

International Evaluation of Swedish Biobanks

March 18, 2005



Preface

Functional genomics research in Sweden has received major financial support from a private fund, the Knut & Alice Wallenberg foundation, to establish two multicenter consortia, Wallenberg Consortium North (WCN) covering central and northern Sweden and Swegene for southwestern Sweden. The funding period started in 2000 and is coming to an end in 2005. One major component in the programmes was the Swedish biobanks, which were initiated several decades ago. To access these and other biobanks the two consortia merged their efforts towards increasing the quality, usefulness and accessibility of the Swedish biobanks in a national biobanking program. The main goal of the program was to develop a system for quality assured collection, handling, storage and documentation of biological samples together with increase the ethical awareness and accommodating new rules and regulations from health authorities. During the program period considerable advances have been made in establishing a national network in biobanking. It is an opinion in the national biobanking program that the Swedish arena for biobank-based research is ready for large-scale genotyping.

To give the Swedish biobanks international credibility, and to facilitate development of research programs based on biobank material a group of international experts convened to give a critical evaluation of the existing Swedish biobanks and the coordinating activities hitherto undertaken and to propose recommendations for further improvements. Members of the evaluation committee were Professor Thorkild IA Sørensen (chairman of the committee), Copenhagen, Denmark; Professor John Bell, Oxford, UK; Professor Jussi Huttunen, Helsinki, Finland; Dr Jaanus Pikani, Tartu, Estonia; Professor Mike Pringle, Nottingham, UK.

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Essential recommendations

Sweden has a special track record and opportunity in Biobanking, not least due to the unique conditions and facilities offered by the Swedish system (health services system, high quality of research, personal identification number, active international collaboration, progressive legislation, positive attitudes among the public, etc.). However, there are major limitations of the biobanking programs as they currently exist. The major issue is how it moves from a relatively disparate and disconnected set of individual programs to one program, which is more coherent with uniform standards, uniform data sets and the possibility of relatively easy access for scientists attempting to interrogate biological samples or databases that emerge from these programs. Although the elaborate and very well and thoroughly described National Biobanking Program gives promises for the future, it seemed to the Evaluation Committee as if the programs are a long way from implementation of this result. There is indeed a great deal of very good activity going on, but it is relatively disconnected and certainly not yet well integrated. It is the opinion of the Evaluation Committee that if major advancement in this area should be achieved in the foreseeable future, say in the next 5 years, the need to establish the systematic and integrated approaches is urgent. The support from the Wallenberg Foundation has put the grounds for the next step, but there is clearly a need for continued support from this and/or other foundations to build the real national biobanking program on these grounds.

Below follow a series of the most essential assessments and recommendations as derived from the critical evaluation and consideration of realistic opportunities:

- The current biobanks are valuable, but of variable quality and need coordination, and especially by a central facility allowing access to and sample retrieval in all the biobanks, and such facility should be based in a strong academic research environment in order to facilitate optimal exploitations of the research opportunities.
- As genotype information is added to the database, their potential will increase greatly.
- There is need for coordinated implementation of the common quality assurance, standard operational procedures, data management systems, and accreditation systems developed in the NBP.
- There is need for harmonized national and regional biobanking organizations.
- There is need for rules of access by different actors.
- There is need for improved rules of intellectual property rights.
- There is need for researcher training.
- Measures should be taken to increase the exploitation of the current biobanks.
- It should be recognized that the developments undoubtedly carry risks for mistrust in confidentiality and loss of societal support.

- There is need for improved public information on ethical issues and on data confidentiality issues, with particular emphasis on using the biobanks for large-scale genotyping.
- There is need for continued development of the international collaboration (especially between Scandinavian countries), also on aspects of legislations and ethics.
- The valuable support from the Wallenberg Foundation should continue.

On behalf of the evaluation committee

Thorkild I. A. Sørensen, *chairman of the evaluation committee*

Definition of a biobank

There are a number of definitions of biobanks and no international consensus. The evaluation panel found the following definition useful for the particular purpose:

A long-term depository of biological samples from an identifiable human population. The content of the depository must be of such quantity and quality that it is suitable for later biomedical analysis in epidemiological and clinical research and for individual clinical purposes.

Comprehensiveness of biobank series

In view of the expectation that the evaluation addresses the Swedish biobanks on a national level, the comprehensiveness of the NBP and of the biobank series presented for evaluation is important.

