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Interview with Jens Mattsson,
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At LifeGene test center, Stockholm



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Editorial board & lay-out: Sofie Petersson, Ann-Sofie Lundin, Loreana Norlin

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Editorial

How to realise the full potential of a biobank infrastructure

Biobanks are playing an increasingly important role in transferring knowledge to health systems and many countries envision that their biobanks will become integral parts of their health care structures. Knowing a patient's genetic makeup in advance could allow a doctor to identify if that patient would respond poorly or adversely to a drug. The astonishing triumph of technology is still hard to take if you remember how tedious DNA sequencing used to be.

Biobanks will also serve as a resource for exploiting new methodologies and developing innovative biomolecular technologies.

So far, most biobank infrastructure initiatives have developed as organisational networking, pure harmonisation efforts in terms of specific data sets, or standardising operational procedures for material collection. While this is important, the full potential of a biobank infrastructure will only be realised if a biobank e-infrastructure is constructed.

Biobank collections often suffer from fragmentation and underutilisation due to lack of commonly applied standards and limited access by investigators. As a result, merely retrieving high quality data on clinically annotated human samples is a time-consuming bottleneck for biomedical research. Compounding the problem is the fact that biobanks contain sensitive data from human donors.

As biobank data become more abundant, the main problem is no longer finding the information as such. What is needed is information about (biobank-) information, or (biobank) metadata. A meta-model for biobank hubs is a first step towards data sharing among biobanks that exhibit tremendous heterogeneities. A common set of attributes defines the minimum dataset. A minimum data set for biobanks and a metadata model for biobank hubs have been developed, and BBMRI.se is the first country to try to implement that model.

The meta model is designed to adopt different kinds of collections and biobanks by using different schemas for study types and as such allowing to achieve integration with high information content while still allow as many biobanks as possible to participate. The latest interoperability and semantic web technologies can be used for building resource description frameworks for data and services providing flexible frameworks that can be used in different data sharing scenarios. In order to obtain a unified view of the semantics of the attributes, each attribute can be defined in a multilingual vocabulary - and this is the first step towards a roadmap for global biobanking.



By Jan-Eric Litton

Work package report (WP6)

Starting to get the value of BBMRI.se

In our previous newsletters we have talked about building up the different parts of BBMRI.se. There is still much development to come, but it's also pleasing to report on some early outcomes, with the first withdrawals and analyses being made on samples banked in BBMRI.se.

The breast cancer study KARMA (also introduced in our last newsletter) is gathering samples and data from 100.000 women in Sweden, over this year and next. So far it has collected samples from more than 15.000 women and now has made its first withdrawal for analysis.

KARMA participates internationally in the Breast Cancer Association Consortium, which has now assembled 100.000 samples in total from different studies. These are genotyped at Cambridge University (using an oncology chip called ICOGS) making the largest genome wide association study ever conducted.

The large scale biobank of BBMRI.se processes KARMA samples routinely now, and by July had extracted DNA from 6000 KARMA donors. Portions of this DNA were sent to Cambridge for the consortium genotyping. Very preliminary analysis shows approximately 25 new susceptibility genes for breast cancer have been identified.

This is a very exciting development, above all for breast cancer research and the study, but

also for BBMRI.se as our first example of how we will gain practical value from the BBMRI.se biobank.

It has also been a *very fast* achievement, thanks to great collaboration between the staff in the study and the biobank. Slow access is a common problem for most biobanks,

“Slow access is a common problem for most biobanks, and this is something BBMRI.se wants to overcome, so this early test case is a promising sign.”

and this is something BBMRI.se wants to overcome, so this early test case is a promising sign. We are grateful to KARMA for helping drive us forward.

Withdrawals from two other BBMRI studies are also now being planned, and we look forward to reporting on some research outcomes in future newsletters.



By Mark Divers

Interview with Jens Mattsson at LifeGene

LifeGene



The LifeGene study is a national collaborative project designed to create a resource for research in all medical disciplines, enabling new and groundbreaking research on the connections between heredity, environment and lifestyle. The study, which is unique in the world, will include a survey of half a million Swedes between the age of 18 and 45. The aim is to create new tools for preventing, diagnosing and treating our most common diseases and health problems such as asthma, allergies, infections, obesity, repetitive strain injuries, chronic fatigue and pain, and major diseases in later life — cardiovascular diseases and cancer.

I meet up with Jens Mattsson, the operating chief of LifeGene, to have a talk about the study. He tells me what makes this study so unique: it gathers information about disease in early life that might have an impact on disease later in life. Jens also mentions that LifeGene is what he calls an event-based study, which means that the study follows people and takes blood and urine samples before, during and after the occurrence of an event/disease — for example the swine flu or a pregnancy. What is also unique is the household-based recruitment of individuals; LifeGene invites whole families to the project.

