Biobanking in translational cancer research

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Biobanking is not just a warehouse of samples

Biobanking: Longterm longitudinal follow-up without having to wait..

- Biobanking roots: samples and baseline data
- Follow-up for disease and cause of death – preferably for decades - is necessary to provide the ”study base” that molecular research can be based on.
- Requires linkage of biobanks to comprehensive registers.
- Requires solid experience of handling personally identifiable data.

Biobanks with follow-up – an essential infrastructure for cancer research

- Molecular research is based on biospecimens.
- Etiological research
  - Search for explanations to differences in cancer occurrence.
    - Causal exposures may have occurred long ago or may change over time.
- Clinical research
  - Search for biomarkers of response to treatment
    - Clinical outcome must be known.
- Prevention research
  - Search for early diagnosis methods/screening tests
    - Future diagnoses must be known.

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Biobank & cancer registry linkages for public health – some examples

- Etiology:
  - Prospective evidence necessary for causality inference.
  - Study base with samples followed-up for 30 years for cancer occurrence.
  - Baseline samples tested for papillomavirus (HPV) – found to increase risk for cervical, vulvar, vaginal, penile, tonsillar & anal cancer.
  - Evidence supporting etiology required for launch of preventive efforts (vaccines)

Biobank & cancer registry linkages for public health – some examples

- Cancer Vaccines:
  - Possibility for long-term follow-up of HPV vaccines using registries & biobanks mandated for approval.
- New screening test implementation:
  - 33 different HPV-based cervical screening tests marketed.
  - Systematic biobanking of cervical screening samples + registry linkages: Study base for longitudinal evaluation of test performance (protection for a screening interval).
  - Public tenders for competition among equivalent tests drive down cost to levels enabling implementation.

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Bottlenecks for biobank & registry-based research

- Lack of systematic specimen collection.
- Study bases not systematically determined (Many biobanks not regularly linked to cancer registries).
- Lack of overview on available biobanks/study bases.
- Lack of standardised description of available materials.

Eurocourse WP7
Interface of cancer registries with biobanks:

- CCPRB-Eurocourse recommendations for Best Practises when linking cancer registries and biobanks.
  - Harmonizing and improving practises.
- Eurocourse-BBMRI recommendation for standardised minimal data set for biobanks intended for cancer research
  - Will facilitate standardised biobank descriptions and pooling of data on a European level.
- Best practises for systematic biobanking in cervical screening.
- Piloting systematic and rapid joint linkage of many sample collections to cancer registry to determine the study base.

Biobanks as ”Biological registers”

  - Infrastructure with information
  - Powerhouse to support population-based cancer research
  - Requirements for personal data handling are similar to those of cancer registries
- Cancer registries essential for follow-up to define study base.
- Overview and descriptions of biobanks for cancer research can be handled by cancer registries.
- Cancer registries are ***the*** disease registers with longest follow-up and experience – can drive the excellence in exploiting biobanks for health.

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BBMRI.se
BioBanking and Molecular Resource Infrastructure of Sweden

Entering the Era of the Large-Scale Biobanking Sciences – Experiences from the launch of BBMRI.se

Joakim Dillner

BBMRI.se

The BioBanking & Molecular Resource Infrastructure of Sweden

The setting for biobanking in Sweden

A. Samples available and identifiable on PIN

B. Accessory information retrievable

C. Complete case ascertainment:

Medical Birth Registry; Malformation Registry; Cancer Registry; Patient Registry

D. Socialised medicine with laboratories serving defined catchment area populations

E. Broad consent to biobanking for research purposes is administered throughout the health care system (About 3 million consents/year collected when samples for clinical diagnosis are taken)

Respecting Integrity:
UNIFORM INFORMATION AND CONSENT PROCEDURE FOR ROUTINE CLINICAL CARE: Agreed for all 25 counties in Sweden

Leaflet with written information is distributed (mandatory)

Physician/nurse asks if the patient has read and gives his/her consent.

