

# Biobanking for Successful Translational Oncology

National Day – Germany's Way Towards Excellence in Biobanking

April 5, 2016/Berlin

PD Dr. med. Esther Herpel

Institute of Pathology  
and NCT Tissue Bank

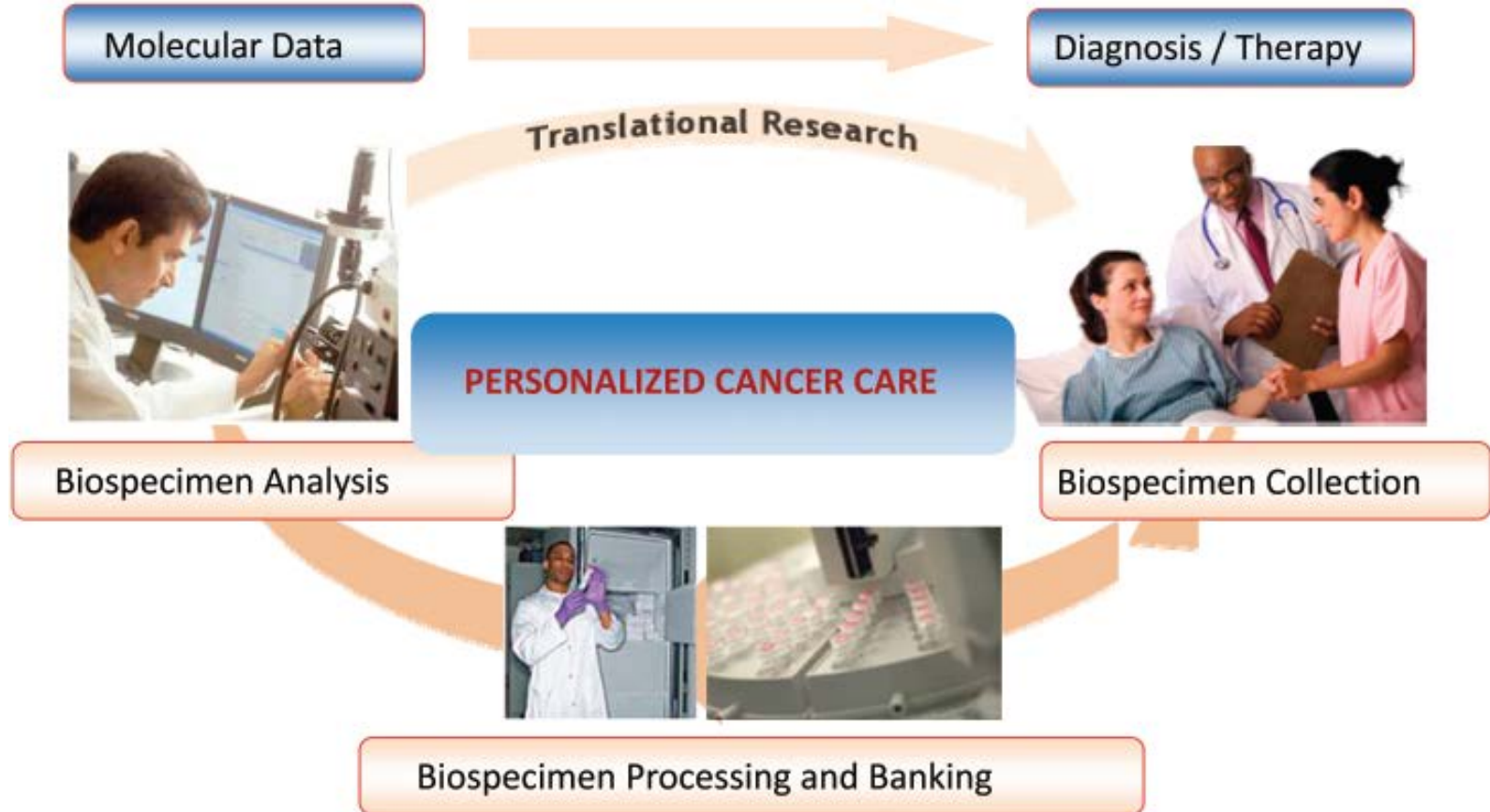
Heidelberg University Hospital  
Im Neuenheimer Feld 224, D-69120 Heidelberg



