Building a shared national biobank infrastructure: the Swedish experience

Mark Divers
Karolinska Institutet & BBMRI.se

1. Nationales Biobanken-Symposium
12. Dezember 2012
BBMRI.se
BioBanking and Molecular Resource Infrastructure of Sweden
Overview

• Background
• The Swedish biobank landscape
• Why biobank (nationally)?... The value
Biobanks work hard to keep things cold!
But biobanks are cooking!
Why is biobanking so hot?

- Huge potential
  - Transformative impact
- New technologies mapping the molecules of life
  - Genes, proteins, metabolites
- Controversial
- Money (cost)
- Real value already coming

➤ Growing impact on medical research
➤ Huge public health opportunity
Yet we still need to keep cool!

NCI discovered big quality problems

Libraries of Flesh: The Sorry State of Human Tissue Storage

By Steve Silberman  May 24, 2010 | 12:00 pm | Wired June 2010

See...
Wired May 2010
Nature July 2011

Quality hot-spots

Samples

- Collection
- Processing
- Storage
- Data
- Access

Donors

- Selection
- Availability
- Informed consent
Today we live in a very rich world of biobanks
and explosions of genetic knowledge and technology

- Gene sequencing 1980s
- Human Genome Sequence 2002
- Single Nucleotide Polymorphisms
- Genome Wide Association Studies
- Epigenetics
- Next Generation Sequencing
- Genetic regulation – ENCODE 2012
...eg the ENCODE initiative
what does all that "non-coding" DNA do?
Populations are now under the microscope

HUNT, Norway
UK Biobank
Kadoori, China
LifeLines, Netherlands
Helmholtz, Germany
LifeGene, Sweden
EpiHealth, Sweden
Saga, Iceland
PACT, Africa
Barshi, India
Es Maestras, Mexico

Millions of individuals helping us study interplay of genes and environment in health and disease
Biobank landscape of Sweden

• 579 Biobanks

With the courtesy of Prof Jan-Eric Litton, KI
Biobank landscape of Sweden – for healthcare

With the courtesy of Prof Jan-Eric Litton, KI
Biobank landscape of Sweden – for research

With the courtesy of Prof Jan-Eric Litton, KI
A good climate for biobank-based research in Nordic countries

*The Scandinavian gold-mine*

Valuable sample collections

Healthcare quality registers

Public support

Personal number system
But sometimes buried deep!

- Complex ethico-legal landscape
- Fragmented infrastructure
- Trust and ownership fears
- Bureaucracy
- ...

- Many oysters
- But few pearls
BBMRI.se is a national initiative to make biobanking better for Swedish medical research

- Funded by Swedish Research Council (VR) and KI
- Based on the EU concept of research infrastructure
- Becoming a reality in Sweden
- 2010-2014
A short history of KI Biobank...

**Progressive growth**
- Capacity
- Competence
- Quality
- Study diversity

**2003/4 kick-off!**
- Lab, data systems, processes
- Ethics and legal compliance addressed
- 1st studies, incl. TwinGene

**2006**
- 1st withdrawals
- Quality System and ISO accreditation
- Data support to external collections

**2010**
- BBMRI.se
- Technical re-development
- Large-scale studies start

**2012**
- 2.5M samples
- 210K donors
- Impact!
The biobanks of KI and BBMRI.se are a rich source of samples: 150 studies, 3M samples

Population cohorts
- TwinGene
- 60y cohort

Disease based studies
- Cancer
- CV
- Neurological
- Inflammatory
- Immunological

Quality registers
BBMRI.se is transforming sample handling

- Modern sample format
- Highly automated
  - Fast in – Fast out
- Highly traceable, secures integrity
  - For donor, sample, data
- Higher quality
- Lower cost
- Continuous improvement
  - Plenty of improvements to come!
Some sample statistics, Nov 2012

