Overview

- Architecture of complex diseases
- Biobanking
- Challenges: from biobanks to bedside
From genomes to health

- Integrate high-throughput technologies, genomics & systems biology to advance translational medicine:
  - new therapies
  - improved diagnostics
  - improved prevention
  - improved public health
  - personalized medicine
‘What is inherited is DNA, everything else is developed’

(Tanner, *Foetus until man: physical growth from conception to maturity*, 1976)
causal nexus for complex disorders/phenotypes

Phenome
Metabolome
Proteome
Transcriptome
Epigenome
Genome
Developmentally
Distribution of disease liability

threshold

affected

g

e

g

e

Distribution of disease liability
Atlas of susceptibility

- High penetrance rare alleles causing Mendelian disease
- Low-frequency variants with intermediate penetrance
- Intermediate frequency modest variants
- Low frequency very rare variants

Rare examples of high-penetrance common variants influencing common disease
Most common variants implicated in common disease by GWA
Rare variants of small effect very hard to identify by genetic means

Borrowed from M. McCarthy
Summarizing Issues about Complex Etiology

- Genetic architecture?
  - Multiple genes & multiple environments?
  - Frequency & penetrance of predisposing variants?
  - What constitutes risk?

- Differential etiology (heterogeneity)?

- Focus on preclinical quantitative variation
  - Recruitment by genotype

- Dynamic processes (i.e. gene-gene interactions, gene-environment interactions)

- Effective genotype varies
  - Over time
  - Over course of disease?
How is this related to biobanking?

- Need access to **very large** sets of biospecimens & associated data
  - Biomolecular
  - Clinical
  - Epidemiological
- Well-curated
- Access to other tools & resources
- Requires coordinated efforts
Interoperability

- Biobanks must be able to communicate with each other on many levels
- Key harmonization platforms identified (Not necessarily standardization)
- Multiple initiatives working in concert
- What sets the pace?
  - Science moves rapidly
  - Evolving ethics frameworks
Example Projects

Population-based research, including special populations
- Public Population Project in Genomics (P³G), PHOEBE, GenomEUtwin, ENGAGE, PHIME, NEWGENERIS, ECNIS, HYPERGENES

- Disease-specific projects in clinical biobanks
  - OECI-TUBAFROST, CCPRB, GENOMEL, EUROBONET, IMPACTS, GenOSept, EUROBIOBANK, TREAT-NMD

- Tools and technologies for biobank research
  - MOLTOLS, MolPAGE, READNA, BioSapiens, GEN2PHEN

- Ethical, legal, social and societal public health aspects
  - PRIVILEGED, GenBanC, TISS.EU, PHGEN

- BBMRI
Aims

- Promote infrastructure, tools and research that maximizes the use of data and biospecimens
  - Population-based
  - Disease-based
  - Clinical-based

- Optimize the ability to:
  - Communicate across multiple platforms
  - Share information and data
  - Collaborate effectively as science & methodologies evolve

- Implications/embeddedness of ethico-legal frameworks?
The science of biobanking & Biobanking-based science (evidence-based)

Enabling new technologies and enabled by new technologies
Evolving science new ethics challenges
Changing perspectives in biobank research: from individual rights to concerns about public health regarding the return of results

Joanna Stjernschantz Forsberg*,1, Mats G Hansson1 and Stefan Eriksson1

1Centre for Research Ethics and Bioethics, Uppsala University, Uppsala, Sweden

During the past decade, various guidelines that imply a duty for researchers to disclose information obtained through research to participants have emerged. The character and extent of this obligation have been debated extensively, with much attention devoted to the decisiveness of the validity and utility of the results in question. The aim of this paper is to argue that individual results from research on materials stored in large-scale biobanks, consisting of samples taken within the healthcare system or of altruistically donated materials, should not be returned. We will defend the thesis that medical research on these biobanks should be viewed as a collective project to improve public health, and that available resources should be utilized to pursue this goal. We argue that there is a need for a change of perspectives. Medical research should not primarily be viewed as a danger that individuals must be protected from, but rather be recognized as constituting a necessary defense against current and future diseases. Research that bears the prospect of advancing medicine and that can be carried out at no risk to individuals should be endorsed and facilitated. This calls for a shift of focus from autonomy and individual rights toward collective responsibility and solidarity.