The biobanks evaluated during the process were those participating in the coordinated national biobanking activities and those responding to the invitation to the evaluation. One of these did not present ((16) Epidemiology group, Preventive Medicine at Sahlgrenska Academy, Gothenburg, Dag Thelle).

The committee has been informed that this series of biobanks is not comprehensive. A major one missing is the so-called PKU biobank, which collects droplets of full blood on filter paper used for screening of all newborns in Sweden a few days after birth for Føllings Disease and other congenital or inherited disorders. The PKU biobank has been established without informed consent. The samples for the whole country are owned by the Stockholm County Council. According to the Director of the biobank, the available resources were not allowing the biobank to be included in the NBP, and it was therefore not included in the evaluation. A number of disease-specific biobanks (*e.g.* on breast cancer, on prostate cancer, on obesity, on the elderly) are also missing.

Criteria for evaluation of the biobanks

The evaluation of the biobanks and the biobanking programmes was based on an overall judgement of what was presented and not on any systematic scoring or predefined weighting. Major emphasis was put on the current and possible opportunities for future research in accordance with the applied definition of biobanks. The following elements came into the evaluation at various levels:

- General aspects
 - Positive features and limitations
 - Significant scientific achievements
 - Cost-effectiveness
 - Time scales
 - Standard operational procedures (SOPs)

- Ethical issues
 - Patient consent
 - Patient withdrawal later
 - Returning to patients for later data
 - Ethics committee approval of biobank
 - Ethics committee approval of studies
 - Policing of use of data for study aims only
 - Intellectual property rights
 - Safety of biobank staff
- Methodology
 - Sample selection
 - Representativeness
 - Prospective data collection
 - Quality assurance procedures
 - Confidence that controls are controls
- Confidentiality and security
 - Reference numbers, patient identification and anonymisation
 - Security of storage of samples and data
- Access to the biobank
 - Preferential access by staff
 - Access by researchers
 - Prioritisation especially of depletable resources
 - Access by commercial companies

Comment on Swedish National Biobanking Programme (NBP)

There has been very considerable progress made with the help of Wallenberg support organising and aligning the multiplicity of biobanks that exist and are being developed in Sweden. The programmes are largely of high quality but all suffer from significant power problems for many of the types of studies that will be demanded in common disease from these samples in future years. Continued development and implementation of the coordinated activities of the Swegene, the WCN and the umbrella organisation, NBP is urgently needed. This does not mean that individual biobanks need to give up their precious samples to a central storage facility, rather better coherent informatic linkage of these programmes so that archived material between different biobanks can be identified within a single database and retrieved with a certain degree of efficiency. This is clearly not now the case and needs to happen if the full added value of Wallenberg support is to be achieved. Owing to differences in the laws for IP in the universities and the health care system, there also remains clear differences in the approach within biobanks to commercialisation that need to be resolved and clear rules need to be established for access to the broad biobank resource which will exist across multiple sites. Only when this is in place will it be possible to describe the multiple biobanks as a single tissue resource for the whole of Sweden, a single serum and DNA resource for prospectively collected samples across the country and a single resource for serum samples related to infectious disease which can be accessed in an integrated way. It may be considered to be an integrated activity in the public health care services.

Considerable progress has been made with Wallenberg support to identify and support a large number of high quality biobanks. Without further integration of these programmes, however, much of this value will be lost. Once integrated, consideration might be given to a new major Swedish biobank but also consideration should be given to improved networking, particularly within the Scandinavian countries and also in the international arena.

Suggestions for improvements in Swedish biobanking

National networking between biobanks

High quality *genetic and epidemiologic research* requires study cohorts of sufficient power, adequate quality assurance systems, open access to all interested scientists, and collaboration both in terms of methodology and study hypotheses. These goals could be reached in Sweden by effective utilization of the existing biobanks the entire research community, and/or by establishing a new large national prospective cohort such as the ones now established in Denmark and under way in Norway (see below).

There are a number of *positive features* that make Sweden is leading country for biobanking:

- An historical collection of samples, many suitable for genotyping
- Samples from large cohorts of the population.
- The Person Identification Number used in all settings – not just health – that can be used to facilitate accurate record linkage.
- A sophisticated legal and regulatory environment that is permissive for biobank development.