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>KIBB</th>
<th>BBMRI.se</th>
</tr>
</thead>
<tbody>
<tr>
<td># studies</td>
<td>155</td>
<td>145</td>
<td>10</td>
</tr>
<tr>
<td># samples</td>
<td>3,400,000</td>
<td>700,000</td>
<td>2,700,000</td>
</tr>
<tr>
<td># donors</td>
<td>275,000</td>
<td>160,000</td>
<td>115,000</td>
</tr>
<tr>
<td># DNA samples</td>
<td>240,000</td>
<td>145,000</td>
<td>95,000</td>
</tr>
<tr>
<td># withdrawals</td>
<td>&gt;335,000</td>
<td>&gt;270,000</td>
<td>&gt;65,000</td>
</tr>
</tbody>
</table>
National prospective cohorts growing within BBMRI.se

<table>
<thead>
<tr>
<th>Large-scale cohorts</th>
<th># donors planned (now)</th>
<th>Collection region</th>
</tr>
</thead>
<tbody>
<tr>
<td>LifeGene</td>
<td>200K (20K)</td>
<td>Stockholm +</td>
</tr>
<tr>
<td>EpiHealth North</td>
<td>150K (5K)</td>
<td>Uppsala</td>
</tr>
<tr>
<td>EpiHealth South</td>
<td>150K (0.5K)</td>
<td>Skåne</td>
</tr>
<tr>
<td>Karma breast cancer</td>
<td>100K (50K)</td>
<td>Stockholm (+Skåne)</td>
</tr>
<tr>
<td>Sthm-2 prostate cancer</td>
<td>100K (25K)</td>
<td>Stockholm</td>
</tr>
<tr>
<td>Scapis CV</td>
<td>30K (2K)</td>
<td>Göteborg + national</td>
</tr>
<tr>
<td>Malmö Diet &amp; Cancer</td>
<td>18K, complete</td>
<td>Malmö</td>
</tr>
<tr>
<td>Malmö Preventive Med</td>
<td>22K, complete</td>
<td>Malmö</td>
</tr>
<tr>
<td>Sthm-3 prostate cancer</td>
<td>200K pilot test</td>
<td>Stockholm</td>
</tr>
</tbody>
</table>

BBMRI.se standards:
- *Unified sample and data format*
- *Open Access Program*
But it’s not all just about populations... 
...squeezed into the biobank

We have space for others too!...
# National patient-based sample collections growing within BBMRI.se

<table>
<thead>
<tr>
<th>National Quality Register collections</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Sclerosis (IMSEII)</td>
<td>Running; clinical trial</td>
</tr>
<tr>
<td>Bipolar Disease</td>
<td>Running</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Advanced planning</td>
</tr>
<tr>
<td>Myelo Dysplastic Syndrome</td>
<td>Started</td>
</tr>
<tr>
<td>Chronic Lymphoid Leukemia</td>
<td>Planning</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other studies</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Rheumatoid Arthritis</td>
<td>Planning; gather pre-existing clinical samples</td>
</tr>
</tbody>
</table>

BBMRI.se standards:
- *Unified sample and data format*
- *Open Access Program*
We can’t do this alone!
An emerging national network for BBMRI.se sample handling

<table>
<thead>
<tr>
<th>Node</th>
<th>Status</th>
<th>Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stockholm, SSB hub</td>
<td>Major facility production &amp; development</td>
<td>Nov 2010</td>
</tr>
<tr>
<td>Göteborg</td>
<td>New facility</td>
<td>Feb 2012</td>
</tr>
<tr>
<td>Skåne</td>
<td>Reformat existing samples, co-develop with new RS Biobank</td>
<td>Nov 2011</td>
</tr>
<tr>
<td>Umeå</td>
<td>Rebuild existing facility</td>
<td>1Q2013</td>
</tr>
<tr>
<td>Örebro</td>
<td>New facility</td>
<td>2Q2013</td>
</tr>
<tr>
<td>Linköping</td>
<td>New facility</td>
<td>3Q2013</td>
</tr>
</tbody>
</table>

- BBMRI.se finances defined sample handling equipment
- Node adopts BBMRI.se sample & data format
- Node provides staff & facilities
- Node participates in BBMRI.se development
- **Node brings new sample collections to BBMRI.se**
BBMRI.se sample network can bring even more collection enrichment

<table>
<thead>
<tr>
<th>Node</th>
<th>Sample collection opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skåne +</td>
<td>Scapis</td>
</tr>
<tr>
<td>Örebro</td>
<td>Swedeheart UCAN</td>
</tr>
<tr>
<td>Umeå</td>
<td>Northpop cohort Västerbotten cohort Monica Marma UCAN</td>
</tr>
<tr>
<td>Linköping</td>
<td>Lifestyle &amp; stress cohort</td>
</tr>
</tbody>
</table>

With built-in BBMRI.se benefits:
- **Unified sample and data format**
- **Open Access Program**
Why are we biobanking?...