NATIONALES CENTRUM  
FÜR TUMORERKRANKUNGEN  
HEIDELBERG

getragen von:  
Deutsches Krebsforschungszentrum  
Universitätsklinikum Heidelberg  
Thoraxklinik-Heidelberg  
Deutsche Krebshilfe

# Central role of biomaterial in translational oncology



# But....



## Research: increasing value, reducing waste 2

Increasing value and reducing waste in research design, conduct, and analysis

John P A Ioannidis, Sander Greenland, Mark A Hlatky, Muin J Khoury, Malcolm R Macleod, David Moher, Kenneth F Schulz, Robert Tibshirani

## An open investigation of the reproducibility of cancer biology research

The American Journal of Pathology, Vol. 185, No. 1, January 2015



### EDITORIAL

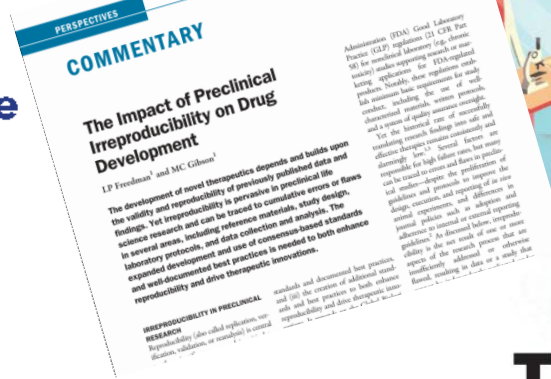
#### Science Isn't Science If It Isn't Reproducible

Kevin A. Roth\* and Audra E. Cox<sup>1</sup>

## Stakeholder Research on Biospecimen Needs and Reactions to the Development of a National Cancer Human Biobank by the National Cancer Institute

Renate Myles, Holly A. Massett, Gretchen Comey, Nancy Atkinson, Dee Allsop, Carolyn Compton

### FEATURES



### PERSPECTIVES COMMENTARY

#### The Impact of Preclinical Irreproducibility on Drug Development

LP Freedman\* and MC Gibson<sup>1</sup>

The development of novel therapeutics depends and builds upon the validity and reproducibility of previously published data and findings. Yet irreproducibility is pervasive in preclinical basic science research and can be traced to cumulative errors or flaws in several areas, including reference materials, study design, laboratory protocols, and data collection and analysis. The expanded development and use of consensus-based standards and well-documented best practices is needed to both enhance reproducibility and drive therapeutic innovations.

#### IRREPRODUCIBILITY IN PRECLINICAL RESEARCH

Reproducibility (also called replication, verification, validation, or corroboration) is essential to the scientific process and is a cornerstone of the scientific method. It is the process of repeating an experiment or study to confirm the results of a previous study. In preclinical research, reproducibility is essential for the development of new drugs and therapies. However, reproducibility is often poor in preclinical research, leading to wasted resources and delayed drug development.

Administrators (FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 312) for animal laboratory (pre-clinical) studies supporting research in new drug applications for FDA-regulated products. Notably, these regulations establish minimum basic requirements for study conduct, including: the use of well-documented materials, written protocols, and a system of quality assurance oversight. For the historical case of successful clinical research, consistent and well-documented research findings were not and are not sufficient to ensure consistently and effectively research results. Several factors are responsible for high failure rates but many can be traced to errors and flaws in practice. We discuss the production of well-documented and reproducible data in new drug applications and reporting of results, design, execution, and reporting of animal experiments, and differences in animal practices such as adequate randomization to control for confounding factors. As discussed below, reproducibility is the end result of one or more aspects of the research process that are insufficiently addressed or otherwise flawed, resulting in data or a study that

