



Biobanking in Biomedical Research

Part 4

***Biobank quality management and
harmonization: current guidelines,
evidence-based standards.***

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Siena, June 2009



Topics

- Why OECD?
- OECD in more detail
 - Map
 - Process
 - Content
- From evidence to European standards and norms
- The Biobank of the Medical University of Graz



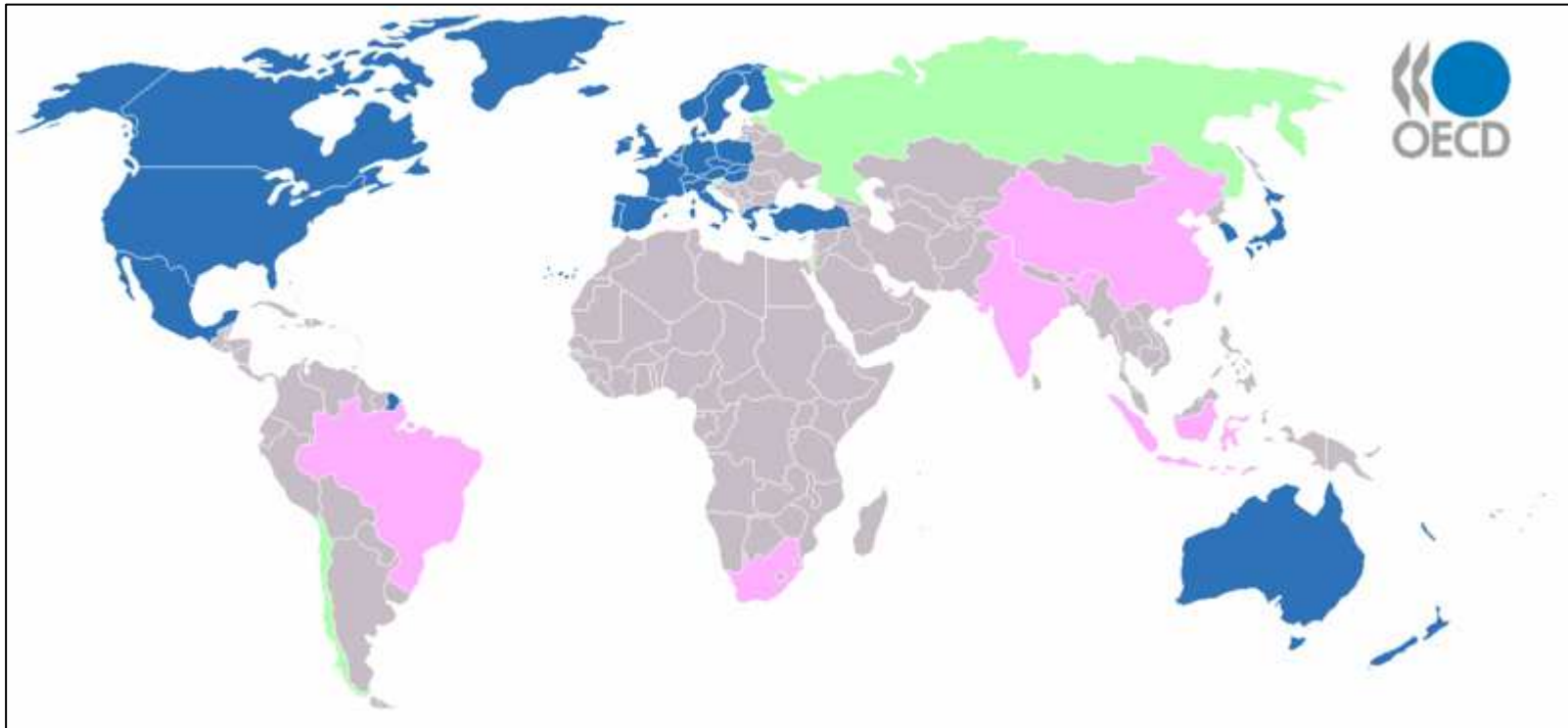
Different Levels of Regulation

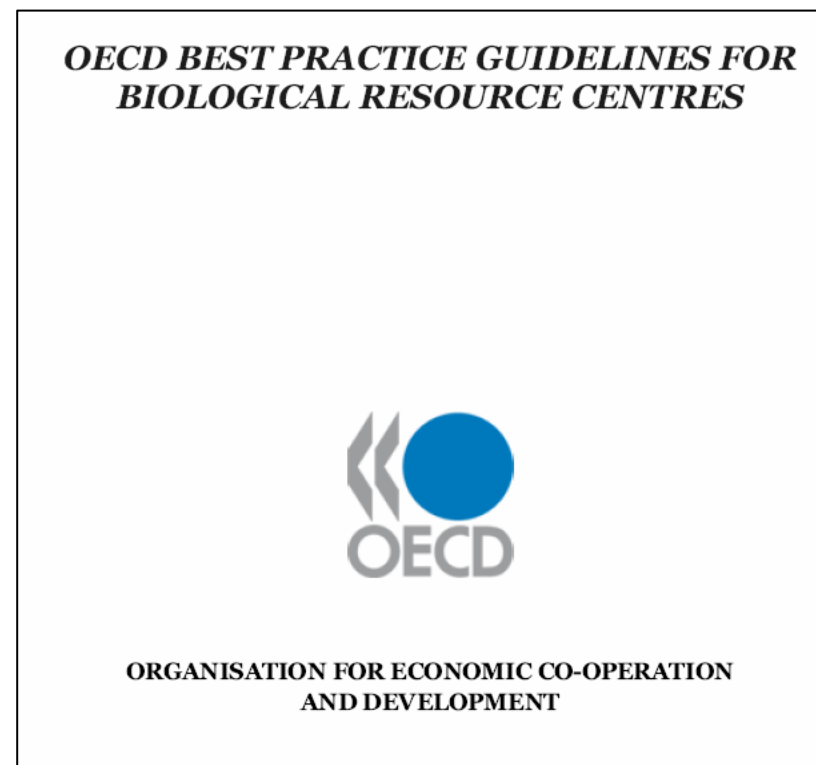
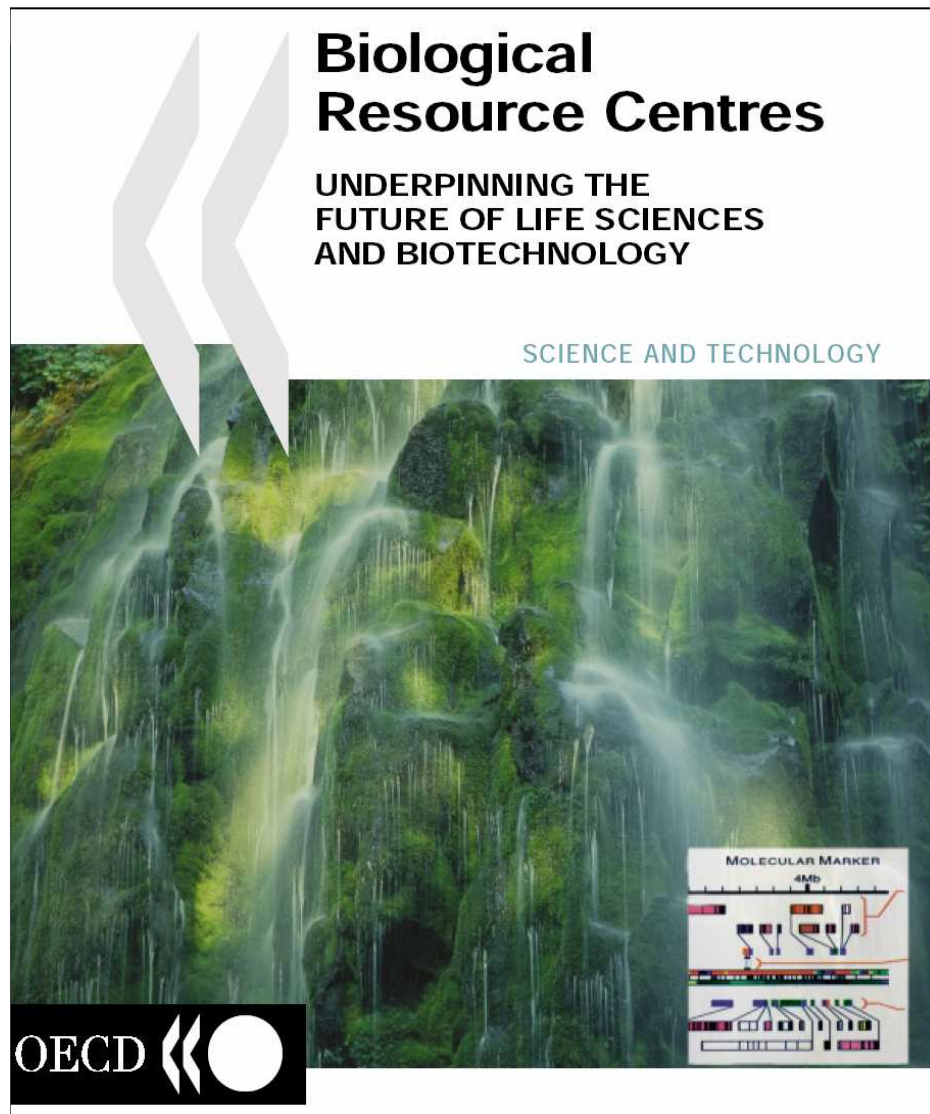
- Legal – soft law – state-of-the-art
- International
 - OECD Guidelines
 - UNESCO Declaration
 - WHO Guidelines
 - Declaration of Helsinki
 - EU Directives (Data Protection)
 - EU Convention (ETS 164)
 - International societies (ESHG, HUGO etc.)
- National
 - Laws

