much more detailed insight into their individual design and aims, but would exceed the remit of the evaluation process.

### ***Format of the evaluation***

#### Precirculated and tabled papers

Documentation on various aspects of the Medical Biobank and DDB were pre-circulated to the Review Panel, including:

1. A review of the Northern Swedish Population Genealogy Project (NORTHPOP) which comprises:
  - i) The Demographic Database (DDB) that, as detailed below, contains comprehensive information on various aspects of kinship, health, and socio-economic and demographic structure, with family reconstructions providing data spanning some 15 generations;
  - ii) The Northern Swedish Research Biobanks, based on the Northern Sweden Health and Disease Study (NSHDS) that in turn incorporates the Västerbotten Intervention Study, the MONICA Project and the Northern Sweden Mammary Screening Project, plus the Northern Sweden Maternity Cohort. In addition, samples are available from the Uppsala Biobank, and U-CAN, the comprehensive Cancer Consortium recently established by the Universities and Academic Hospitals of Uppsala and Umeå;
  - iii) The Science for Life Laboratory in Uppsala offering core facilities in Genomics and Proteomics;
  - iv) eSSSENCE, a joint initiative by Uppsala and Umeå Universities for the development of new (bio)informatics applications in medicine, the social sciences and humanities.
2. The Biobanking and Molecular Resource Infrastructure of Sweden, BBMRI.SE, which aims to establish a Swedish National Biobank funded by the Swedish Research Council. This body will include the various Northern Swedish biobank cohorts and a number of existing Malmö-based Biobanks.
3. The GEN-STUDY which utilizes specific aspects of the NSHDS and to date allows for 25 year follow-up of individuals diagnosed with breast cancer, colorectal cancer or gliomas in Northern Sweden.
4. The GLACIER study (Genome-Lifestyle interactions And Complex traits Involved in Elevated disease Risk) which aims to discover predisposing gene variants dependent on environmental context, with cross-sectional and longitudinal assessments of gene x lifestyle interactions on cardio-metabolic traits.

At the request of Knut Borch-Johnsen, Göran Hallmans had pre-circulated to the Review Panel written responses to a list of specific questions on the proposed structure and format of the Evaluation, the envisaged role of the Review Panel, the current facilities and support for the proposed initiative within Umeå University, legal, data safety and data availability issues, and the degree of willingness to share samples and information with other national and international researchers.

At the Evaluation, information was tabled on publications by DDB from 1970-2008, and the Medical Biobank/NSHDS from 1989-2010, the latter with impact factors appended. An additional document on the DDB Security Policy for material subject to secrecy also was tabled.

### The evaluation process

The evaluation was hosted by Prof. Anders Brändström of DDB and was conducted on February 25-26, 2010 in the Social and Behavioural Sciences Building of Umeå University. Besides the Review Panel (Appendix 1), the participants included representative academic staff and clinicians from the DDB and Medical Biobank, who on day 2 were joined by members of the Medical Biobank Steering Groups (Appendix 2).

The programme for the evaluation is listed in Appendix 3. Day 1 consisted of a 2 hour Introduction aimed at illustrating the scope and potential of the proposed Strategy for Biobank Research at Umeå University, with presentations on DDB, the NORTHPOP Project, and the application of DDB genealogical data to genetic research. Short presentations of specific projects followed, highlighting aspects of the GLACIER Study, NSPHS and the multi-national EUROSPAN Study, and the GEN-STUDY. At the conclusion of the presentations there was a round table discussion on how the multigenerational DDB database could be used in the study of present-day chronic diseases, ranging from diabetes to Alzheimer disease, and including disorders showing epigenetic transmission.

Day 2 commenced with a discussion of the scientific value for future generations of scientists of combining population-based genealogical data with prospectively collected biobanking and high-throughput genomic and proteomic analysis. This discussion flowed on to the differential roles and potential of individual patient cohorts affiliated with the Umeå Biobank, the development of the Swedish National Biobank (BBMRI.SE) and the role of the proposed Nordic Biobank, including the international competitiveness of the latter two institutions. The evaluation finished with a free-ranging discussion in which members of the Umeå Biobank Steering Groups were invited to participate.