Given these assets, Sweden should continue to support initiatives on biobanking. In doing so, it should concentrate on maximising the value from its best current biobanks.

The relatively large number of different type of human biological samples and health data collections in Sweden is thanks to the *enthusiasm and personal motivation* of researchers as well as practicing doctors. This type of voluntary commitment has resulted in an invaluable resource, but one that has been underexploited due to its fragmentation. In contemplating steps to improve biobanking in Sweden, one has to be aware of the dangers in centralising the structure of biobanks. However some centralisation is inevitable if the real value of the existing collections is to be exploited.

Achieving the right *balance between autonomy and organisation* is a major challenge for Swedish biobanking system. One option would be to develop a harmonised basic biobank software infrastructure that could be updated centrally. An important feature of this type of solution would be the possibility to add locally tailored modules to meet the special interests of local researchers. Such a development would require careful promotion and the training of people involved.

Consideration should be given to reinforce the implementation of the well-developed national scheme for *regulating the quality assurance and accreditation* of biobanks. The process has been adequately initiated by the NBP and enables, if taken forward, for networking researchers with suitable biobanks and databases; and possibly for managing access to samples so as to maximise research while protecting a depleting resource. Certainly some central coordination to ensure equity of access using rules acceptable to the scientific community is necessary. Those biobanks that contain high quality samples, which can be used for research analysis and genotyping, should be identified and quality assured. A census of the samples and their quality should be undertaken. This group of

accredited biobanks should be publicised to researchers and their exploitation encouraged.

The *collaboration between the Swedish biobanks* has improved during the recent years due to the development of the coordinating organisations and especially the NBP, but is still far from ideal. Only a part of high quality biobanks is open to all interested scientists, as they should be under ideal conditions. The situation could be improved by agreeing on terms by which the “open access” policy could and should be pursued under different circumstances. Networking and collaboration is possible only if information on the existing biobanks is available to all interested parties. A comprehensive register (including both the true biobanks, but also sample collections of individual research groups) would be a powerful tool for promoting joint exploitation of the biobanks.

An effective tool for enhancing the collaboration between biobanks and researchers is *education and training*. Courses directed at disseminating knowledge on potentials as well as limitations concerning the use of biobanks in biomedical research would increase the awareness of their potential and, simultaneously, stimulate collaboration between the groups working in Sweden. And there will be a requirement for clinicians and others who fully understand the meaning and significance of the content of datasets to ensure high quality science. There is a real need to promoting research among life science students. The huge amount of data is useless without well-trained researchers exploiting them.

The *potential for linking data* between biobanks themselves and between biobanks and other databases should be exploited. In particular links to electronic clinical records would be a significant breakthrough. Using the unique patient identifier, the linkages should be reliable and the research potential resulting should be substantial. The effective use of biobanks and linked databases is a high skill activity. There is a need to stimulate academics to develop the skills to formulate questions and answer them using these complex datasets. There will be a need for a cadre of skilled programmers and statisticians to work alongside the researchers.

Although the *legal framework* for biobanks is clear, the more that the public understand and support the creation and continuation of biobanks the better. There is a real risk of a cultural backlash. It would therefore be advantageous to undertake two initiatives. One would be to reinforce research governance and access controls; the other would be to inform the public and lead a debate on the ethical implications of this work. In particular, the rules for commercial exploitation need to be clear before the first attempts to exploit the biobanks commercially.

The *Regional Biobanking Registries* outlined in the summary of the National Biobanking Programme and partially operative in Region Skåne are an ideal way of promoting collaboration in the regions. Establishment of a national registry would further promote collaboration and provide practical solutions and advise to ethical, legal and logistic problems in the use of biobanks for research. The Wallenberg Foundation could promote the collaboration by giving start-up support both to several new regional registries and to establishing a national registry, which should be hosted by a strong academic research environment securing the high quality support and exploitation.

Establishment of new biobanks

If Sweden were to consider a new national biobank cohort, it should consider carefully what that should be and how it should be structured. Any national biobank needs to have open access to all scientists in Sweden and ideally should be accessible to scientists on the international stage.

Except for the PKU biobank, no pregnancy-birth cohort currently exists in Sweden, whereas it has been established in Denmark and is under way in Norway. Similarly, a cohort with extensive environmental exposure data associated with biological samples and of the size necessary for genetic epidemiology studies also do not yet exist. The establishment of such cohorts could be facilitated by involvement of the strong epidemiological research groups in Sweden.