# THE CANCER TEST

A nonprofit's effort to replicate 50 top cancer papers is shaking up labs

By Jocelyn Kaiser

arrived in Richard October 2013 was the writer was part archers who "are

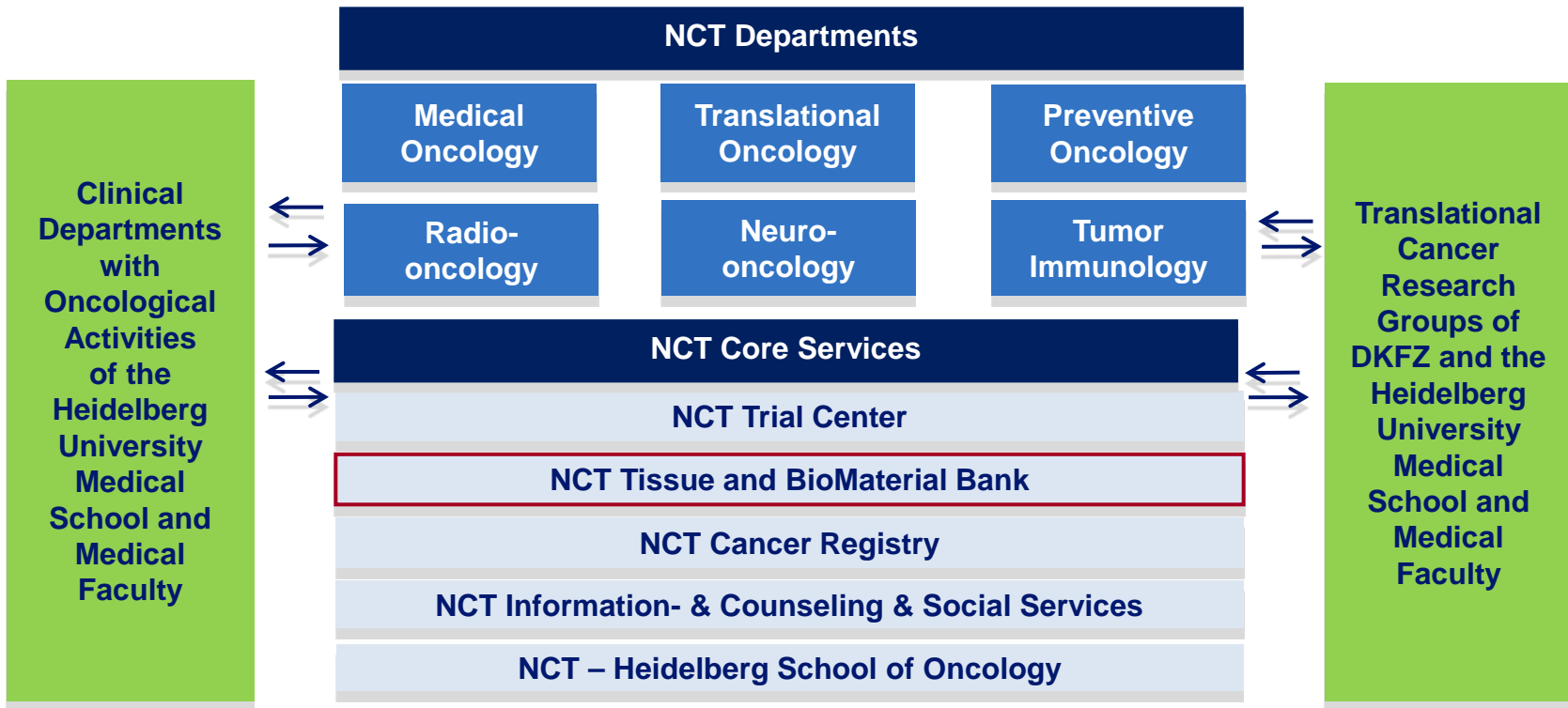
spurs tumor growth was among 50 high-impact papers chosen for scrutiny by the Reproducibility Project: Cancer Biology. The group might need help with materials and

plied, they still wanted to repeat it. But they needed more information about the protocol. After weeks of emails back and forth and scrambling by graduate students and



# Which issues are important?

# 1. Align your Biobank upon your objectives and local circumstances



# 1. Align your Biobank upon your objectives and local circumstances

## NCT Tissue Bank

since 2005, Head: E. Herpel

- Focus: cancer
- Cryopreserved Tissue: >25.000 FFPE (archive): >500.000 Proben
- >1900 successfully completed projects
- Established quality and project management, technology platform
- Accreditation since 2009