If the patient says No- Form asking for the specific type of No is handed out. All “No-forms” forwarded to the Regional Biobank Registry.

It is not possible to send a sample for pathological or microbiological analysis without certifying either of three alternatives: Patient gave consent/Patient is not conscious/Patient said No and a No-form was sent to the Regional Biobank Regsitry.

Retraction of consent

Can be done at any time, also for all previously stored samples (even for 100 year old samples).

Send a “No-Form” specifying the type of No to the Regional Biobank Registry (RBR).

RBR will locate where samples are stored and ensure that they are destroyed/not used for purposes for which the consent has been retracted.

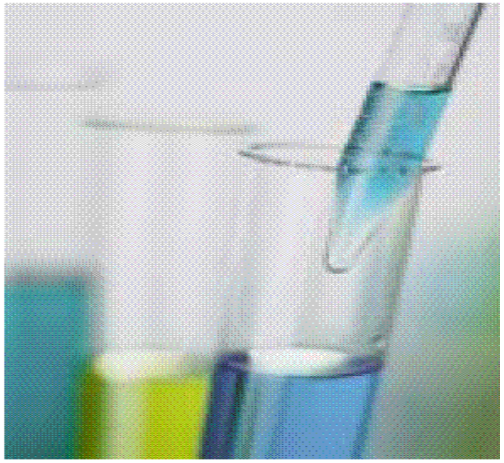
Clearly defined and simple possibility to retract consent addresses some of the ethical problems in longitudinal studies

Broad consent to research is administrated throughout the health-care system

Only 0.2% of patients decline storage and use for ”medical research”.

Till dig som lämnar prov

Som patient behöver du ofta lämna prover, till exempel blodprov eller vävnadsprov. Prover tas också vid de hälsokontroller som landstinget erbjuder. Vissa prover sparas rutinmässigt i en så kallad biobank. En biobank är en samling prover – blodprov, cellprov eller andra vävnadsprover – som tas i vården och sparas längre tid än två månader och som kan härledas till en viss person.



Mer information

Vill du ha mer information kan du fråga din läkare eller vända dig till Regionalt biobanksregister,

Sweden is well prepared for building a national biobanking infrastructure

- **Established national biobanking network**
  - Large National Biobanking Program in 2002-2007: All medical universities in Sweden network of population cohorts & disease-based biobanks. Goal of joint standards of quality, documentation and ethics.
- **Established international coordination roles**
  - FP6 IP ”Molecular Tools” program; high-throughput molecular analysis techniques (Ulf Landegren - Uppsala)
  - Informatics WP5 of FP6 Coordinated Action PHOEBE on harmonization of biobanks (Jan-Eric Litton - KI)
  - FP6 Network of Excellence CCPRB and FP7 EUROCOURSE on quality standards for biobanks (Joakim Dillner - KI)
  - **FP7 BBMRI** (WP4 Landegren – Uppsala; WP5 Litton – KI)

Wallenberg Consortium North
WCN

SWEGENE
The Postgenomic Research and Technology Programme in South Western Sweden

The Swedish National Biobanking Program

Joint national programme of the medical universities in Sweden (2002-2007). Total budget 6M Euro. Comprehensive participation of major Swedish biobanks (www.biobanks.se)

AIM: Promote Accessibility and Quality: All participating biobanks committed themselves to work using **common quality standards** and to provide **access to samples** after prioritisation on scientific grounds only.

Method: Strategic Initiatives – initiated and supported pilot excellence projects at each university. E.g. KI Biobank; Uppsala fresh frozen tissue biobank; TwinGene Biobank; Malmö Biobank Consortium; Swedish Multigeneration Register expansion.