International collaboration between biobanks

The availability of a range of molecular tools for analysing materials stored in biobanks has excited the international biomedical research community to the extent that large biobanking programmes are either in place or being proposed in a number of different countries.

The USA has proposed a large prospective cohort, while such cohorts are currently being collected in the UK (UK Biobank), Mexico City, Japan and China. Canada is also considering a prospective cohort, but has yet to agree on its exact size and scope. "Genome Canada" has been instrumental to support an initiative P3G (Public Population Projects in Genomics) that is aimed to harmonise the human biological sample and data collection. The founding members of the not-for-profit organisation are Quebec project Charagene, GenomEUtwin project led by Finnish researchers and Estonian Genome Project. Several Swedish cohorts have been used in international research collaboration (*e.g.* EPIC). The Nordic countries have had the health care infrastructure most conducive for the development of biobanks. Substantial biobanks exist in Denmark, Norway, Finland and Sweden, and some of them are currently coordinated in the Nordic Serum Bank Network (headed by Joakim Dillner), but these activities could be brought much further if the resources are available.

Legal constraints may prevent complete integration of these programmes, but closer affiliation of the Swedish biobanks with other such initiatives within Scandinavia would greatly enhance the potential power of these programmes. Given that even the largest biobanks being proposed (*e.g.* the UK Biobank) will be underpowered for many common diseases, the use of multiple national biobanks to solve major problems in genetic epidemiology will be essential for the success of these programmes.

There are several ways in which networking between biobanks could be used for the benefit of the Swedish biobanking programme.

Firstly, alignment of the structure of these biobanks will allow the same questions to be asked in several different samples if information and biological materials collected in different biobanks are similar. It would be an important way forward to motivate local

“biobankers” with enhanced funding through national and international collaboration, available only in the harmonised environment. Harmonisation is needed not only in data and sample collection, but even more so in developing the ethical and legal environment. For example, the current regulation of informed consent varies, leading to potential confusion in international collaboration projects. Another example is the commercial use of samples and data. Numerous international initiatives both by inter-governmental (OECD, EU etc) and non-governmental organisations (*e.g.* P3G) have started to address the issue of harmonisation

Secondly, much is currently being learned about best practice in terms of storing biological samples and sharing this knowledge between different countries will avoid new biobanks “reinventing the wheel” every time they set up a biological store.

Finally, there is a significant human capacity problem that needs to be solved in the near future for these biobanks to be properly mined for useful information. As a matter of urgency, training programmes need to be established and some of these may involve exchanges between scientific programmes that rely on biobanks in different jurisdictions. This could significantly enhance the attractiveness of this field to young investigators and would also form natural collaborations between the sites.

Thus, as with networking within Sweden, which needs considerable improvement, networking of Swedish biobanks externally to other national biobanks will be important to ensure best practice, to achieve the power necessary for some of these studies, to help develop training programmes for young scientists and to ensure that Sweden gets the best value for money out of its programmes.

Comments on the individual biobanks

Tissue biobanks

Fresh Frozen Tissue Biobank (1), Uppsala University; *Johan Botling*

This is a clinical biobank with priority to diagnostics. The collection is divided into two parts: (1) old biobank, sampling started in 1970s; (2) new or pilot biobank starting from 2001. The biobank contains over 20 000 tissue samples that are accompanied in some cases by cell pellets, imprints, DNA-,RNA- and protein extracts. The samples are stored in -80C freezers. Additionally, app 20 000 cryovials with vital cells, mostly lymphoma and leukaemia cases, in DMSO/serum are stored in liquid nitrogen.

The Fresh Tissue Biobank represents an example of impressive collection of non-fixed tissue samples. Being a clinical biobank there is very limited phenotypic and background environmental data directly collected into the database. Although, the unified ID number enables to retrieve clinical data from existing patient charts, the non-harmonised recording of clinical events and historical differences in diagnostic patterns will make the process extremely troublesome for large scale use. Access to the resource is controlled by a steering committee, and the final decisions are made by the Head of the Clinical Pathology Dept. Whether there is need for informed consent is decided by ethics committee on the basis of the Biobank Act.