Biobanking Guidelines and Regulations (Examples)

Title	Organisation	Link
Tissue banking for Biomedical Research	National Cancer Centre	http://www.bioethics-singapore.org/resources/pdf/AppendixB-Dr%20Kon.pdf
Biorepository Protocols	Australian Biospecimen Network (ABN)	http://www.abrn.net/pdf/ABN_SOPs_Review_Mar06_final.pdf
Biological Resource Centres: underpinning the future of life sciences and biotechnology	Organization for Economic Co-operation and Development (OECD)	http://wdcm.nig.ac.jp/brc.pdf
OECD best practice guidelines for biological resource centres	Organization for Economic Co-operation and Development (OECD)	http://www.wfcc.nig.ac.jp/Documents/OECD.pdf
European Human Frozen Tumor Tissue Bank TUBAFROST	The European Human Tumour Frozen Tissue Bank (TUBAFROST)	http://www.tubafrost.org
Common Minimal Standards for Biological Resource Centers	International Agency for Research on Cancer, World Health Organization	http://www.iarc.fr/News/RecommendationsBRC.pdf
Human tissue and biological samples for use in research. Operational and ethical guidelines	Medical Research Council (MRC)	http://www.mrc.ac.uk/pdf-tissue_guide_fin.pdf
Best Practices for Repositories I: Collection, Storage, and Retrieval of Human Biological Materials for Research	International Society for Biological and Environmental Repositories (ISBER)	http://ehs.sph.berkeley.edu/Holland/Biorep/BestPractices2005.3.5.pdf
First-Generation Guidelines for NCI-Supported Biorepositories	National Cancer Institute (NCI)	http://biospecimens.cancer.gov/biorepositories/NCI_First_Generation_Biorepository_Full_Guidelines.pdf
Transport of infectious substances	World Health Organization (WHO)	http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2005_22r%20.pdf
UN Recommendations on the Transport of Dangerous Goods. Model Regulations.	United Nations Economic Commission for Europe (UNECE)	http://www.unece.org/trans/danger/publi/unrec/rev13/13files_e.html
A Cold Greeting: an Introduction to Cryobiology	Biotech	http://www.biotech.ubc.ca/Bioengineering/AColdGreeting/
Specimen Collection, Preparation, and Handling	Labcorp	http://www.labcorp.com/datasets/labcorp/html/frontm_group/frontm/section/speccol.htm

Global Integration of BBMRI by Implementation of the OECD GBRCN Concept in Europe





Endorsed by CSTP in March 2007

“Biological resources – living organisms, cells, genes, and related information – are the essential raw material for the advancement of biotechnology, human health, and research and development in life sciences“

The OECD Process

Committee for Science and Technology Policy
(CSTP)



Working Party of Biotechnology (WPB)

Public
Consultation



Task force



Experts



Development of the Scope

1998: Japan proposed microbial BRC to WPB

2001: BRC concept extended to all biological systems

2001: GxP

2005: Standards

2006: Guidelines

2007: Best practice guidelines



Table of Contents

- Part I: Rationale and development of the project
- Part II: Best Practices
 - BP Guidelines for all BRCs
 - BP Guidelines on biosecurity for BRCs
 - BP Guidelines for the micro-organism domain
 - BP Guidelines on human-derived material



BP Guidelines on Human-Derived Material

- Organisational requirements
- Staff-qualifications and training
- Premises
- Equipment
- Documentation
- Informatics
- Services
- Preparation of samples
- Accession of deposits
- Preservation
- Supply of biological material
- Quality audit and quality review



Informatics

- Data
- Security of data
- Internet publication

Furthermore:

- Certification
- Minimal data set
- Recommended data set



Differences and Similarities of the OECD GBRCN and HBGRD Documents

GBRCN

- Facility
- Personnel
- Biosecurity
- Traceability
- MDS,RDS
- Data protection
- Certification
- (Old collections)

HBGRD

- Informed consent
 - IC process
 - IC document
- Governance
- Stakeholder
- Involvement of donors
- Data protection
- Change of scope
- (Old collections)



Strengths and Weaknesses of OECD Guidelines

Strength

- “global” scope
- Impact on national legislation
- Good instrument for harmonization

Weakness

- Complex consensus finding process
- Minimal compromise



Need for Evidence-Based Standards

- Basis for harmonization of guidelines
- Requires global cooperation
- Implementation by journals
- Implementation by funders
- Integral part of good scientific practice

Caveat: misuse of standards to generate competitive advantage



Reproducibility Depends on Quality

OBBR Office of Biorepositories
and Biospecimen Research

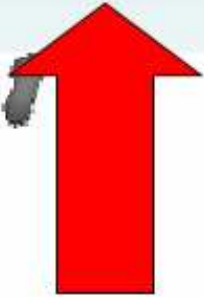
GARBAGE IN \Rightarrow GARBAGE OUT



Many SOPs Around the World: Which are the Best?