### ***Description of the resource and scientific ideas***

The Demographic Database (DDB) at Umeå University was established in 1973 and houses the largest database in Europe for longitudinal historical and societal information. Currently, the DDB covers the period from 1700 to 1949 and has the ability to add-on other excellent registers available via at Statistics Sweden. The DDB comprises two parts:

1. A historical database POPUM with individual level and detailed life-course data on one million people and a depth of more than 10 generations over the period 1700-1899;

2. A new multigenerational research infrastructure POPLINK which links POPUM to current Swedish registry resources (1950 – present) by digitising Swedish population data over the period 1900-1950. These high quality Swedish population resources include registers on family structure, work, and socio-economic conditions, plus the health registers maintained by the National Board of Health and Welfare.

The rich information available in POPLINK comprises 300 variables, including demographic, kinship, health, and socio-economic data over the life course. The scope and depth of available information is internationally unique, and the inclusion of both survivors and non-survivors in each generation makes the data particularly suitable for genetic epidemiological research. POPLINK will cover data from nine parishes in the Skellefteå region of northern Västerbotten in its first phase (by 2013), and through linkage with POPUM will make available life-course data on about 275,000 individuals covering up to 15 generations. In so doing, it will significantly surpass the deCODE genetics resource in Iceland. The second phase will incorporate the Umeå region, thus covering 2/3 of the population of Västerbotten county. The NORTHPOP proposal seeks to extend POPLINK further, to include data from inland parishes included in POPUM, which include several sub-population exhibiting wide genetic and lifestyle diversity.

It is proposed to link this unique database to the Northern Sweden Research Biobanks resources contained in the Medical Biobank at Umeå University. Samples and data are available from the NSHDS (which as previously noted combines data from the Västerbotten Intervention Project, the MONICA Project, and the Northern Sweden Mammary Screening Project) and the Northern Sweden Maternity Cohort. In total these biobank resources comprise blood samples and questionnaire data from 169,000 individuals. Since participation rates were very high, the data are regarded as truly representative of the constituent population. Further blood samples, questionnaire data and tissue samples are available in additional sample sub-sets. The NORTHPOP proposal would extend this facility to additional areas in northern Sweden covered by POPUM, and to other biobanks such as the Uppsala Biobank and the U-CAN Comprehensive Cancer Consortium (Uppsala-Umeå). The intention then would be to form strong scientific links with the emerging Science for Life Laboratory in Uppsala, and the Genomic and Proteomic Medicine and eSENCE Informatics initiatives, so that internationally leading laboratory and informatics expertise in Sweden can support this initiative.

#### Research niche

The proposed resource will make possible a wide range of demographic, social science, epidemiological, genetic epidemiological and population genetic research. Within genetic epidemiology these studies will include not only gene discovery through family-based association and linkage approaches, but novel designs, such as multigenerational studies of genetic, environmental and gene-environment interactions, and studies of epigenetic effects by linking historical exposure data to current genetic studies. The resource also will facilitate powerful and highly efficient approaches to mutation identification, such as homozygosity mapping and targeted sequencing studies, by identifying highly informative individuals and those with close links to founders.

### Evaluation of the Strategy scientific value / potential

We consider the proposed Genetic and Genealogical Strategy of Biobank Research to be a resource of international excellence. The Strategy would be very competitive for national and international funding support if linked to a focused programme to develop a Centre of Expertise in Multigenerational Studies which uniquely would be made possible. Umeå could lead and act as a fulcrum for international efforts to develop new methods in this novel and exciting field, with the potential to make seminal and scientifically distinctive contributions in the emerging field of epigenetics. The Strategy could also make important contributions to the rapidly developing field of life course epidemiology and should be developed as a national and international resource which could complement other major medical research investments in Sweden. The successful development to date of the NSHDS and the GLACIER study give some indication of the scientific potential, but there is substantial further scope to develop a true international Centre of Expertise in Umeå.

### Uniqueness of the resource

We consider that these research resources are internationally unique in their potential scale of generational coverage, and they will remain scientifically competitive at least over the next 10-20 years. A time-scale of this nature offers a secure platform on which to build a team with appropriate expertise for the optimal development and exploitation of the available resources. The Strategy should be seen as an opportunity for Umeå to develop a research facility which would become internationally established as a Centre of Expertise in Multi-Generational Studies.