## NCT Liquid Bank

since 2011, Head: R. Kirsten

- Focus: cancer
- Liquid samples: blood and derivatives, urine, stool, sputum, DNA/RNA,..
- >200.000 samples, 35 projects
- SOP guided sample storage and processing



# 1. Align your Biobank upon your objectives and local circumstances

**One comprehensive Biobank.....**

**Because the benefits are e.g. ....**

- Efficient use** of valuable biomaterial resources
- Use of synergies** (sample preparation, data storage, informed consent, sample storage systems, staff and training)
- Implementation of common **quality standards**
- Transparency** and an **interdisciplinary structure** (core-function, consistent regulations, access)
- Platform for numerous project designs** (epidemiological studies, complex projects, joint research, international co-operations)
- Reduced stress for patients** (blood draw, informed consent procedure, data safety)

## 2. Note the legal requirements and ethical aspects

- Comprehensive ethical vote for tissue acquisition
- Compliance with legal regulations
- Data safety concept
- Standardized informed consent for all biomaterials and respective data
- Hospital admission contract
  
- Priority of clinical diagnostics and therapy
- Release of retrospective tissue collection



# 3. Take care for clear data management

Informed consent documentation



Patient

Gewebe



Arzt / Chirurg

- Control completely by QR-codes / Touchscreen
- Automatic label printing with receipt number, time and dignity
- Duplicate- and error checking

Access to sample data



Dokumentation

Pseudonymisierung

Metadaten-Zuweisung



STARLIMS

Steuerung

Weiter Zurück Empfang schließen

Empfang abbrechen

Stückzahl

1 4 5 6



Gewebeprobe +  
Einsendeschein

Initialregistrierung mit:  
Röhrchen-IDs,  
Eingangsnummer,  
Material,  
Füllmenge

Gewebe-Entnahme NCT-Gewebebank				
Kryo-Zeit:	12.03.2014 12:22	Arzt:	FA:	TA:
E 2014:				
NCT-Nummer	Dign.	Organ		A
FC	TG			3
FC	TG			3
FC	NG			3



TA 1

Probe  
aliquotieren



Rack mit  
Aliquots

Lagerort im  
Freezer zuweisen



TA 2



Rackscanner

Rack-ID,  
Röhrchen-IDs,  
Positionen (x, y)



registriertes Rack  
mit Aliquots



Freezer (Lagerung)

Samplemanagement, Quality assurance (SOPs)

Rackscanning and analyser compatibility

# 4a. Build a "living" quality management (QM)

## Only high sample quality may ensure succesful translational oncology

QM = active and integrated system that ensures the quality of a process/project.

- Written SOPs
- Data management
- Emergency management
- Measurable quality objectives (Feedback of customers, publications...)
- Quality control (Entry-/ Exit control)

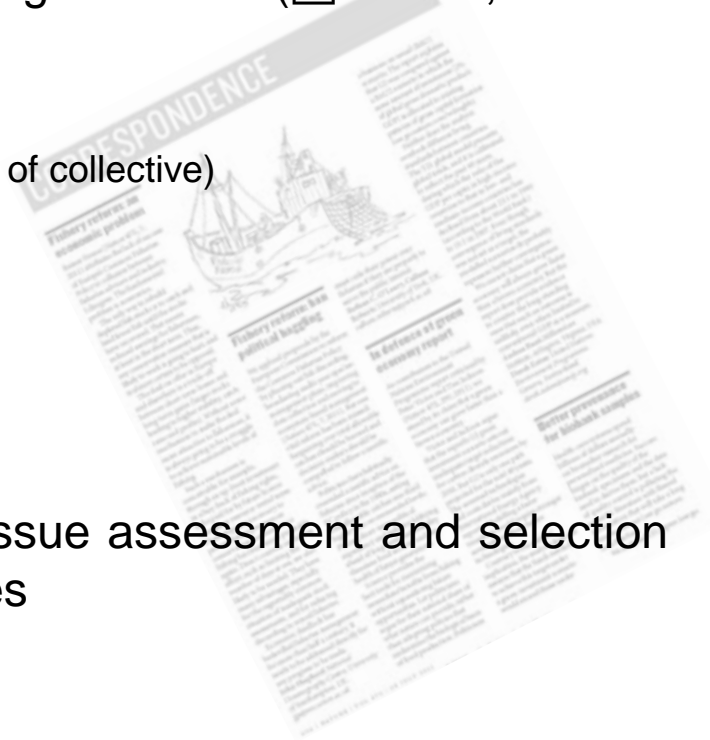
## NCT Tissue Bank:

Accreditation since 2009/2013 in accordance with  
DIN EN ISO/IEC 17020



# 4a. Provide high quality of biomaterial

- >50% of studies using homogenised human tissue derivatives are based on insufficiently characterized/documented starting material (□ Perren, Nature 2011)
  - Lack of:
    - Expert-evaluation (diagnosis, quality, composition of collective)
    - Trial specific parameters
    - Standardized entry- and exit-controls
    - Standard reporting and documentation
  
- Good scientific practice in pre-experimental tissue assessment and selection is the decisive basis of work with human tissues



## 4b. Provide high Quality of biomaterial

- Processing of biomaterial under regard of the respective research projects
- Projects require different quality
  - Type of fixation (FFPE vs. Fresh Frozen)
  - Immunohistochemistry vs. homogenization
- Result report (exit-control) = quality control
- Handover protocol including a MTA (e.g. instructions on how to handle the samples, quoting in publications)
- Tracking

# 5. Ensure transparency and clear structures

- ❑ Resources/ Infrastructure
- ❑ Interdisciplinary structure
- ❑ Advisory Board
- ❑ Competent head of biobank
- ❑ Rules of procedure/ Organisation chart
  
- ❑ Access rules, project management:

**Anforderungsbogen Gewebekbank**

Anforderungsbogen für ein PC und/oder Gewebekbank an der NCT. Bitte füllen Sie diesen Bogen aus und senden Sie ihn an: NCT, Postfach 10 15 53, 53115 Bonn, Tel. 0228 275-2222, Fax 0228 275-2223, E-Mail: nct@nct.de

**Anforderung (Bitte beschreiben):**

**Aktuelle Problem:**

**Beteiligte Institutionen:**

**Studienkriterien + Anzeigearbeitsgruppe:**

**Projektziele:**

**Antragnummer:** \_\_\_\_\_ **Projektnummer:** \_\_\_\_\_

**Genehmigung:** \_\_\_\_\_ **Nach:** \_\_\_\_\_

**Kooperationspartner:** \_\_\_\_\_ **Datum Genehmigung:** \_\_\_\_\_

**Bemerkungen:** \_\_\_\_\_

## 6. Protect your samples and data

*Things always seem to happen when you least expect them...*



*It does not matter to foresee the future but to be prepared for the future*

An emergency management defines preventive and reactive measures

- Which measures in case of emergency?
- Responsibilities, information?
- How will “normal” conditions be recovered?

# 6. Protect your samples and data

## Some Measures of NCT Tissue Bank:

- 24 hours monitoring of freezers + daily visual controls of temperature
- Emergency phone list
- Access restriction
- Labeling of freezers
- Backup-Freezer; alternative storage location
- Regular “emergency training”
- Separate servers for data
- Daily data backups

Gewebebank des NCT  
am Pathologischen Institut

Leitung der Gewebekbank  
Dr. med. E. Herpel

Truhenbelegungsplan

Anlage 4 zur Arbeitanweisung  
Lagerung Frischgewebe

**NCT Gewebekbank-Gefriertruhen  
zuständige Mitarbeiter**

im Notfall benachrichtigen:

Ärzte/Mitarbeiter	Telefon-/Handy- Nummern
Bettina Walter	37564 (Klinik) 06221-767533 (privat) 017864099837 (mobil)
David Jansen	34749 (Klinik) 015733129762 (mobil)
Dr. Sabrina Schmitt	39864 (Klinik) 06224-9022312 (privat) 017662795768 (mobil)
Gloria Laukemper	34749 (Klinik) 06221-6729754 01777992947 (mobil)
Christiane Zgorzelski	36288 (Klinik) 06221-7258568 (privat) 0152-28770905 (mobil)
Dr. med. Esther Herpel	39306 (Klinik) 06221-599082 (privat) 015254648455 (mobil)