OBBR Office of Biorepositories
and Biospecimen Research

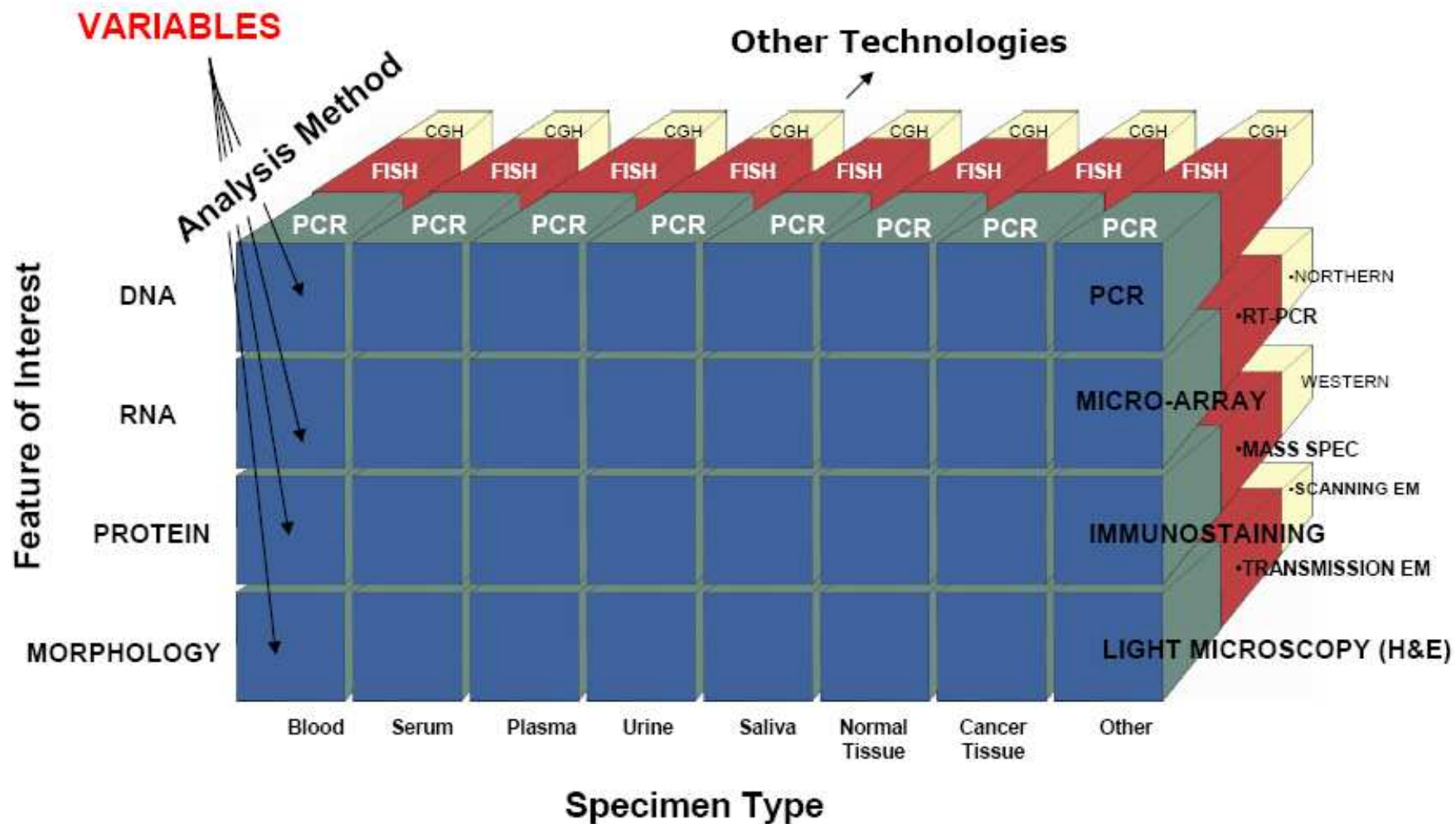
- 
- Impossible to call any one “best” (even NCI’s)
 - All have strengths and weaknesses
 - No single set of SOPs are applicable to all clinical and research analytical platforms
 - Very few SOPs are based on **scientific evidence**



Where we need to go

Framework for Development of Evidence-Based Standards Operating Procedures

OBBR Office of Biorepositories and Biospecimen Research

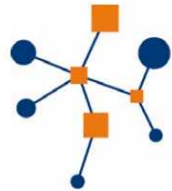




European FP 7 Large Integrated Project: SPIDIA

- Evidence-based quality parameters
- New stabilization procedures
- New sampling procedures
- Evaluation of morphology
- Evaluation of antigenicity
- Evaluation of DNA, RNA, proteins, metabolites
- Validation in international ring trial
- European Norm (CEN)

Forum for International Biobanking Organisations (FIBO)



BBMRI
Biobanking and
Biomolecular
Resources Research
Infrastructure



ISBER



International Agency for Research on Cancer

Centre International de Recherche sur le Cancer

OBBR

Office of Biorepositories
and Biospecimen Research

Harmonization: The Adaptor Model



- Define criteria
 - Which samples and data can be combined?
 - Need for evidence-based standards
- Develop tools
 - Data exchange
 - Sample transport



The Genome Austria Tissue Bank: A Brief History

- 1911 centralized pathology service in Austrian monarchy
- 1980 Pathology service
 - University hospital
 - 33 Public hospitals
 - 10 Private hospitals

} ~ 1.2 Mio Pop, 7 000 beds
- 1983 Computer system
- 1993 Industry cooperation (BI; frozen tissue, data base, 1 FTE)
- 2001 Industry cooperation (Oridis Biomed; TMA robot, 3 FTE)
- 2002 GEN-AU I (Archive – Biobank)
- 2006 GEN-AU II (joint ELSA project, international coop.)
- 2008 Central research infrastructure of Medical University (20 FTE)
- 2009 GEN-AU III (prospective cohort metabolic dis., BBMRI)



Form an Archive to a Biobank: Research Topics

- Ethical and legal clearance
- Quality control
- Analysis tools (new technologies, screening platforms)
- IT-Infrastructure (diff. structured data, confidentiality)
- Sample preservation (new fixatives, cryobiology)
- Public perception
- Associated research projects
 - Cancer
 - Metabolic diseases
 - Infectious diseases
 - Biomarkers



IT-Infrastructure: Projects

Development of data bases

Sample DB IoP, Uni. Klagenft. (Gen-Au I, CD-Lab)

Clinical DB IoP, Uni. Klagenft. (Gen-Au I)

Data MART IoP, Uni. Vienna (EU-PONT, Gen-Au I/II)

TMA DB

TU Graz (CD-Lab, BIN)

cDNA DB

TU Graz (CD-Lab, BIN)

Data protection

Gen-Au II

Sample tracking

Gen-Au II

Sample annotation tools

IoP, CRIP

Visualization&analysis tools

GenView

IoP, TU Graz (ZUFO)

Vipem

IoP, TU Graz (FWF)

Genopticum

IoP, TU Graz (FFG)

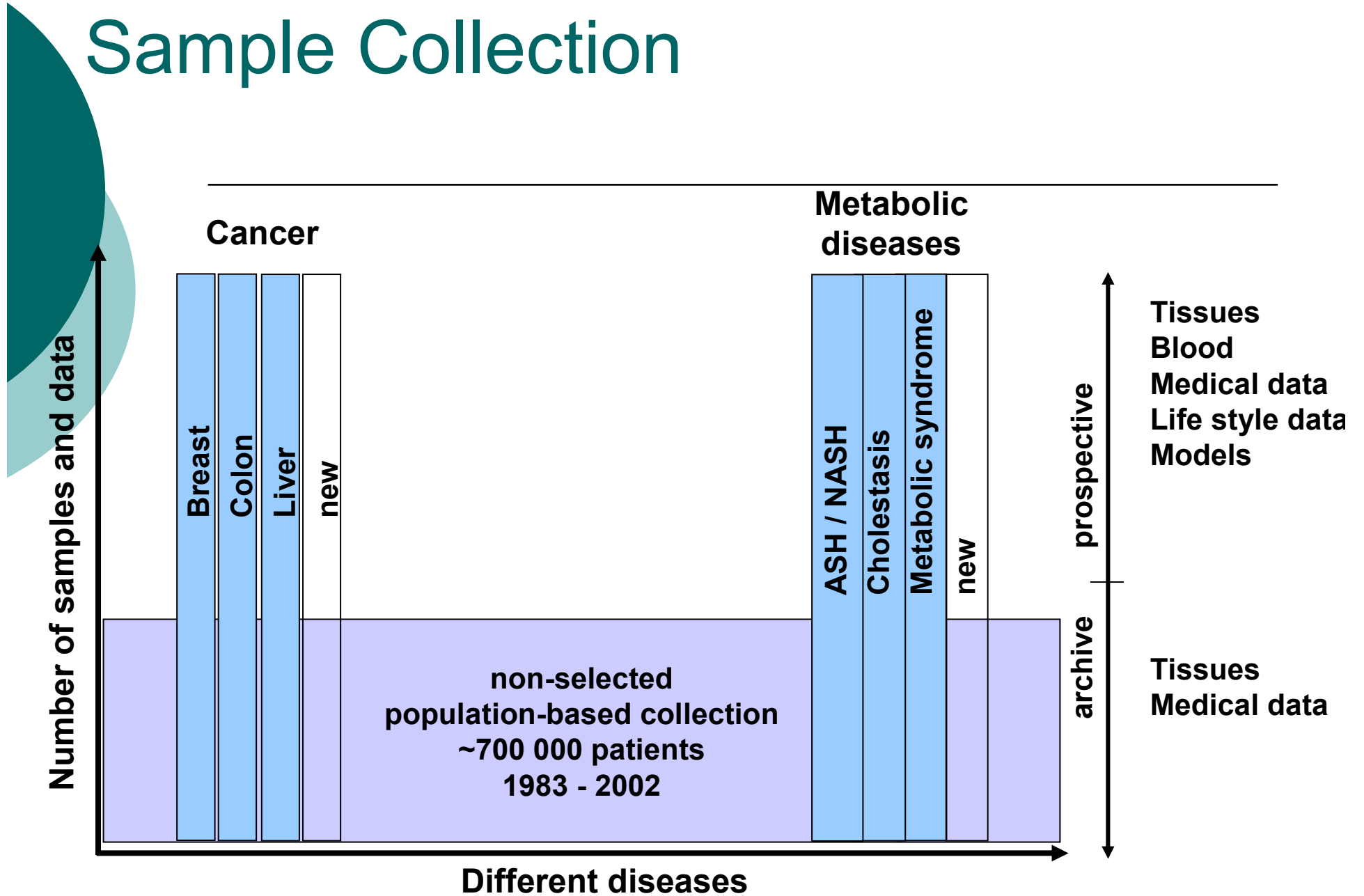
Digital Pathology Archive



Data Protection at Biobank of the Medical University of Graz

- Approval of biobank and IC by REC
- Registration of biobank at data protection agency
- Specific IC for biobanking; broad consent for research use
- Coding of samples in biobank
- Approval of research projects by REC
- Research projects may use only coded data and samples