In the last issue of **biobank SWEDEN** I interviewed Lars Lind, the project leader for EpiHealth in Uppsala. LifeGene and EpiHealth have a close collaboration and together they cover almost the entire age range in Sweden. LifeGene invites participants between 18-45

years of age and EpiHealth participants between 45-75 years of age.

Jens believes that BBMRI.se is an important infrastructure, essential for LifeGene. He comments that there is a growing demand for a large-scale bio-banking facility like this, with a standardized sample handling. LifeGene is a unique study and has been normative for other large scale studies.



Jens Mattsson

I ask Jens if LifeGene has generated any research results so far and he tells me there have been two scientific publications from the pilot study. The first call for proposals from the “real” LifeGene study will be opened shortly. Jens points out that LifeGene is a platform for a myriad of researchers and research projects - researchers not only in the fields of biomedicine and biotechnology but researchers in behavioral and social sciences may also benefit from having access to LifeGene.

Today LifeGene have two running test centers, one in Stockholm and one in Umeå. The future plan is to open up a test center in every city in Sweden with a medical university.

Behind LifeGene are all Swedish universities with medical schools.

LifeGene is funded by grants from the Research Council, Karolinska Institutet, AFA Försäkring and Torsten and Ragnar Söderberg Foundations.



By Sofie Petersson

Work package report (WP2)

Coordination of population-based biobanks — an example of osteoporosis

WP2 has employed research coordinators at the major medical universities, which form a network enabling strong national cohort cooperation. The national process has already started with a large number of projects, including organisation and reusing of national WGA materials, development of a joint model for ethical applications within WP2 concerning complex projects, stimulating the development of different national disease registers, development of the Meta-Health strategy, but also to identify national projects with a high international potential and if possible a world-leading position in biobank research.

The WP2 coordinators will also be involved in the direct coordination of different national research projects, including for example national cancer projects, national cardiovascular projects, projects including autoimmune and chronic inflammatory diseases,

neurodegenerative diseases, and osteoporosis projects.

A national network for osteoporosis-researchers was established in 2008 already by professor Karl Michaelsson, Uppsala University. This network is supported by grants from the Swedish Research council and meet twice a year. At the latest network meeting in Uppsala in May 2011, Ulrika Pettersson Kymmer, which is participating in the osteoporosis network and a national coordinator for osteoporosis within BBMRI.se, WP2, gave a brief description of the aims with BBMRI.se with special attention to WP2. The information was well accepted and there were many good discussions on how to improve the cooperation and reuse of osteoporosis material in Sweden, either by replication studies or meta-analysis.

Article continues on next page

The overall aim of BBMRI.se work package 2 (WP2) is to:

- ***integrate the major population-based research biobank cohorts in Sweden***
- ***enforce state-of-the-art technologies for further collection and processing of samples and data. Quality assurance is an important part of the Wp2 concept.***
- ***establish the best possible coordination of large-scale and smaller biobanks (and their databases) in Sweden for specific projects.***

Work package report (WP2) continued...

During the meeting, several national osteoporosis materials and several WGA samples used for osteoporosis studies were identified from different universities in Sweden (Table 1). These materials could be used for validation studies in the future. There were also discussions about the possibility to use sam-

ples from other national biobank resources, such as the Swedish maternity cohorts and the microbiological serology cohorts for studies on osteoporosis and all participants were encouraged to develop new research ideas until the next network meeting in November 2011.

Table 1

Region	Study name	Approximal number	Type of sample
Uppsala	ULSAM	2200	blood, BMD, fx data*, DNA
	Mammography study	5000	blood, BMD, fx data, DNA
	MrOS	1000	blood, BMD, fx data, DNA
Göteborg	GOOD	1000	blood, BMD, fx data, GWAS
	MrOS	1000	blood, BMD, fx data, GWAS
Malmö/Lund	OPRA	1000	blood, BMD, fx data, DNA
	PEAK25	1000	blood, BMD, fx data, DNA
	MrOS	1000	blood, BMD, fx data, DNA
	PEAK 25 men	1000	blood, BMD, fx data, DNA
Umeå	UFO	6000	blood, BMS, fx data, DNA, GWAS (1100)
Stockholm Linköping	-		

* fx data = data on fractures



Report**SPIDIA meeting**

June 13, 2011 in Prague, Czech Republic



The SPIDIA project (<http://www.spidia.eu/>), funded by the European Union FP7 programme, brings together a consortium of 16 leading academic institutions, international organisations and life sciences companies.

The project is coordinated by QIAGEN GmbH and aims to tackle the standardisation and improvement of pre-analytical procedures, such as sample handling, stabilisation and storage. The work varies from the development of stabilisation technologies for tissues, blood, and non-invasive samples, such as swab samples to the integration of multiple pre-analytical steps into an automated workflow.