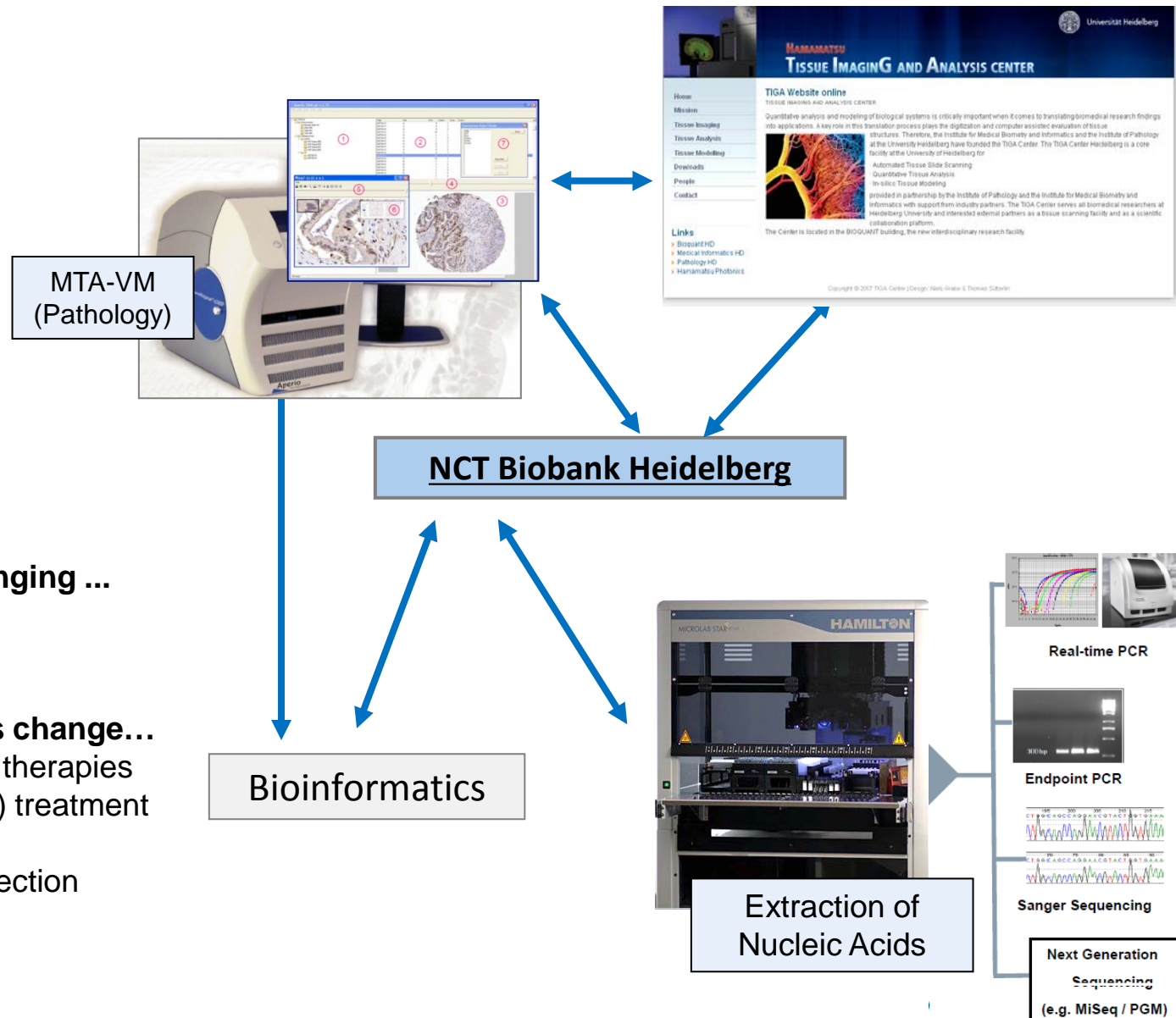
Überprüft:  
J. Berger  
Datum: 17.09.2012