ESFRI established the European BBMRI in 2008

BBMRI
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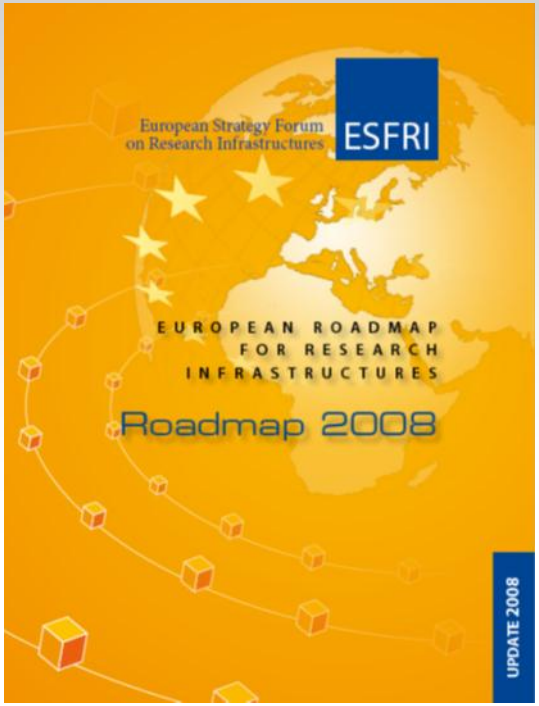


- Network structure: International state-of-the-art centers cooperate with national centers, who in turn cooperate with regional centers
- International comparability, context and perspective

2009: Swedish Science Council call for applications for “infrastructures outlined in the ESFRI roadmap”

*Building on experiences from BBMRI-PP and from the Swedish National Biobanking Program.

*Positioned as the Swedish hub of BBMRI – BBMRI.se

*Funded by the Swedish Research Council-
15 M euro for the first 5 years + regional co-financing.

*Structure similar as BBMRI – but in addition also operation of a national, large-scale biobanking facility

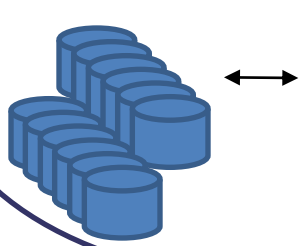
BBMRI.SE – a unified Swedish infrastructure for biobanking

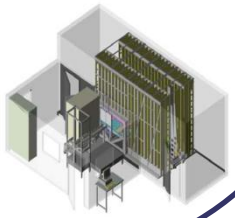
WP1 – Project management

WP2 & WP3	WP4	WP5	WP6	WP7	WP8
Collection: Input	**Analysis: Output**	**IT**	**Physical Facility**	**Ethics**	**Financing**
Coordinate & harmonize sample / data collection from populations & hospitals	Optimize interface to analysis resources	Enforce a unifying national IT platform	Create an efficient national, large scale sample handling facility	Provide national expertise and forum to address ethical issues	Ensure long-term financing

Distributed sample handling at local biobanks and hospitals

Central storage and withdrawal





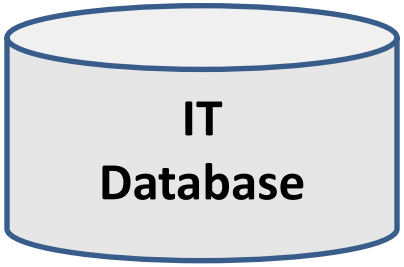
Deep freezing stores ~100 million tubes = “hard drive”

Automatic repicking unit at -80° C. Fast withdrawal of tubes = “processor and RAM memory”

The Science of Biobanking - optimal storage and use of valuable samples

Biobank deposit → **Storage** → **Biobank use**

- **Input**
  - **Ensure valuable biological samples optimally stored**
- Ethics
- Quality control
- Sample handling and processing
- Data gathering
- Links to registers



- **Output**
  - **Ensure biological samples are optimally used**
- Ethics
- Platforms for high throughput sample analysis
- Data handling
- Biostatistics

Example of a BBMRI.se project: Clinical Cytology Biobanking

Women of Sweden Cohort

The cervical screening program targets all women in Sweden between 23-60 years of age (~650.000 samples/year). Cervical cellular samples collected in a liquid preservative, ensuring stability of large amounts of high quality DNA, RNA, proteins and intact cells - even after many years of storage.