**The Review Panel recommends that Umeå University recognize the scientific potential for international excellence by establishing a Centre of Expertise in Multi-Generational Studies in Umeå, at the same time supporting this decision by giving priority to the provision of appropriate related organizational, human resources and research infrastructure support.**

### ***Organisational and “political” recommendations that could strengthen the initiative***

#### Ambition, vision and strategy for the new ‘Centre’

At present, the Medical Biobank and DDB represent separate entities in which collaborative projects are largely based on the interest of individual researchers, with the role of the Medical Biobank and/or DDB in some projects primarily as “data-providers” rather than initiators and coordinators. The absence of a joint organizational entity, combined with the fact that the researcher remains in control of the projects, makes the interaction between the Medical Biobank and DDB less robust. If a Principal Investigator leaves Umeå to take a position at another university (nationally or internationally), this could potentially lead to a conflict on ownership of data and the research project in question. The absence of a common Centre also weakens the branding potential of the collaborative effort, as branding will be related to individuals, projects and the University, with the consequent risk that the true nature and scope of the collaboration/interaction is not apparent.

**The Review Panel recommends that the proposed body formed by the linkage of the Medical Biobank and DDB should be clearly identified as a single entity with its own new name and logo.**

**To facilitate this process the Review Panel recommends that the Medical Biobank and DDB create a common platform through the creation of an institute/unit within the University combining the research strengths of the Faculties of Medicine and Social Science.**

**The Review Panel also recommends that a common strategy, ambition and action plan is prepared for this common research entity based on the strengths of the collaborating bodies. The plan should include very clear milestones for the new combined entity focusing on 1, 3 and 5 year perspectives.**

#### Platform for the linkage of minds

At present the two collaborating bodies, the Medical Biobank and DDB, are based in scientific communities representing different scientific methodologies, environments and cultures. This situation is common to numerous other interdisciplinary units world-wide, and for most of these units their differences limit exploitation of the full potential of their collaboration. Collaboration between institutes and institutions under these terms may well lead to a sharing of resources but lack the comprehensive linkage of minds that is necessary for the creation of a genuine ground-breaking and innovative cross-disciplinary research entity. History does not provide clear, practice-based guidelines indicating a solution to this problem. In the opinion of the Review Panel, the most successful models have included physical unification of the partners in an open environment which creates a platform for daily, informal interaction. This type of interaction has the potential to extend collaboration beyond a common protocol based on existing expertise drawn from each individual discipline towards the creation of new protocols, incorporating innovative and synergistic interactions, that fully utilize the competencies within both scientific domains. A meeting of minds of this nature does, however, require daily interaction between researchers at all levels, from the most junior PhD student to established senior faculty.

**The Review Panel therefore recommends that a new, inter-faculty institute/unit is created, organisationally as well as physically. As part of this process it is recommended that a new facility be established, with appropriate support provided by the University to existing management in the Medical Biobank and DDB in the preparation and implementation of this challenging but crucial task.**

#### Local positioning (University and County)

Evidence was presented to indicate that both the Medical Biobank and DDB are highly regarded by the University, and that there is strong support for the creation and establishment of a combined body that would benefit synergistically from the inputs of both existing bodies. For any such initiative, financial and logistical support from the local community is also a critical factor. In this respect the Evaluation was assured of strong ongoing support from Västerbotten county, which has been an enthusiastic supporter of existing biobank studies originally established to improve the health of the local population, and which have been highly successful in achieving this central aim. The unequivocal statement by Anders Brandström that within a period of five years approximately 80% of the research work undertaken by DDB would be dedicated to the new combined research body augured very well for the perception of the initiative, both within the University and the wider local community.

**The review panel recommends that the unique opportunities of the collaboration is acknowledged formally by the University of Umeå and the County of**

**Västerbotten, and that creation of a combined centre and funding of core facilities in the centre is considered.**

Positioning and interaction with other centres – nationally and internationally

As discussed elsewhere in this Report, to date a large majority of the studies undertaken by researchers in the Medical Biobank and DDB have been initiated and conducted by specific individuals, often with collaborators outside Sweden. This strategy is entirely understandable, since it is notably cost-effective and provides access to analytical expertise that may not be readily available locally or even within the country. The resultant research output, whether as conference presentations or in high impact journals, also provides a useful and effective advertisement for the research capability of Umeå University faculty. The creation of the proposed new Biobank Research facility with the DDB as an integral partner changes the picture very substantially, and with appropriate support from the University it is highly probable that in future Umeå will more be regarded as a Centre of Research than a peripheral player. Progress in this respect will be significantly facilitated by strengthened links with other Swedish Centres of Excellence, as exemplified by the NORTHPOP Project and the BBMRI.SE.