The processes in the biobank are organised in accordance with the NBP Good Biobanking Practice. The pilot biobank involves extensive development activities on sample collection technological process, particularly on RNA quality tests. The well-established QA is an outstanding feature of the Fresh Tissue Biobank.

At the same time not all historically collected samples are fed into the electronic format. However, there might be questions about using old samples for new purposes. Historical diagnoses may not stand.

Even though the number of withdrawals has been relatively high (17) in 2004, the number of samples per research projects has been limited. Only four publications emanating from the biobank have been reported during recent years.

The Fresh Tissue Biobank represents a good example of valuable resource that can contribute to the well-organised network of various data sources in existence of common linking denominator. This type of collection could be more of value if the basic harmonised electronic patient data recording will be introduced in coming years.

There is a huge need for this kind of biobank, which can be used with new tools, but it must have better background data, put in an electronic database. Important opportunities are to identify specific infectious material and to conduct proteomics studies.

Brain Tumor Biobank (2), Karolinska Institutet; *Monica Nistér*

The narrow targeted brain tumour tissue biobank to collect non-fixed tissue samples removed at neurosurgery. The collection has started in Uppsala in mid 80s and in Stockholm in 2002. There is currently app 600 with no extensive clinical data attached,

but patient ID and clinical diagnosis. The exemption is low-grade gliomas from Uppsala region, where special research project has been carried on. In recent years also DNA and plasma samples from patients has been collected. The storage is taken place at -70C in two separate locations: (a) Karolinska Tissue Biobank and (b) Pathology Biobank in Uppsala. While there is no joint database for two sub-parts currently, ethics committee permission has been obtained for a joint tumour biobank

During 2004 withdrawals for five projects with 90 tissue samples and 20 blood samples has been performed. The attached list of publications by PI contains over 30 entries. Approximately one third of these, however, seem not to be directly connected with this particular biobank.

The Brain Tumour Biobank has been active in development of sample handling technology and QA for genomics and proteomics under National biobanking program. The QA manual is still under construction.

As a special purpose “boutique”, it would be probably more cost-effective, if the biobank could be linked under an umbrella of more professional database organisation that could provide harmonised database engine and operational procedures, e.g. the tissue biobanks of Uppsala or KI. This could also facilitate the wider enrolment area and external use of the valuable resource.

Tissue Biobank for Cancer Research (3), Lund University; *Bo Baldetorp (presented by Henrik Simán)*

This tumour tissue collection at the Lund University Hospital has been started in 1980. It contains app 40 000 samples from app 30 000 individuals. It is more diagnostic collection than properly designed biobank with standardized data collection and operational procedures. There is no approved QA system but freezers electronic temperature control. The samples are kept at -80C.

No clinical/phenotypic information attached to samples. Additional data can be retrieved either from Regional Tumour Registry or patient charts at Oncology Centre of the Hospital.

Sample retrieval is controlled by different research groups, except for breast tumour samples, which are decided on by a tumour bank committee. It has been reported app 15 projects with app 1500 samples carried out on the biobank material in 2004 with no external projects distinguished. 414 publications have been published with the help of Tissue Biobank from 1980 to 2004.

To develop this sample collection to a tissue biobank, it will be necessary to build and add the biobanking facilities as described in the NBP.

Tissue Biobank Karolinska Institutet (14); *Bertil Hamberger*

This is a collection of selected pathology material, mainly endocrine tissue, from 1986 onwards with 5368 samples from app 4500 patients. During recent years other types of tissue samples have been added to the biobank. The abovementioned Brain Tumour Biobank's Stockholm part is administered by this biobank. The sample retrieval is

authorised by a single responsible person without back-up in an organisation, which may make it sensitive to conflicts of interest very likely to a “one man “shows. It has no approved QA manual yet. The number of publications listed 2001-2004 is 24. There is no data on external use of material.

To be able to participate in a national program, the biobank need to be associated to a database, thereby facilitating coordinated exploitation. It is missing a control mechanism of what samples are put in and what are taken out. The easiest way to improve the utilization of the resource would be, perhaps, to link the tissue biobank to the KI Biobank database infrastructure.