At the Prague SPIDIA meeting the project leaders Dr Uwe Oelmüller (QIAGEN GmbH, Hilden, Germany) and Prof. Mario Pazzagli (University of Florence, Italy) reported on two Ring Trials (DNA and RNA) that have been performed with the aim to develop evidence-based quality guidelines for the pre-analytical phase of blood samples. Uniform blood samples were shipped to various European laboratories and the participants extracted DNA according to their current standard procedures. The isolated DNA samples were returned to SPIDIA laboratories (DNA Blood: 118, DNA Plasma: 62) and analysed

for DNA quantity and quality. A similar ring-trial was executed for the analysis of cellular RNA from blood samples. Uniform blood samples, collected in different blood collection tubes, were shipped to 102 participating laboratories that isolated cellular RNA and shipped it back to SPIDIA laboratories. The received RNA samples (91) were analysed for quality, quantity, RIN value, by several RT-PCR assays and for the presence of interferences by RT-PCR assays.

“The aim of the SPIDIA project is to tackle the standardisation and improvement of pre-analytical procedures, such as sample handling, stabilisation and storage.”

The results will form the base for a second ring-trial that eventually will lead to assurance schemes and guidelines for the pre-analytical phase of blood samples for DNA and RNA analysis.



By Joakim Galli

Report

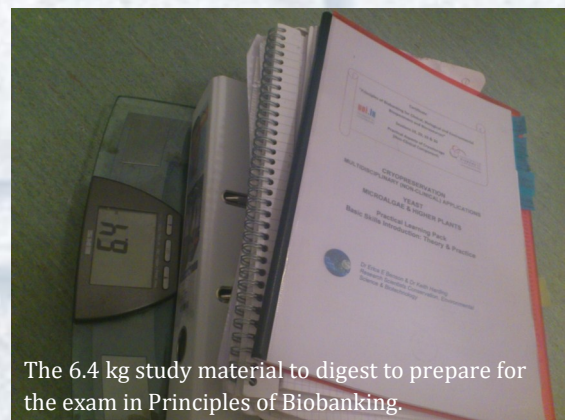
Principles of biobanking for clinical, biological and environmental biospecimens and bioresources

June 6-24, 2011 Luxembourg University, Luxembourg

With rapidly expanding knowledge, the science of biobanking is becoming increasingly complex. This necessitates formalised education in the biobanking sciences, preferably in an internationally harmonised way. In June, I attended a three weeks biobanking course at the University of Luxembourg that was organised by International Biobank of Luxemburg (IBBL) and had a curriculum developed and endorsed by the International Society of Biological and Environmental Repositories. After having completed this demanding course and passed the exam, I am now a proud possessor of a Certificate of education in the Principles of Biobanking.

The main tutor was Dr. Fay Betsou, scientific director of IBBL, who shared her biobank skills with great energy and with a flair for quality assessment and quality control. Dr Keith Harding and Dr Erica Benson were the experts in low storage temperature who taught the subject of cryopreservation and biopreservation in a variety of settings, e.g. the conservation of potatoes at the iso-certified (ISO 17025) International Potato Center (CIP) in vitro Genebank in Peru. It is obvious that clinical biobanks have a lot to learn from environmental cold preservation. A common angle to the course was how to validate methods and samples: how will you have full confidence in sample quality and will we be able to use sample after a long

time? What are the preanalytical measurements that should be performed? For the latter question, Fay Betsou and ISBER have developed the so-called SPREC-code which is a good tool to understand the quality and the variation of the samples. SPREC is a 7-variable international code assigned to each specimen to identify common elements in the preanalytical process chain. Is the sample fit for purpose? Biobank samples are expected to hold a high standard of quality by scientists



The 6.4 kg study material to digest to prepare for the exam in Principles of Biobanking.

and the industry. Therefore, it is important to establish international guidelines for an accreditation that optimally ensures usefulness of the samples. International biobanking networks such as ISBER and BBMRI have an essential role to play here.

The course was quite intensive. That a novice has to learn a lot in the field of biobanking, was reflected in the amount of course litera-

Report continued...

ture to read through — the total weight of the literature was 6.4 kg! We were also taught about pitfalls when buying LIMS-systems, how to fixate tissues, ethical issues & biobank laws, different types of informed consent, the cost recovery calculations that are required for any simple biobanking operation, how to prepare for audits and what to include in a SOP. Both for audits and for SOP-writing the 5 M-rule was proposed: 1) Method 2) Manpower 3) Material, 4) Matter (the samples) and

5) Means (the equipment). Finally, we also studied the epidemiological aspects of sample collection and trained the power calculations for this.

With students from 8 different countries with different background experiences we had many long and interesting discussions and also learnt a lot from each other. I can warmly recommend the course to anyone with an interest of working with biobanking.



Course attendants, from left to right, top row: Andrea Kühn (DE), Sara Demiroglu (DE), Alexandra Fiott (MT), Audur Thorlaksdottir (IS), Stephan Schäfer (CH), Céline Degallier (BE).

Bottom row: Rania Labib (EG), Maria Anderberg (SE), Fabienne George (BE), Fay Betsou (LU), Britt Peeters (BE), Rita Lawler (IT) and Alexandre Bulla (CH).

By Maria Anderberg