Keywords: biobanks; returning results; solidarity; public health; altruism
New Heights

- Multiple projects tackling these issues
- Synergy between projects (essential)
- Can’t progress unless there is an ethos of sharing
- Major achievements reached
  - tools
  - technologies
  - compatible informatics
  - Information repository & catalogues
  - best practices
  - Information portals
  - codes of conduct
  - standards
  - project-specific collaborations
  - active and networked community
  - scientific collaborations
  - biobank prototypes
  - Evidence-based
Paradigm shift

- Partnership model
  - Must work together
  - Multidisciplinary
  - Stakeholders engagement
  - Strategic alliances
    - Funders
    - Governments
  - Multi-mileu
  - Public-private partnerships
  - Rethinking incentives
  - New continuums
10 IDEAS CHANGING THE WORLD RIGHT NOW

- Why Your Job Is Your Most Valuable Asset
- Repurposing the Suburbs
- Survival Store Shopping
- Biobanks: Saving Your Parts
- Need Land? Rent a Country
- The New Calvinism
- Ecological Intelligence
- Amortality: Forever Young
- Africa: Open for Business
- Reinventing the Highway
Biobanking

- Biobanks are engines for translation research
- Integration knowledge & technologies
- Driving new wave of ethical challenges/thinking
- Harmonization enables science through the use of data and specimens
  - Across data sources
  - Across national boundaries
  - Across traditional disciplinary boundaries?
Why Population Aging Matters
A Global Perspective
Unsustainable health costs
YOUNG CHILDREN AND OLDER PEOPLE AS A PERCENTAGE OF GLOBAL POPULATION

PROJECTED INCREASE IN GLOBAL POPULATION BETWEEN 2005 AND 2030, BY AGE

The increasing costs of increasingly longer lives

Projected population structure and age-related spending

Old-age population (ratio to working-age population)\(^1\)

Estimated increase in age-related government expenditure from 2011 to 2050\(^2\)

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1 Working-age population is ages 15–64.  
2 As a percentage point of GDP.

Sources: IMF, WEO April 2007; United Nations Secretariat; European Commission; US Congressional Budget Office.
Biobanks for health

- National Biobanking Infrastructures
  - EU-BBMRI
- Large national investments
- Biobanks becoming embedded in national health care infrastructures
Good Biobanks-Better Health
(June 2008)
• BBMRI.NO
• BBMRI.SE
• BBMRI.NL

plus several other countries
Good biobanks better health

- Recommend establishment of a long-term national platform for:
  - Coordination of use of biobanks and health data in research.
  - Development of infrastructure to ensure secure & effective system for use and exchange of biobank related information and health data.
  - Pilot project to prepare hospital based biobanks for research.
  - National register of individuals who don’t want biobiological material collected for diagnostic purposes to be used in research.
New horizons new continuums

- Bridging clinical and non-clinical domains
- Patient research-population research
- Doctor-researcher
- Participant-patient
- Research-diagnostics
- Individual rights-public health
- Flexibility to respond to progress
- Different ethico-legal frameworks
Example Challenges-I

- From high-throughput to deep sequencing
  - Small impact on risk to possibility of large impact on risk
  - Ethically difficult not to give feedback
  - Is gene mapping in the clinic diagnostics, research or both?

- Incidental findings
  - Which information should be fed back?
  - What is enough information?
  - Who should define this?
Example Challenges-II

- How do we decide if an illness can be prevented?
- How do those enrolled define what they want to know?
  - Evidence based?
- Implications beyond individual
  - Relatives, family planning etc.
  - What is a good enough background to make an 'informed' choice?
From Biobanks to Bedside

- Biobanking: an engine for translation
  - Provides & coordinates raw materials needed to advance research and development in public health
  - Is becoming a key feature of health care infrastructures
- Biobank-based consortia studies already elucidating causal factors of disease
- Tackling complexities & translation of findings depends upon:
  - Maximization of resources
  - Harmonization
  - Ethico-evolution?