Sample Collection

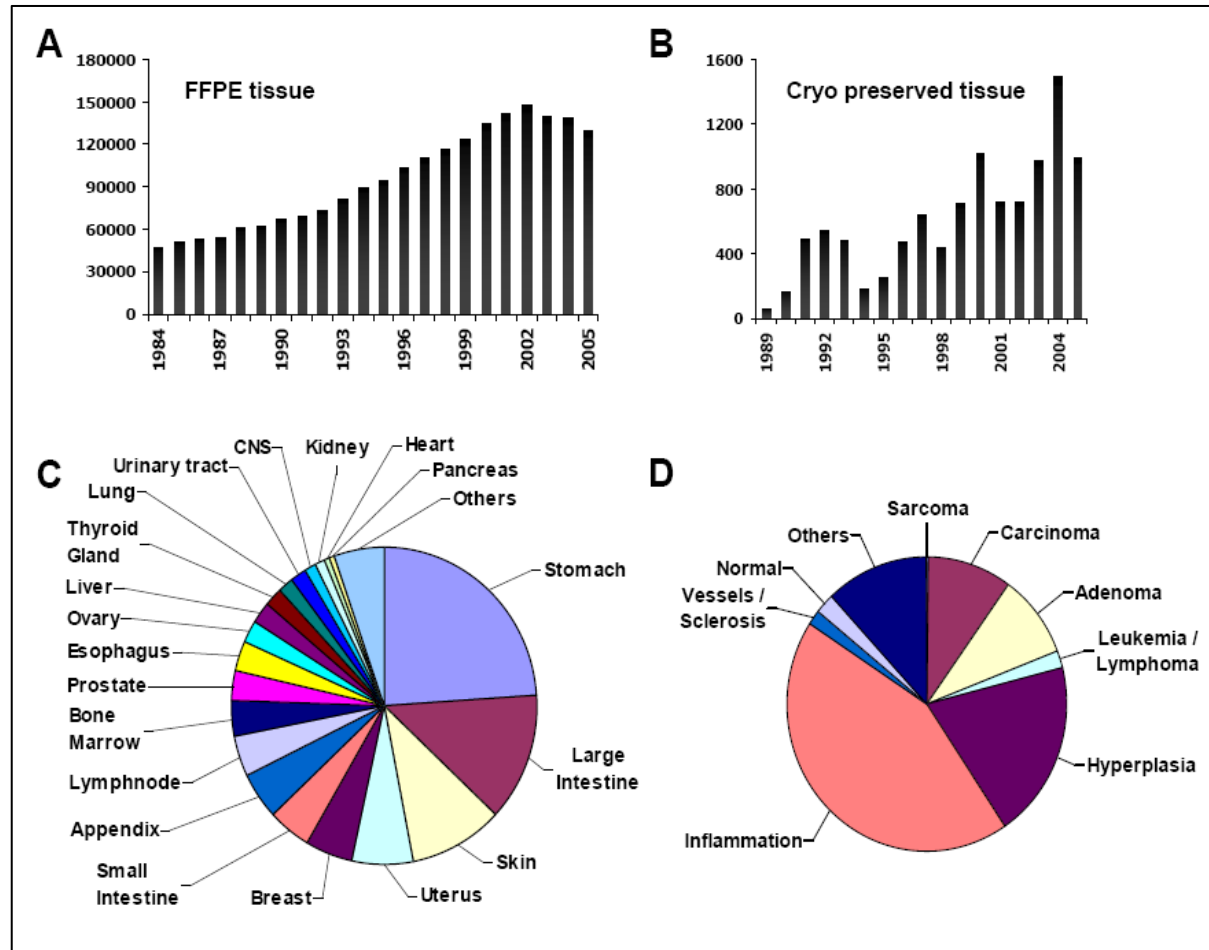


GATiB: Diseases and Tissues

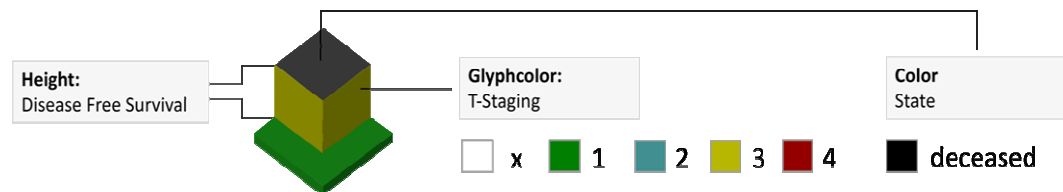
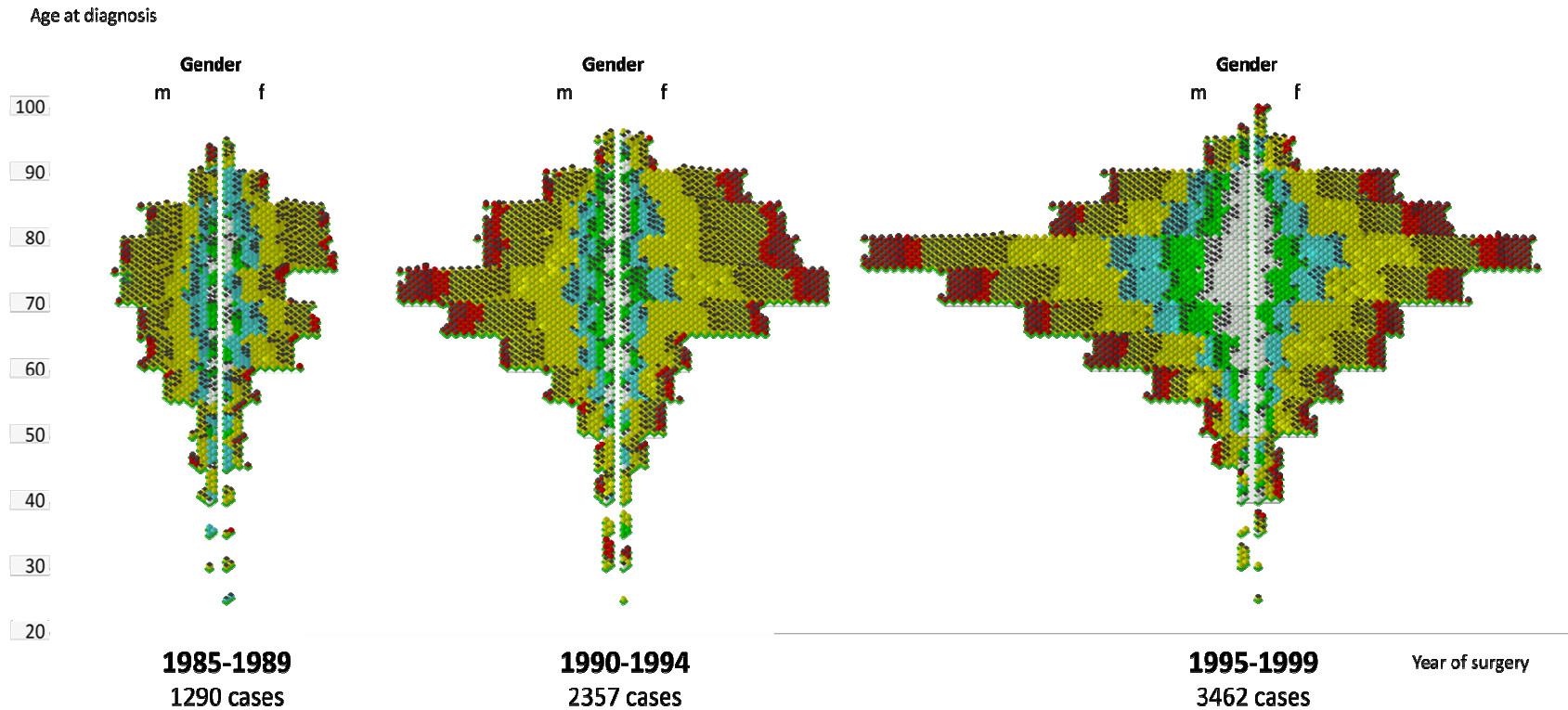
Total number of patients:

860 000 patients (FFPE)

24 000 patients (CRYO)

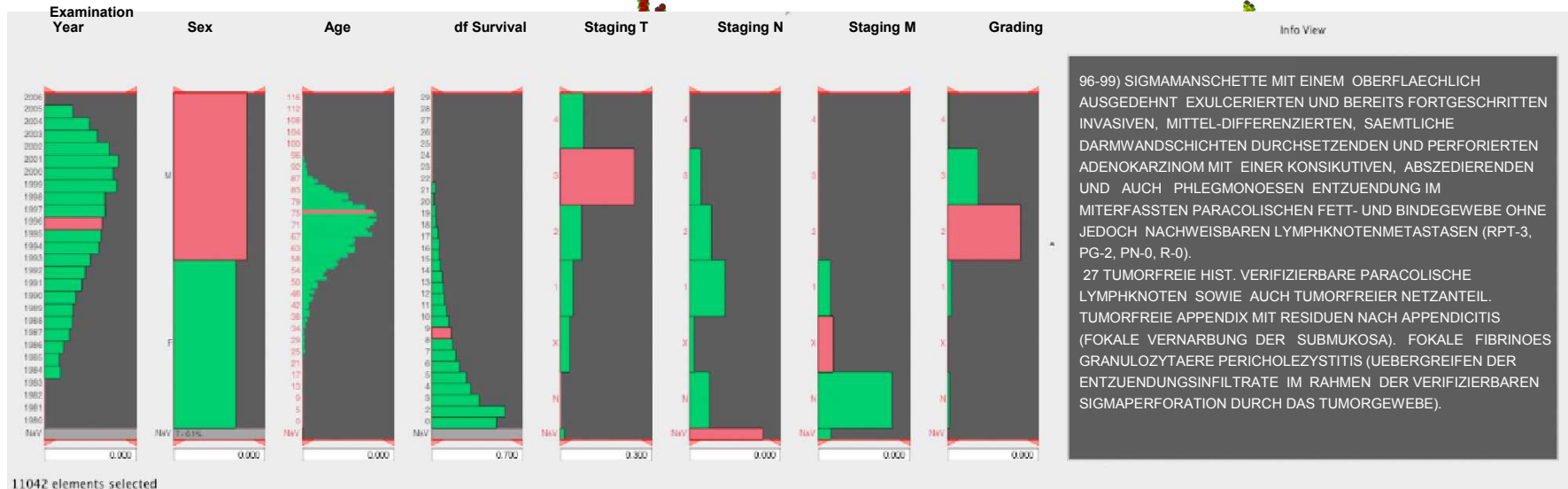
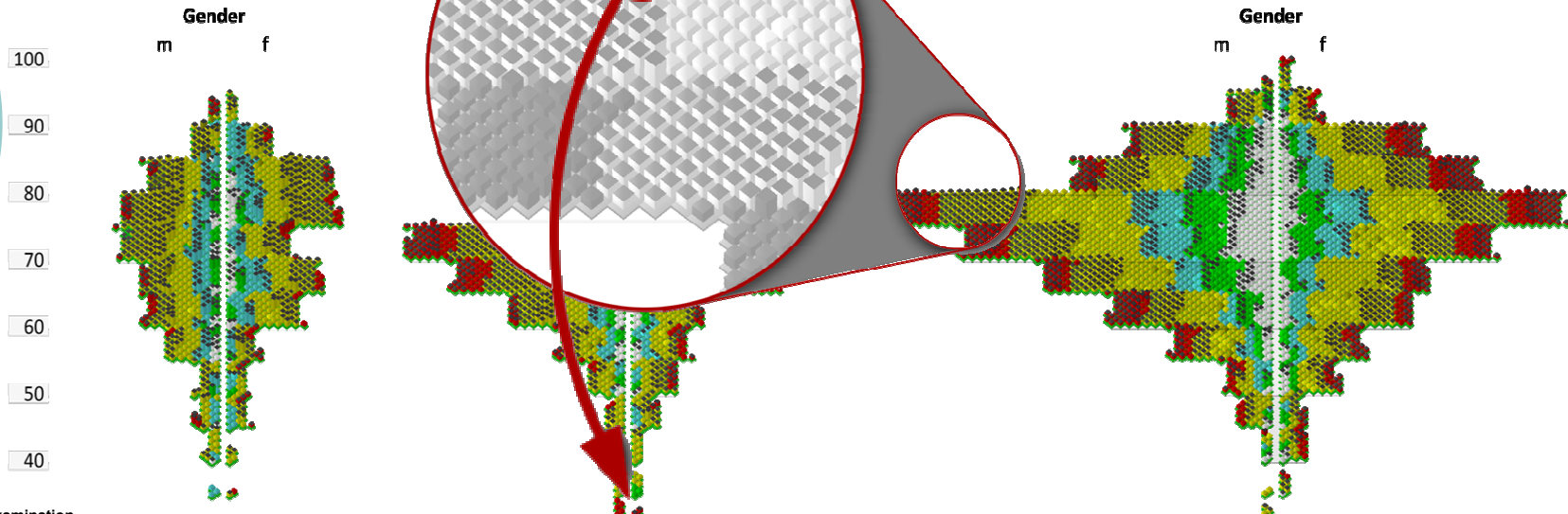