Epidemiological cohort biobanks

Medical Biobank (5), Umeå University; *Göran Hallmans*

This is an excellent biobank with long follow-up and information on phenotype and clinical information from over 100 000 subjects. The cohorts consist of the Northern Sweden Maternity cohort and Northern Sweden Health and Disease Study (the Västerbotten Project Cohort, The Northern Sweden Monica Cohort, and The Västerbotten Mammary Screening Cohort) combined with about 20 smaller biobanks collected by scientists from different parts of the country. The number of individuals is ca. 100 000 (a large part of the population), and samples have been collected on almost 300 000 occasions. Buffy coats have been collected since 1990 with app. 145 000 samples. In principle, the access is free for interested scientists. The quality control system covers all activities of the biobank. The data has been extensively exploited in a large number of epidemiological studies.

The problems include insufficient long-term financial support and lack of equipment for DNA extraction. The Wallenberg Foundation has supported the Umeå Medical Biobank, and there are all reasons to continue the support. Ideally, the Umeå Biobank should be organized in a similar way as the region Skåne biobank system. Continuation of the re-sampling is important. Overall, this is one of the best Swedish biobanks and can be utilized in various genetic and epidemiological studies in the future. The panel was informed about the legal process on the way in the Umeå biobank, but did not discuss the matter in detail.

Malmö Preventive Project (6), Lund University; *Göran Berglund*

The Malmö Preventive project is a prospective epidemiological study set up in 1974 by the late professor Bertil Hood. The total number of person-years of follow-up was 730,000 in the end 2004. Plasma, serum and DNA samples have been collected from 33,000 individuals. A quality control system started in 1990 and appears to be at least satisfactory. The study is seriously understaffed and poorly funded, which may endanger the future of the project, when the Principal Investigator retires within a few years.

The value of the project is based on long follow-up and large amount of information collected during the study. The main emphasis has been on the epidemiology of cardiovascular diseases. The study has not, however, been adequately exploited even in this area. The cohort is probably too small for genetic research, but would be very

valuable for research on the aetiology and mechanisms of chronic non-cardiovascular diseases.

Malmö Diet and Cancer Study (7), Lund University; *Göran Berglund*

The Malmö Diet and Cancer Study is a part of a large European collaborative study on the role of diet in the aetiology of cancer (European Prospective Investigation on Cancer, EPIC) coordinated from IARC in Lyon. The total number of the unique individuals who have donated samples (erythrocytes, granulocytes, cryo-preserved lymphocytes, plasma, and serum) to the Swedish cohort is ca. 28,000. The quality control system is adequate. The cohort is open to all researchers.

Even though the entire EPIC study encompass more than 500,000 subjects and is among the largest cohorts in the world, its power is barely sufficient to give meaningful answers to hypothesis about low excess risk exposures such as the diet-cancer association, and therefore, the Swedish sub-cohort will be able to contribute to such hypothesis only as a part of the whole study. The problems include relatively low participation rate (40 %), high costs of the biobank and lack of interest of granting bodies in Sweden. The number of scientific papers published so far is relatively low, but there is a great potential, particularly if continuation and external collaboration with other biobanks are secured. The lack of a staff securing the continued activities implies that retirement of the Principal Investigator may cause difficulties for the continued follow-up the cohort.

The Swedish Twin Biobank (9), Karolinska Institutet; *Ulf de Faire*

The Swedish Twin Biobank is based on the Swedish Twin registry containing information on environmental and life style factors and disease phenotypes by repeated questionnaires and interviews over 30-35 years. The Swedish Twin Registry has provided a remarkable resource for the study of environmental and inherited factors in disease. The purpose of the biobank is to study functional genomics in complex diseases. Blood has previously been collected and DNA extracted in selected sub-samples of the twin cohort, and systematically from ca. 900 individuals since 2004. Blood sampling and data collection will continue through the next years. The Biobank is using the Karolinska Institute (KI) biobank infrastructure, and is available to external research groups, both national and international. The project has, as a part of the KI Biobank, explicit procedures for quality assurance. All laboratory procedures have been documented.