Systematic biobanking improves both clinical diagnostics for the participating women, evaluation of new screening tests and research on cervical cancer and other diseases that affect women.

BBMRI.se provides development of standardised automation solution, IT & QC system. National tenders for equipment and supplies. Ready-to-use, nationally standardised biobanking solution offered to collaborating cytology laboratories.

Creating a BBMRI.se national network

- National profiling of competences, services and biobanking R&D
  - Biobanking legal and ethical issues: Uppsala
  - Sample management: Stockholm
  - Molecular analyses platform: Uppsala
  - Genealogy linkages: Umeå
- Regional BBMRI.se satellites improve nationwide utilization of BBMRI.se services
  - **Deposit services: National biobanking projects**
  - **Use services: National biobank-based studies**
  - Improve interaction and collaboration with regional activities in the biobanking area.

How can we help?

Input customer – New collection project

1) Large-scale services, subsidised by the Swedish Research Council, results in:
    1) Low costs to customer
    2) Standardised & internationally recognized format & quality.
2) National critical mass of competences & experiences in biobanking sciences assist with:
    - Study design for enrollment
    - Data collection tools
    - Advise on optimising collection to suit analys needs
    - Study design for sample handling
    - Ethical and legal issues

Key BBMRI.se Concepts

Biospecimen open access

All sample owners who deposit samples in BBMRI.se make committment to make samples available at nominal fee for both academic and commercial customers.

Stakeholder dialogue

Stakeholder dialogue on possible future uses of samples - to ensure that samples will be collected that are optimally useful for later stakeholder use.

Key BBMRI.se Concepts

A large national/international organisation to manage biospecimens in Sweden.

-BBMRI.se unified formats in a) physical biobanking and b) data management enables valid use in nationwide & international studies.

-Very large tenders will drive down purchasing cost of equipment and supplies, will make biobanking less expensive and further enlarge operations

Customers will want to use BBMRI.se to ensure valid use, low cost and efficient management.

Input customers mostly in academia and health care - open access requirement

How can we help?
Output customer – Biobank-based study

National critical mass of competences & experiences in biobanking sciences assist with:

- Study coordination services
- Contacts with biobanks all over the country (one contact person per university city)
- Registry linkages (cancer registries et c)
- Data collection tools
- Advise on optimal analyses
- Services with sample handling
- Ethical and legal issues

BBMRI.SE will implement a much needed national, unifying biobanking infrastructure

- **National large scale automated facility with cost efficient sample deposit, storage and withdrawal**
- Nation-wide consolidation & standardization of collection of biospecimens from patient cohorts
- **Integrated with parallel international activities - makes resources internationally useful**
- Availability of comprehensive and high quality archives of patient biospecimens will make Sweden an attractive partner for efficient clinical research.

BBMRI Nordic -

Nordic Council of Ministers- funded Collaborative Network between the National Biobanking Infrastructures in the Nordic Countries, chaired by BBMRI.se

- Similar health care and health data registry infrastructure creates a Nordic competitive advantage for biobanking.

- A Nordic collaboration, that works to exploit the Nordic advantages: enriching biobanks with registry data on exposures, phenotypes and endpoints + health-care-derived specimens

- Pilot joint Nordic biobank-based study demonstrating the advantages of a common infrastructure for biobanks:
  Identifies all specimens and all data available for joint studies on a pilot disease.

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The Era of the Large-Scale Biobanking Sciences

-The input scientist: Freely chooses among many biobanking facilities, also in other countries, to find the most cost-effective & high quality services.

-The output scientist: Has easy access to massive numbers of well-characterised, ready-to-use samples and rich accessory data from many countries.

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