**The review panel recommends that ways to optimise the positioning of the unit within the frames of a national collaboration should be considered as part of the strategy and action plan.**

Research support strategies

The Review Panel considers that the current secondment of postgraduates for training in international institutions should be subsumed within a wider overall plan to develop scientific expertise and retain high quality staff in Umeå. To develop new methods, and identify and capitalise on scientific opportunities afforded by the unique data resource in Umeå:

**The Review Panel recommend that a series of international workshops be held in Umeå on topics related to multigenerational genetic epidemiology studies with leading scientists invited to participate.**

From this starting-point, joint fellowships could be established with the institutions from which the visiting scientists are drawn, to encourage their younger scientists to spend periods of time in Umeå becoming familiar and working with the available data and methods. The Review Panel believes that an initiative of this type would greatly raise the international profile of Umeå researchers, help to confirm their role as leaders in this field, and provide many opportunities for local scientists to interact with, learn from, and form new collaborations with, visiting scientific experts.

External Scientific Advisory Board

**The Review Panel recommends that an External Scientific Advisory Board be established to help develop and direct the vision for the proposed new entity. The Board would bring an international perspective to the development of the entity by challenging strategies and activities, and providing advice on funding and areas of priority.**

The Board should be composed of internationally recognized scientists with technical expertise in multigenerational studies and recruited from institutions which would be willing to jointly develop these new methods and help fully utilise this unique resource. The Board should meet annually in Umeå and will serve to engage internationally

excellent scientists in the development of the proposed new entity, improve interaction between local scientists and scientists from other leading institutions, and help to raise the international profile of the new entity.

### *Specific recommendations*

In addition to these general recommendations, **the Review Panel made the following, more specific recommendations:**

**1. Give priority to completion of the POPLINK 1900-1950 programme**

There is a gap in the data held in DDB for the years 1900-1950, a period which overlaps with the establishment and/or implantation of a number of crucial, Swedish health-related databases from 1940-1960. This time gap in the DDB significantly diminishes its value in biomedical research and its closure merits priority status.

**2. Identify and prioritise key regional and national data sources which could be incorporated into the DDB to significantly increase its value**

In discussions with DDB it became clear that there are potentially very valuable sources of individual-based medical information which have not yet been digitised for inclusion. These sources may include information on hospitalisations (including diagnoses), possible important exposure variables such as birth-weight, and key markers of growth. The Review Panel recommends that a Joint Committee be established to explore the possibility of expanding DDB to include these health-based data, with the Committee to be responsible for prioritisation of these possibilities, and for advising management and the Board how to maximise the value and cost-effectiveness of future collaborative efforts.

**3. Strengthen epigenetics and biostatistical support at senior levels to develop the methodologies needed in the analysis of multi-generational cohort studies**

As already outlined, in international terms the existing resource is truly unique, opening numerous possibilities for the conduct of multi-generational cohort studies, and adopting this multi-generational approach to design case-control studies and case-cohort studies with significantly greater power than current conventional designs. A project of this nature would, however, represent a major methodological challenge. The Review Panel therefore recommends that relevant expertise is attached to the initiative, either through the appointment of one or more senior epidemiologists and/or epidemiologists with expertise in the field, or by attaching experts as consultants/advisors on part-time but long-term contracts.

**4. Create greater focus on this specific research area, with a shift from individually focused to combined programmes**

As previously stated, a long-term strategy should be developed with focus areas identified in which the proposed new entity in Umeå has the expertise to become THE international centre of excellence. These areas should then be the focus of future research initiatives within the entity.

**5. Accord greater visibility within Umeå University to the new entity and prioritise it in terms of support**

The new entity should be provided with the necessary funding to maintain core activity and be independent of add-on projects. In the opinion of the Review Panel it is crucial that Umeå University acknowledges the uniqueness of this resource and consequently prioritises the initiative for internal support and funding. While a major part of the funding should still come from sources outside the University, including

Västerbotten County and the Swedish Research Council, the Review Panel considers that long-term, dedicated University support for infrastructure and key senior staffing is essential. Support of this nature would demonstrate the willingness of the University to ensure sustainability, which in turn would encourage the funding of large-scale projects by external funding bodies.

## **Appendix 1 Membership of the Review Panel for the International Evaluation of the Genetic and Genealogical Strategy of Biobank Research at Umeå University**

**Prof. Knut Borch-Johnsen, MD, DMSci** is Director of Steno Diabetes Center in Copenhagen and Professor of Clinical Epidemiology at the University of Aarhus, Denmark

- Professor Knut Borch-Johnsen has initiated two large scale European and global networks and common data bases within diabetes epidemiology and public health (DECODE and DETECT-2), and data from surveys conducted within Västerbotten County have been included in these data bases.