Overview on 7109 Colon Cancer Cases

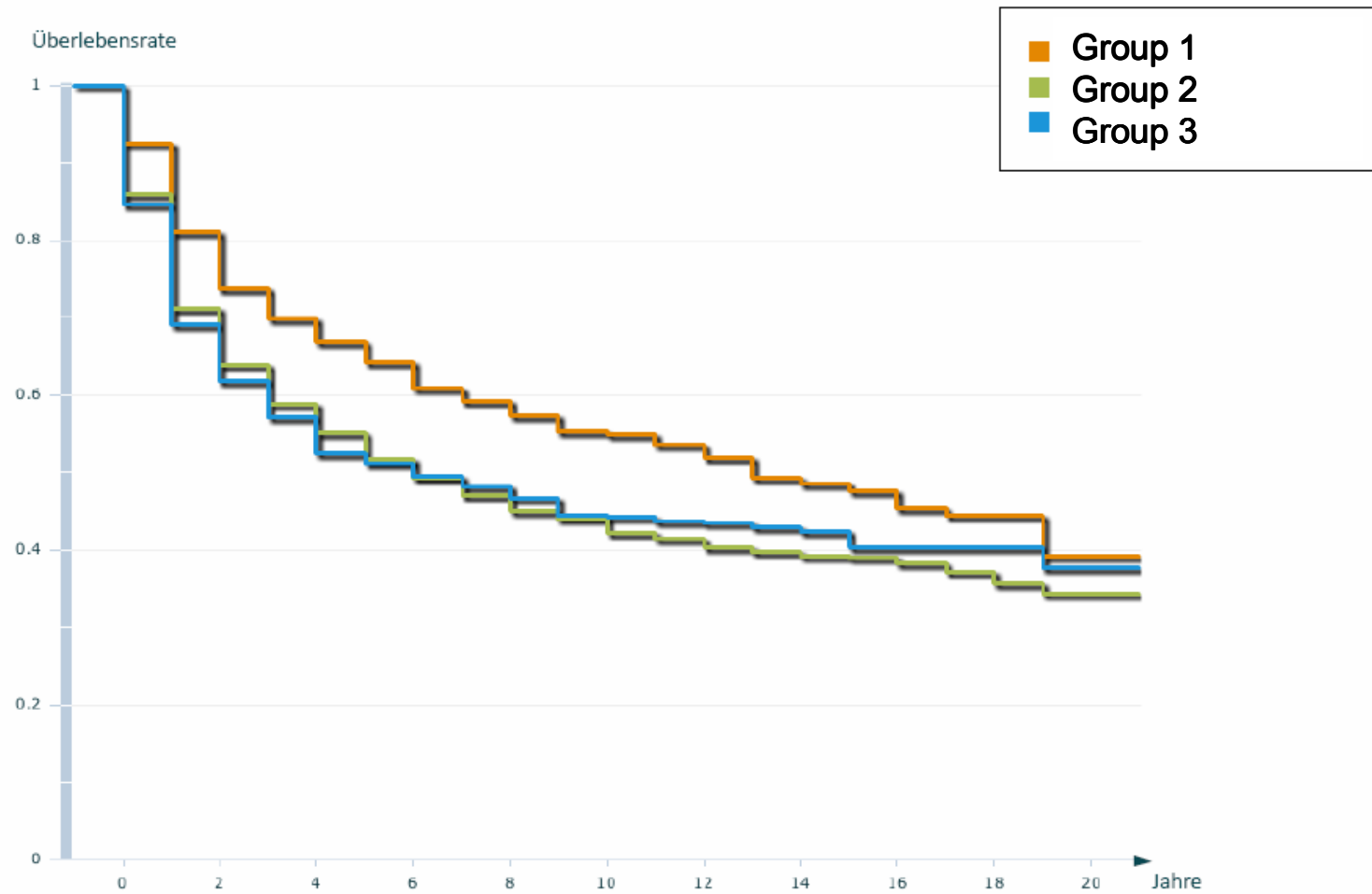


Overview on 7109 Colon Cancer Cases

Age at diagnosis



Colon Cancer Survival





The Biobank as an Interdisciplinary Research Infrastructure

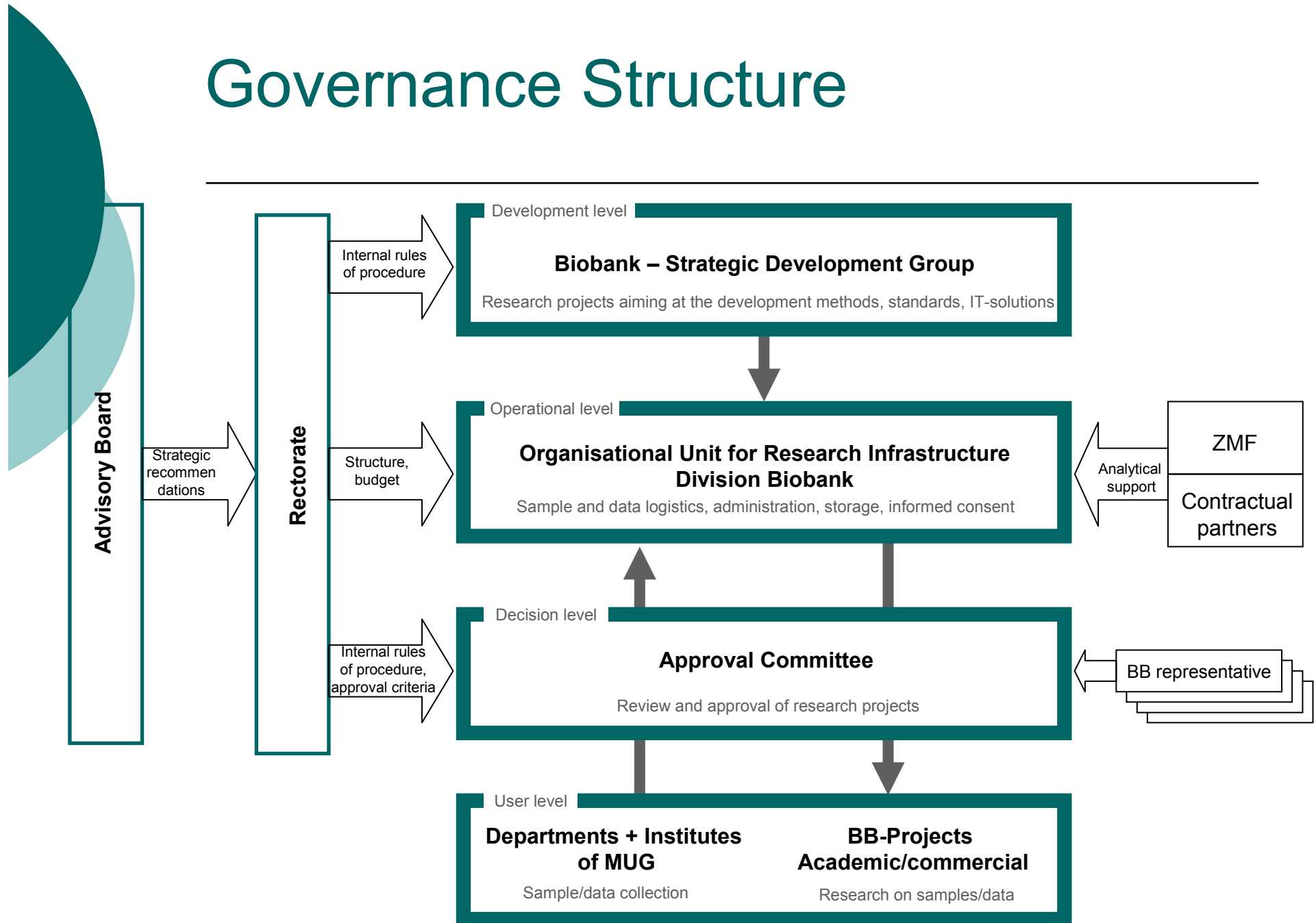
Advantages

- Integration of different sample types and medical data (tissue, blood, urine; whole medical record)
- Harmonization/standardization
- Informed consent (one IC for the whole University, tracking system)
- Data protection (data trusty)
- Increased capacities
- Preferred partner (one stop shop)

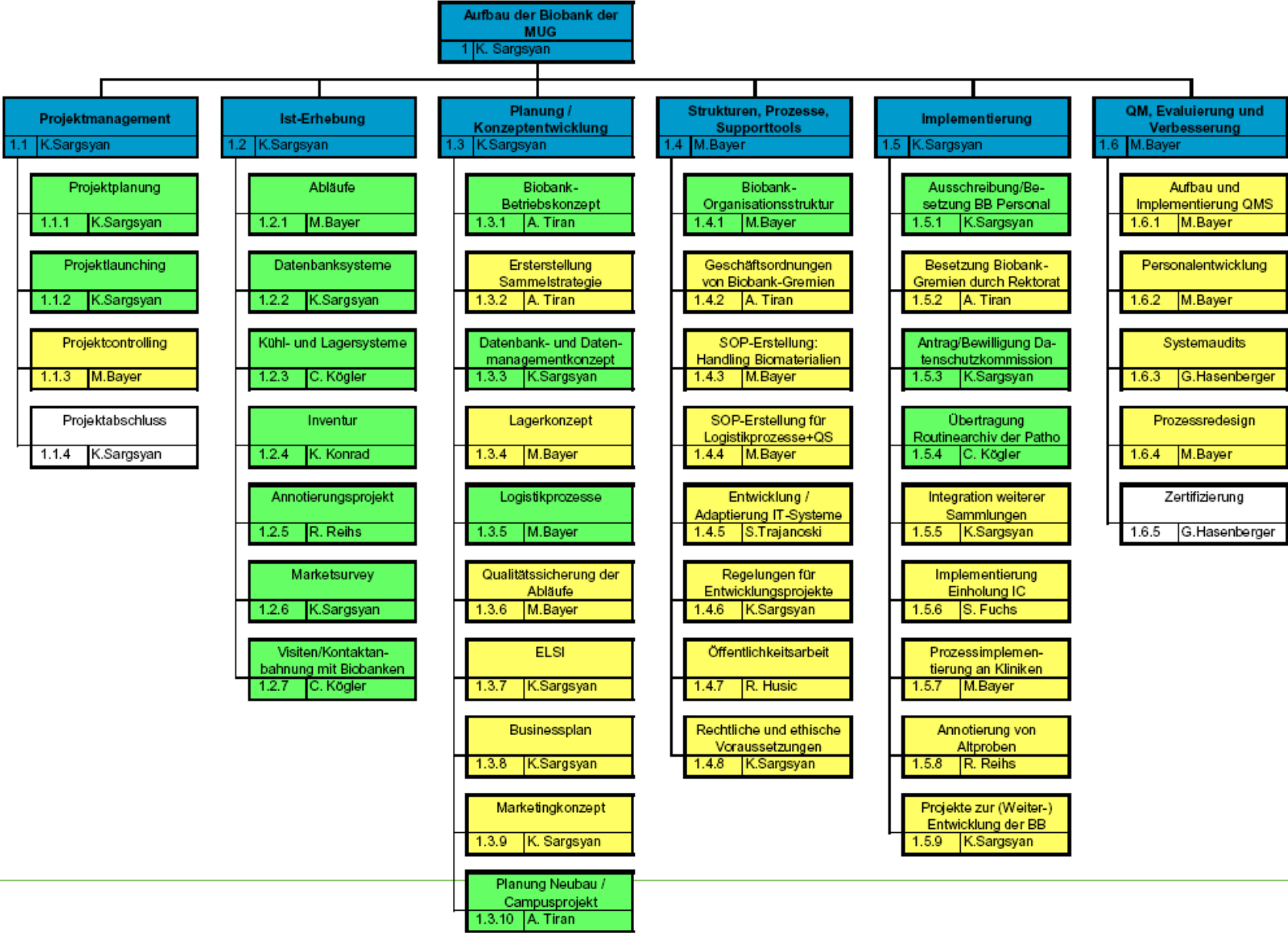
Biobank of the Medical University of Graz