The Swedish Twin Biobank is an extremely valuable source for investigating the relationships between environmental factors, biomarkers and diseases. There is potential for collecting relevant information and blood samples for e.g. genetic studies from over 10,000 twin pairs, born in 1958 and earlier, with collection from the whole of Sweden and stored at KI. Nevertheless, the amount of biological material currently stored will prove to be inadequate for most of the genetic studies that are being proposed, although studies of biomarkers may be facilitated even with the material currently collected. Even when 10,000 pairs have been collected, the power to detect genetic effects will often need collaboration with other twin programmes and therefore, national and international collaboration is an absolute necessity. The Study Group is already integrated in several ongoing large international research networks. This will be greatly promoted by the

existing European network, now launched under the EU FP5 project, the GenomEUtwin project, coordinated from Helsinki, Finland. The crucial target, therefore, for this Twin Registry will be to collect much more biological material over the next few years and to maintain its lead as one of Europe's biggest and most influential twin registries. Sufficient funding of the Twin Biobank is of paramount importance, not only during the initial part of the project, but also later. It is a problem for the individual researcher to get information about what samples and data are already collected and this shortcoming must be dealt with.

Uppsala Longitudinal Study of Adult Men (ULSAM) (10), Uppsala University; *Lars Lannfelt*

The Uppsala Longitudinal Study of Adult Men was initiated in 1970 and is based on the follow-up of a representative population sample of 2322 men who were 50-year old at the outset, so the survivors are now app 84 years old. The investigations have been repeated on regular intervals and the last examination was finished in April 2005. The follow-up data contains very valuable detailed information on the phenotypes and medical history. DNA has been collected at the end of the 1990's. The aliquots are stored at -70C. The database has been extensively utilized over the years.

The strengths of the study include long-follow up and careful collection of the phenotype data. The cohort is too small for any meaningful genetic studies, but is very useful for epidemiological studies of age-related diseases. Maintenance of the biobank is at risk because of the funding problems. Because of the small size of the cohort is not at the priority list for funding from the National Biobank Programme.

All Babies in Southeast Sweden (ABIS) (11), Linköping University; *Johnny Ludvigsson*

The All Babies in Southeast Sweden was initiated in 1997 with the purpose to study the environmental factors for the development of Type 1 diabetes, but also other autoimmune diseases, such as allergy and celiac disease. Data and various biological samples (including DNA) have been collected from app. 16,600 children and mothers and 2500 fathers. Registration of environmental data is extensive. Storage of the samples appears to be appropriate, although there is not a comprehensive quality assurance system.

The cohort does not have enough power to give any meaningful answer to the initial study hypotheses (environmental causes of the Type 1 diabetes), which explains at least in part the difficulties met in the funding of the project. The publication record is mediocre, one reason being lack of collaboration with other groups working in the same area. The strength of the project is extensive information collected in a representative population sample. So far, the exploitation of the biobank has rested on its founder only, but it is the opinion of the committee that the study would definitely benefit from national and international level and from extending the focus from Type 1 diabetes to common diseases of childhood. The funding attempts will fail without collaboration and broadening the focus.

The Botnia Study, Lund University (15); *Leif Groop (presented by Göran Berglund)*

The aim of the Botnia Study is to elucidate the genetics of Type 2 diabetes. The study has collected comprehensive environmental and clinical information and biological samples from ca. 9000 individuals, in part from Finland. The group has an excellent publication record and scientific reputation. The database (including the biological samples) is typical for one single research projects and does not fulfil the criteria of a biobank. The project is definitely worth of funding but not as a part of the National Biobank Programme.

Microbiological biobanks

Swedish Institute for Infectious Disease (SMI) Control Biobank (12); *Ragnar Norrby*

SMI has a national role as testing lab for infectious diseases and is also a regional asset for Stockholm region running microbiology service. The samples stored in this biobank date back to the 1950s when collection was started by the State Biological Laboratory, whose samples have been inherited by the Swedish Institute for Infectious Disease Control. There are now approximately 750,000 samples at -20° , including serum, plasma and CSF, each accompanied by demographic and limited clinical data. The rather high storage temperature may affect the quality of the samples, and validations will be necessary for analysis of substances that may degrade at this temperature. Access to the resource is controlled by a steering group, which meets quarterly.

This biobank has some considerable assets. It has a large number of samples from a 50-year period and each sample can be linked to the patient's unique registration number. It can be used to retrospectively track the emergency of and changes in infections and, if linked, could allow follow up of clinical outcomes.

However, it is not used extensively. Of the five references given, the most recent was for 1998 and in 2004 there were only 4 withdrawals of samples. The samples are, due to the nature of the two organisations contributing, not representative of general population samples and their use for research may be limited. The age of some samples may adversely affect their usability, reducing this biobank's unique strength.