... to advance medical research!

- Combine with modern bio-analysis
  - Systematic
  - Statistical power
- Huge potential for public health

<table>
<thead>
<tr>
<th>Study</th>
<th>publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>GALLSTEN</td>
<td>4</td>
</tr>
<tr>
<td>PAIN</td>
<td>2</td>
</tr>
<tr>
<td>BAMSE</td>
<td>8</td>
</tr>
<tr>
<td>SCALE</td>
<td>15</td>
</tr>
<tr>
<td>Ekonomiskt beteende</td>
<td>2</td>
</tr>
<tr>
<td>TwinGene &amp; Euroclot</td>
<td>13</td>
</tr>
<tr>
<td>HARMONY &amp; SATSA</td>
<td>12</td>
</tr>
<tr>
<td>KTS</td>
<td>1</td>
</tr>
<tr>
<td>CAPS</td>
<td>40</td>
</tr>
<tr>
<td><strong>Totalt</strong></td>
<td><strong>97</strong></td>
</tr>
</tbody>
</table>

Emerging highlights
- Multiple Sclerosis
- TwinGene
- Broad
- Influenza Like Illnesses
- Prostate Cancer
Some great examples
Examples of research progress, 2011

- Bipolar disease (SBP) Mikael Landén
  - New susceptibility gene, calcium channel (GWAS)

- Multiple sclerosis (IMSE, EIMS) Tomas Olsson, Lars Alfredsson
  - Genetic susceptibility (GWAS)

- Lymphoma (SCALE) Karin Ekström-Smedby
  - Hodgkins lymphoma genetic susceptibility (GWAS)

- Prostate cancer (SPSC-1) Henrik Grönberg
  - Genotyping for better diagnosis (SNP)
Main findings of the iCOGS chip, Spring 2012

Approximate number of new disease associated loci 75:

- Breast: 42
- Prostate: 23
- Ovary: 5
- BRCA1/2 carriers breast: 3
- BRCA1/2 carriers ovary: 2

- The results roughly doubles number of known loci for these cancers
- Several surprising overlaps between cancers have been identified
- 13 papers about to be submitted

With the courtesy of Prof Per Hall, KI
What is the real value of biobanking?...

Multiple Sclerosis research gives a great example*

- ~17K MS cases in Sweden
- Many represented in KI Biobank
- New therapy, Tysabri™
  - Monoclonal antibody
  - Very effective, very expensive
  - Serious side effects for some (polyoma viral cross-reacton)
- Screen MS biobank for polyoma virus
  - Save big drug cost (200KKr/patient/yr)
  - Save some lives, improve others
  - Match a good drug to the right patients

* T Olsson et al

New Tysabri label to personalise treatment

WORLD NEWS | JANUARY 23, 2012
PHARMATIMES

Eliot and Biogen have been given a green light from the US Food and Drug Administration to update the product labelling for their multiple sclerosis drug Tysabri (natalizumab) to help identify those at most risk of developing the rare but potentially fatal viral brain infection PML (progressive multifocal leukoencephalopathy).

The labelling now suggests patients should be tested to see whether or not they have previously been exposed to the JC virus – prior infection and a corresponding anti-JCV antibody positive status means a multiple sclerosis patient runs a greater risk of developing PML, particularly if they have also received immunosuppressant therapy and have been on Tysabri for more than two years.

In analyses, patients who were anti-JCV antibody positive had a greater chance of developing PML, to varying degrees depending on prior IS use and duration of Tysabri treatment, irrespective of treatment, around 55% of MS patients are anti-JCV positive, the companies note.