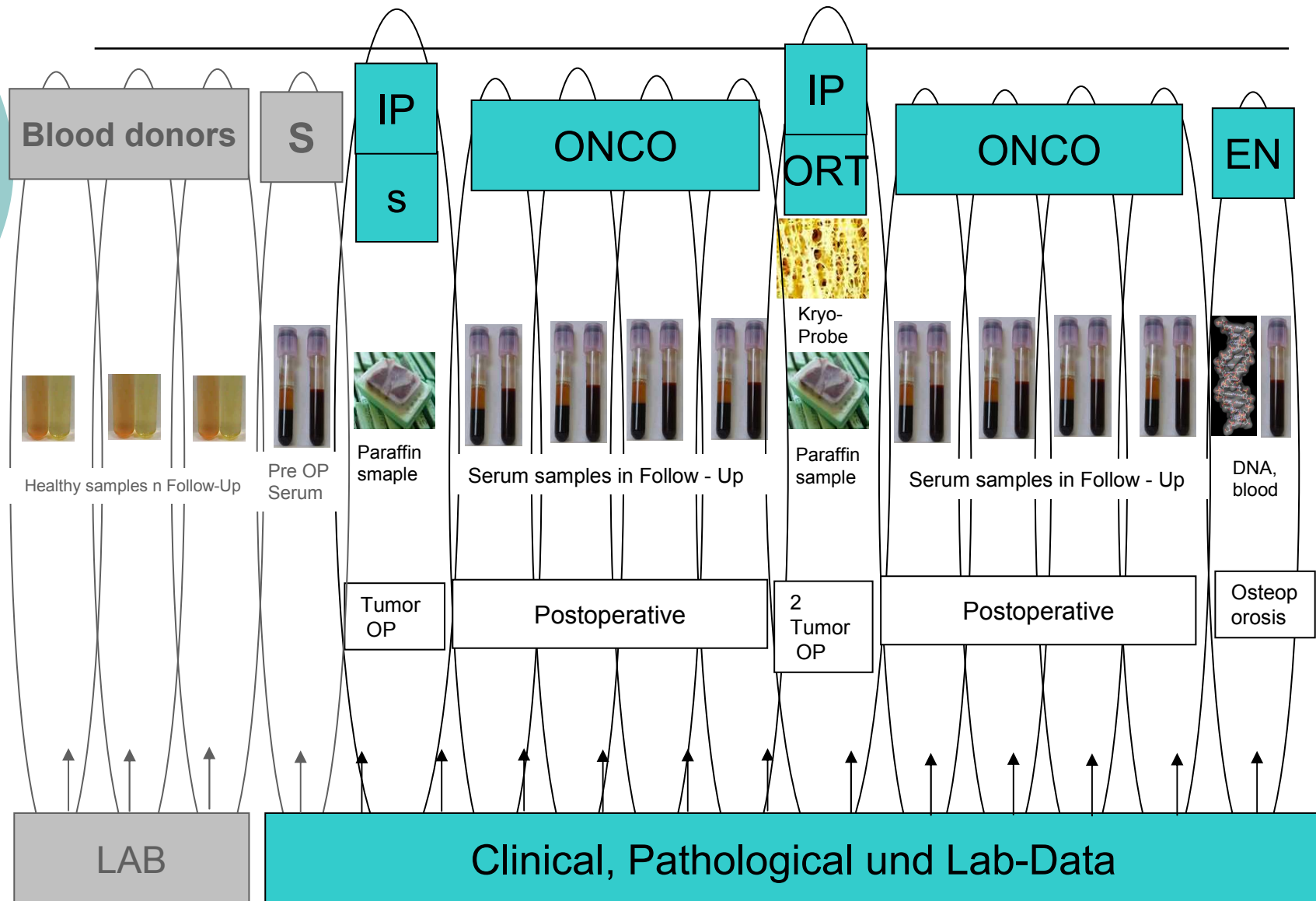
Governance Structure



Projekt Plan for Certification



The Medical History in the Biobank: An Example



4.2 Number of collected biological samples

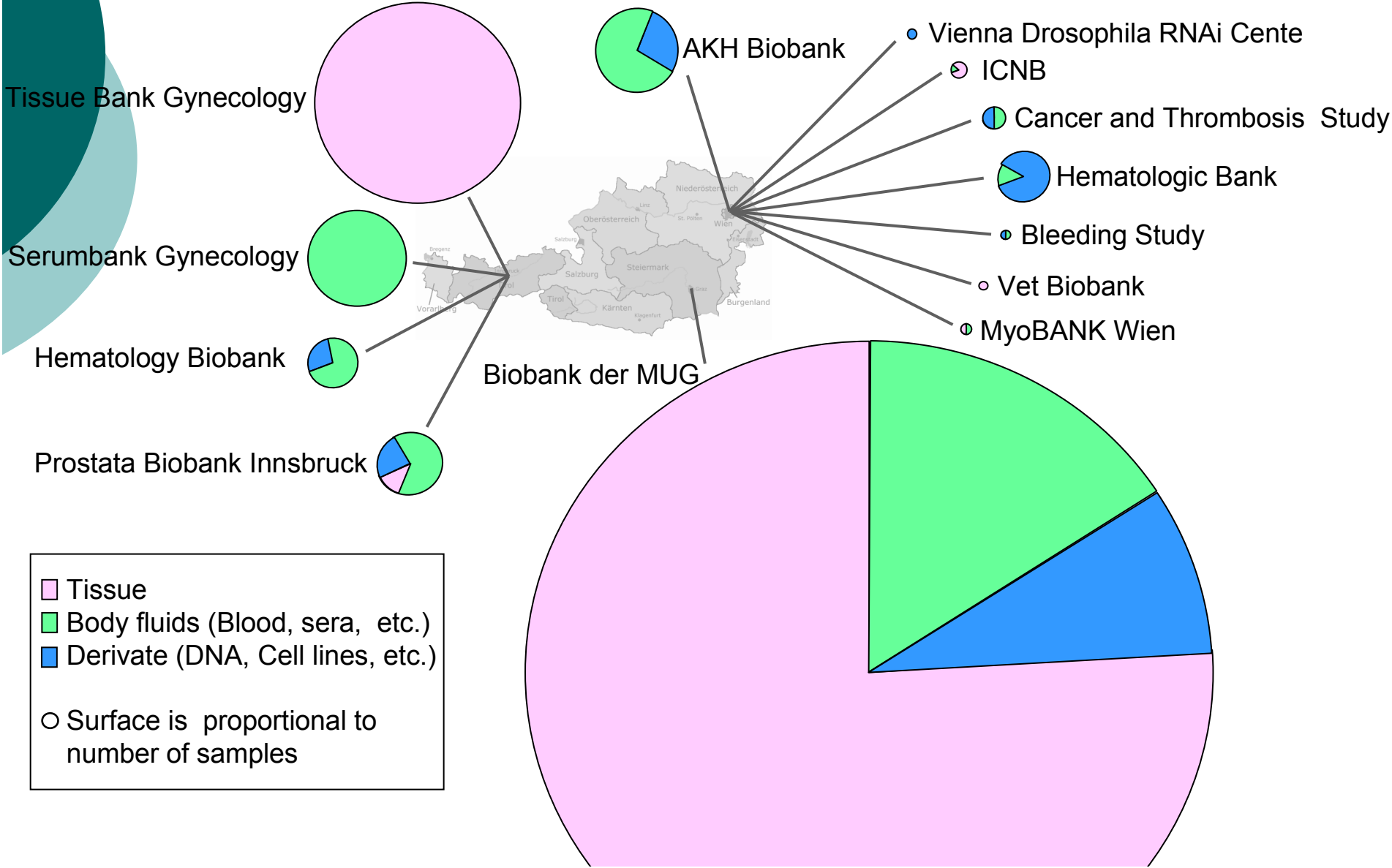
For how many people have biological samples (not aliquots) been collected (*select those applying and specify numbers*)?