This biobank can only be used effectively if the potential to use the patient registration number to link to other databases and biobanks could be exploited. There are a number of ethical issues to be addressed in doing so. Overall, the potential of this biobank appears limited, but could be increased if linked up with facilities of other already established biobank systems.

Malmö Microbiology Biobank (13), Malmö University Hospital; *Joakim Dillner*

(Joakim Dillner was not present during the discussion of this biobank)

While only started in 1969, this biobank has nearly a million samples from the regional population in Southern Sweden, and is growing at 100,000 samples a year. It is primarily a serum bank (much of which was taken for maternity testing and blood donor screening, and will represent a reasonable coverage of the adult population). Access to samples, which are stored at -20° , is through approval by the chairman of the biobank and quality assurance systems have been in place since 2000.

An important use of this bank is to explore the relationship between antecedent virology and subsequent development of cancer, using links through the patient registration number to the cancer registry. The size of the population with samples in the biobank (half a million) should allow studies on relatively uncommon outcomes, such as many cancers. When substantial numbers of samples have been genotyped, this biobank will become even more valuable.

There have been very few external requests for access (only 2 in 30 years) and in 2004 only one internal project. Despite this the publication rate has been satisfactory, if not as high as might be expected from such a resource. The procedure for accessing the biobank needs clarification and strengthening, and there needs to be much wider knowledge of the biobank's existence and research potential. To avoid conflicts of interest, at least in principle, it should be considered to separate the responsibility of being PI from being chair of the steering committee. The biobank is already integrated in the Skåne Biobank system, and continued development of links between this biobank and other databases will further increase its research potential and use.

Biobank infrastructures

Region Skåne Biobank (4), Lund University; *Thor Alvegård (presented by Henrik Simán)*

This biobank is perhaps a model as to how biobanks are likely to develop nationally around Sweden and ideally around all European countries where nationalised healthcare provision is available. It has the advantage of being very large and systematic providing a collection of patient samples that could cover the population of 800,000 individuals in Skåne province. The programme requires significant additional input to ensure that it is properly used. In particular, the distributed nature of the sample storage needs a highly efficient QC and QA structure and relatively easy systematic access to these samples needs to be assured using the currently developing biobank information management system. It is not clear that, in the end, a distributed sample storage structure will be the optimal solution to such a programme, but it is a good place to start and one could eventually transfer this programme to a more coherent centralised storage facility. The Swedish healthcare system is ideally suited for such a structure. This is the most exciting biobanking concept within the Swedish system and will pioneer this model for a range of other regions in Sweden as well as for the international community.

However, there are some problems to be solved. The way to achieve consent is very risky, and they may be playing on thin ice, and they run a high risk of a media scandal. Ethical issues are going the same way in the Western world. The Committee recommend a more solid ethical structure. Financing is a risk, by not being controlled by the scientific community, but the maintenance is essential for the health care authorities, which are obliged to be able to identify and destruct samples if consent is withdrawn. The central registration of all samples is not yet complete, but must be done if this should be a model for the rest of the country.

KI Biobank (8), Karolinska Institutet; *Gunnel Tybring (presented by Helena Andersson)*

The KI Biobank is still in its infancy and currently consists of some sample-handling infrastructure and is backed by a significant expertise in epidemiology and genetics that exists at the Karolinska Institute. It is highly appropriate that the Karolinska become actively involved in biobanking in Sweden in the future, but it was clear that the exact role planned for the KI Biobank had not yet been agreed. Karolinska could provide the host facilities for a biobank similar to the Region Skåne model except that it would be for a different region. At the moment, such a regional role would seem most appropriate. If and how a KI Biobank can contribute to the biobanking activities at the national level depends on the future development of the various elements in the NBP.

It is important to recognize that the Karolinska has been relatively slow in establishing the necessary infrastructure for biobanking, but has as strong an academic program to support such activities as any program in the country. What are needed now are local leadership and a coherent plan as to the exact role of the KI Biobank infrastructure within KI and the region and in relation to the NBP.

Appendices

- A Letter of invitation to committee members.
- B List of panel members.
- C The National Biobanking Programme
- D Biobanks planned to be evaluated
- E Form for information about the biobanks
- F Program for the presentations of the biobanks
- G List of participants at the presentations
- H The evaluation process