**Prof. Alan Bittles MA, PhD, ScD, FRCPath** is Adjunct Professor and Research Leader in the Centre for Comparative Genomics, Murdoch University, and Adjunct Professor of Community Genetics, Edith Cowan University, both in Perth, Australia.

- In 2004-2005 Prof. Bittles was Visiting Researcher in the Centre for Population Studies, Umeå University

**Prof. Harry Campbell MD, FRCPE, FFPH, FRSE** is Professor of Genetic Epidemiology and Public Health, Centre of Population Health Sciences and Institute of Genetics and Molecular Medicine, University of Edinburgh, Scotland, UK

- Prof Campbell is coordinator of the EUROSPAN consortium which includes the Northern Sweden Population Health Study led by Prof Gyllensten

## **Appendix 2 Participants in the International Evaluation of the Genetic and Genealogical Strategy of Biobank Research at Umeå University**

Ingvar Bergdahl  
Anders Brandstrom  
Lasr-Olov Bygren  
Fredril Elgh  
Elisabeth Engberg  
Sture Eriksson  
Paul Franks  
Ulf Gyllensten  
Göran Hallmans  
Urban Janlert\*  
Anders Johansson  
Gerd Johansson  
Johnny Karlsson\*  
Per Lenner  
Börje Ljungberg  
Jack Lysholm  
Beatrice Melin  
Tommy Olsson  
Ulrika Pettersson  
Olov Rolandsson  
Dmitry Shungin  
Gunnar Sjöblom\*  
Roger Stenling  
Torgny Stigbrand\*  
Annika Westberg  
Åsa Ågren

\*Member of a Biobank Steering Group

### **Appendix 3 Programme for the International Evaluation of the Genetic and Genealogical Strategy of Biobank Research at Umeå University**

**Thursday, 25 February**

12.30            *Lunch at Hotel Björken*

#### **Program at DDB - Introduction**

13.30 - 13.40 Welcome, presentation of participants, Göran Hallmans

13.40 – 14.05 The Medical Biobank, the Northern Sweden Health and Disease Study and the National Swedish Biobank Strategy, Göran Hallmans

14.05 - 14.25 The Demographic database (DDB), Anders Brändström and Elisabeth Engberg

14.25 - 14.45 The NORTHPOP project – a vision, Ulf Gyllensten

14.45 – 15.10 Introduction to the science of genealogy, Alan Bittles

15.10 - 15.20 Discussion

15.20 – 15.40 *Coffee break*

#### **Presentation of projects**

15.40 – 17.00 Short study presentations followed by discussions

The GLACIER study, Paul Franks

NSPHS - Northern Sweden Population Health Study and EUROSPAN, Ulf Gyllensten

Combining genetic, environmental and genealogical data; Multigenerational gene-environment interaction modeling and genotype imputation, Paul Franks

The GEN-STUDY, Genetic Epidemiology of breast cancer, colorectal cancer and brain tumours in Northern Sweden, Beatrice Melin

#### **A combined genetic and genealogical strategy of biobank research**

17.00 – 18.30 Round table discussion on how a population-based multigenerational genealogy database with health and social information from historic to the extant generations can be used to study the risk of chronic diseases of today

17.00 - 17.25 Diabetes, introduction: Paul Franks. Comments Olle Bygren, Olle Rolandsson

17.25 - 17.45 Cervical cancer, introduction: Ulf Gyllensten

17.45 – 18.30 Discussions concerning other disease areas:

Epigenetics in colo-rectal cancer research, Richard Palmqvist

Infections - chronic diseases in extant generations, Anders Johansson and Fredrik Elgh

Breast Cancer, Per Lenner

Kidney cancer, Börje Ljungberg

Alzheimer's disease, Sture Eriksson

*19.30 Dinner at Rex*

## **Friday, 26 February**

08.30 – 09.45 Discussion of the **scientific value for future generations** of scientists by combining:

A population-based multigenerational genealogy database with health and social information from historic to the extant populations and

population-based and prospectively collected biobanking

ultra-sensitive high-throughput methods in genomics and proteomics

09.45 – 10.15 **The Swedish (Nordic) Biobank Challenge**

Can Sweden/BBMRI.SE/Nordic countries be an international leaders in biobanking?

What is the role for different cohorts in the challenge? Should they be combined? Should we focus on some cohorts? Strategies for international collaboration? Other ideas?

*10.15 – 10.30 Coffee break*

10.30 – 12.00 Meeting and discussion with members of the Steering Groups

*12.15 – 13.30 Lunch at DDB*

13.30 – 14.30 Review Panel discussion