Please also specify the numbers collected/issued per year for the year 2007.

Total Numbers				Numbers per year			
Donors		Samples		Donors	Samples		
<i>Affected*</i>	<i>Relatives[§]</i>	<i>Affected*</i>	<i>Relatives[§]</i>	<i>Collected</i>	<i>Collected</i>	<i>Issued</i>	
20.000	1.000	40.000	2.000	2.000	4.000	2.000	DNA, derived from: EDTA Buffy coat or whole blood
2.000	0	2.000	0	400	0	0	cDNA / RNA, derived from: [redacted]
40.000	1.000	80.000	2.000	4.000	8.000	2.000	Whole blood
5.000	0	5.000	0	100	100	300	Blood cell isolates (buffy coat, etc.)
150.000	1.000	350.000	3.000	12.000	36.000	6.000	Serum
1.000	0	1.000	5.000	1.000	1.000	0	Plasma
0	0	0	0	0	0	0	Fluids (urine, etc.)
40.000	0	120.000	0	6.000	18.000	6.000	Tissues, cryo preserved
980.000	0	3.100.000	0	130.000	380.000	6.000	Tissues, paraffin embedded
0	0	0	0	0	0	0	Cell lines
1.000	0	1.000	0	500	500	0	Other, please specify: amniotic liquor
1.239.000		4.399.000					Total number

Inventory of Biobanks in Austria

BBMRI – AT



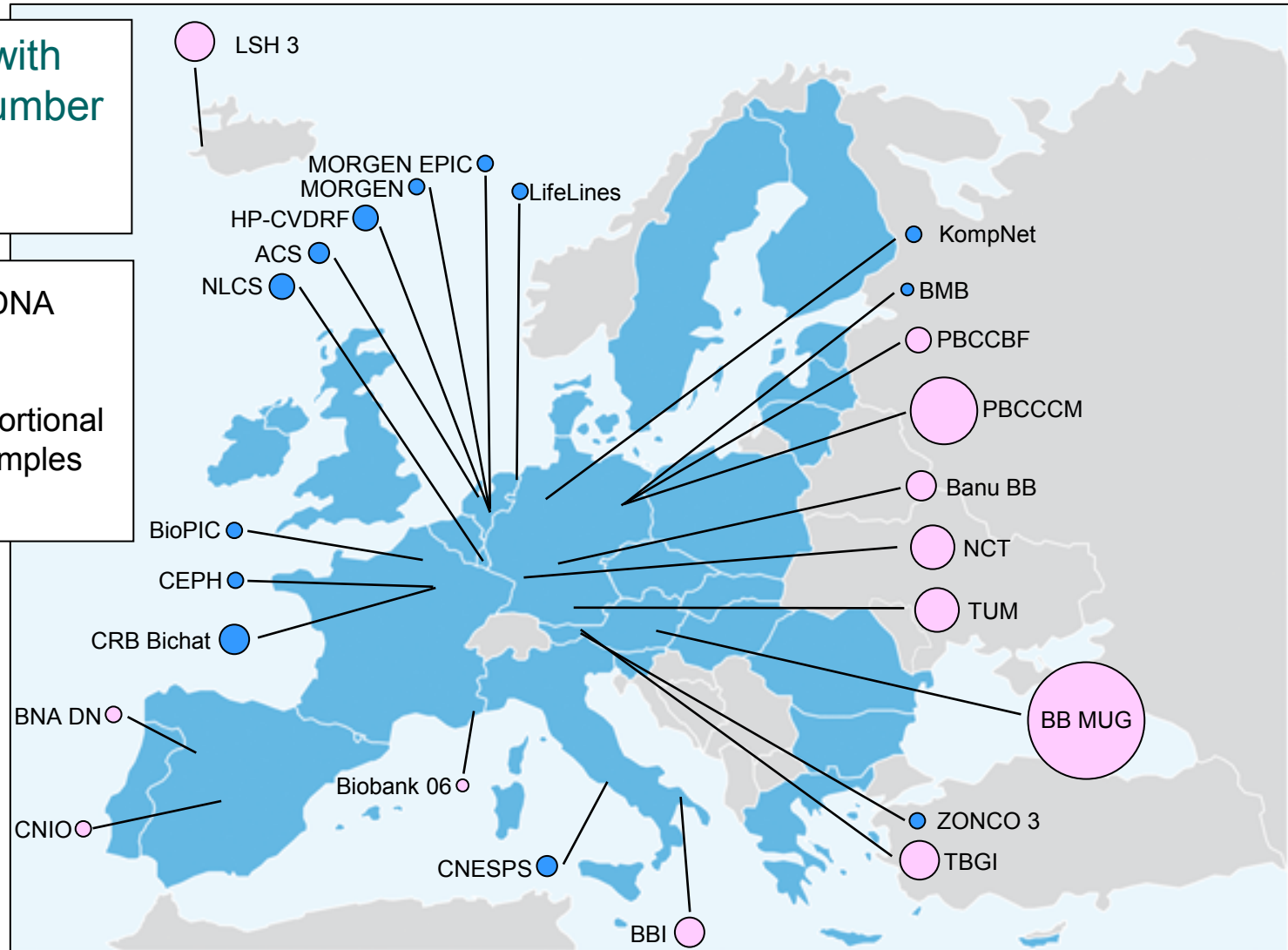
Inventory of Biobanks in Europe

BBMRI –Europe

25 Biobanks with
the highest number
of samples
April 2009

◻ Tissue, Blood, DNA
◼ Blood, DNA

○ Surface is proportional
to number of samples



Developments in Personalized Medicine Require Large Collections

Total number of patients

880 000

Breast cancer cases

10 600

tumor type

tumor size

lymph node metast.

hemat. metast.

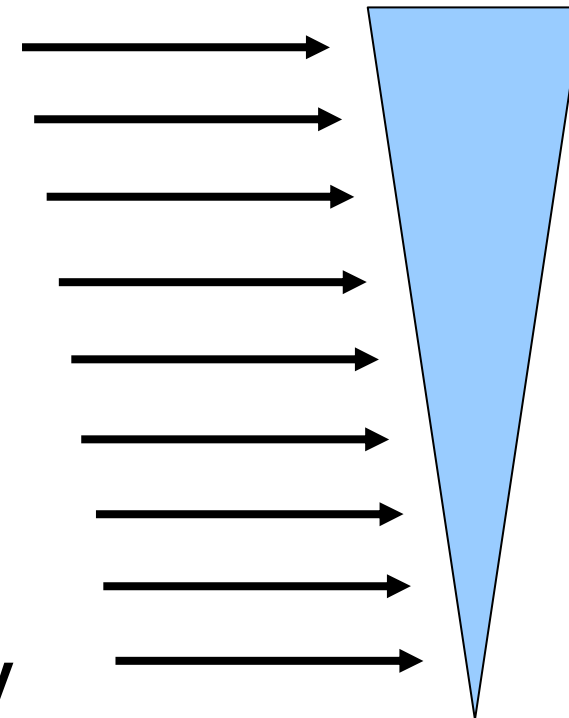
hormone receptors

HER-2, EGF-R

treatment

survival

family/patient history



Cases for specific study

~ 100 - 300



Collaboration is the Only Choice

Thank You!