These attempts to personalise medicines means that a product that a few years ago might have been taken off the market because of the small but possible risk of PML, can now be used effectively in a targeted group of patients. “Our development of the risk stratification algorithm and subsequent efforts to support the commercial availability of anti-JCV antibody testing reflect our commitment to providing patients and their physicians with additional guidance to help them make more personalized treatment decisions,” notes George Scangos, chief executive of Biogen.

Tysabri is one of the key drivers of growth at Biogen, bringing $277.3 million into its coffers, up 26%, in the third quarter of last year. Overall its profits were up 38% to $351.8 million for the period.
Conclusion:

Biobank-based research adds big value

Clinical practice
Better screening, diagnosis and treatment match; eg HPV

Health economy
Better public health for lower cost
eg HPV, MS, RA

Drug development
Matching patients to treatments
eg MS, HIV, HPV

Ethical credibility
Increased trust and support
eg all of the above

Mark Divers
A new wave of biobank studies

- Power of large numbers and...
- ...Sharp focus on specific disease areas
  - Prostate cancer
  - Breast cancer
  - Cardio-vascular disease
- Plus healthcare quality registers
- Big opportunity for early impact
  - Clinical practice
  - Health economics
Karolinska Mammography Project for Risk Prediction of Breast Cancer

With the courtesy of Prof Per Hall, KI
With the courtesy of Prof Per Hall, KI
Stora studien inom prostatecancer

Biobanking to support big decisions:
• Diagnosis
• Treat or not treat localised cancer
• Which treatment for advanced disease
• Is patient cured

Start 2013-01-01
PI prof Henrik Grönberg
Karolinska Institutet

250 000 individuals

With the courtesy of Prof Henrik Grönberg, KI
Costs of prostate cancer care in Sweden today

• 2003 estimated direct cost of 1,5 billion SEK
• 1100 MSEK direct care
• 400 MSEK drugs

With the courtesy of Prof Henrik Grönberg, KI
Prostate cancer diagnosis: Today

- Insensitive diagnosis based on 1 biomarker, PSA
  - 2 of 3 positive diagnoses are incorrect
  - 15-20% of all severe cancers are missed

With the courtesy of Prof Henrik Grönberg, KI
Annals of Internal Medicine

Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement
Virginia A. Moyer, MD, PhD, on behalf of the U.S. Preventive Services Task Force*

Recommendation: The USPSTF recommends against PSA-based screening for prostate cancer (grade D recommendation).

What the U.S. Preventive Services Task Force Missed in Its Prostate Cancer Screening Recommendation
William J. Catalona, MD; Anthony V. D’Amico, MD; William F. Fitzgibbons, MD; Omofolasade Kosoko-Lasaki, MD; Stephen W. Leslie, MD; Henry T. Lynch, MD; Judd W. Moul, MD; Marc S. Rendell, MD; and Patrick C. Walsh, MD

Prostate Cancer Screening: What We Know, Don’t Know, and Believe
Otis W. Brawley, MD

CONTROVERSIAL !!!!

With the courtesy of Prof Henrik Grönberg, KI
Prostate cancer diagnosis: Tomorrow

Improved diagnosis based on combination of 100+ markers

• Enables exclusion of 50%
• Differentiate severe from non-severe tumors
• Significant reduction in unnecessary biopsies
• Reduce anxiety – improved quality of life

With the courtesy of Prof Henrik Grönberg, KI
So what about the future?

**Bad?...**
- Ethical fears take over
- Legal constraints increase
- Abuses of integrity
- Technology fails to deliver
- Cost pressure
- More fragmentation

**Good?**
- More research progress
- Healthcare quality increases
- Public faith grows
- Samples and data shared
- Technology delivers

➢ Banking crises spread to biobanks

➢ Public health improves
The future can never be fully predicted...

...but we must look forward!
A wise investment...

... biobanks help health

If you think research is expensive, try disease

Mary Lasker (1901-94)
What do you think?

Bright or gloomy future?
Acknowledgements

- Staff of KI Biobank and BBMRI.se
- Staff of our homebase, KI MEB
- Our 155 customers
- Our suppliers
- And some others

17 December 2012
More info on KI Biobank and BBMRI.se services...

www.ki.se/kibiobank
www.ki.se/scarab
www.bbmri.se