Dagüß:  
Prof. Dr. med. P. Schramacher  
Datum: 18.09.2012

Freigegeben:  
Dr. med. E. Herpel  
Datum: 24.09.2012

09.12rev. 1 QMC-NCT 2.3 88d  
Truhenbelegungsplan\_1001201 Seite 1 von 1

# 7. Be open to new scientific developments



**Science is constantly changing ...**

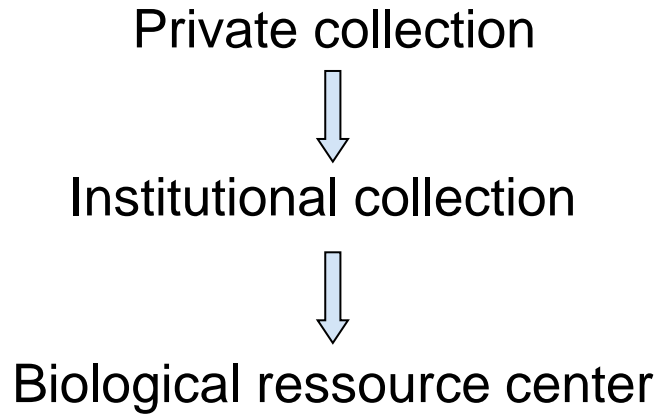
- New issues
- New technologies

**Medical Treatment options change...**

- Less "aggressive" surgical therapies
- Preoperative (neoadjuvant) treatment forms
- New methods for early detection



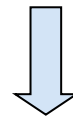
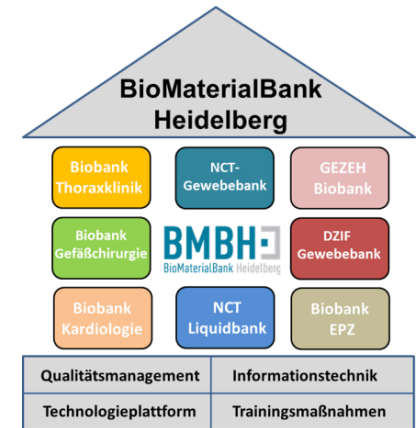
# 8. Be willing to share



Single Biobank



Network



# 9. Provide sustainability

## In terms of

- Standardized quality
- Guaranteed data safety
- provision of resources/ biomaterial

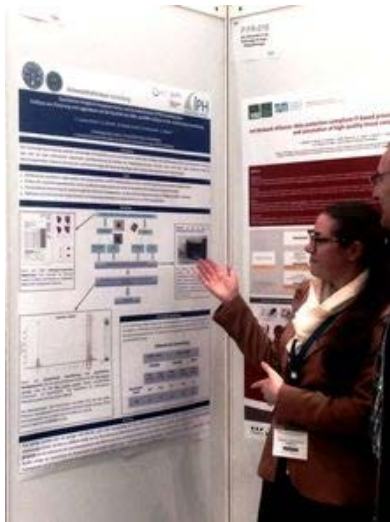
high efforts – high costs  
insufficient infrastructure  
and financing options



## Development of a sustainable financing concept

- Acquisition and documentation of single expenses and structures
- consideration of these expenses in case of biomaterial requests
- Where applicable, fees for services (internal customer vs. external customer)
- Commercial activities (e.g. industrial co-operations)
- Integration at local centers

# 10. Do good things and talk about it



Talks/Poster with topic Biobanking



Open House Day NCT

**Universitätsklinikum Heidelberg**  
**BIOBANKING UPDATE**

II. Nationale / Internationale Biobanking Aktivitäten

Meeting 2016 in Berlin

Die Bundesgesellschaft für Biobanking und Gewebekbanking (BGG) hat am 10. und 11. September 2016 ein Meeting in Berlin durchgeführt. Das Meeting wurde von der BGG und dem Deutschen Biobanknetzwerk (DBN) organisiert. Die Teilnehmerinnen und Teilnehmer haben sich über die aktuellen Entwicklungen im Biobanking und Gewebekbanking informiert und die Zusammenarbeit zwischen den verschiedenen Akteuren im Bereich Biobanking und Gewebekbanking diskutiert.

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**Deutscher Biobanknoten (DBN)**  
Das DBN ist ein zentrales Kontakt- und Vermittlungsstelle für die deutschen Biobanken. Es bietet eine Plattform für die Kommunikation zwischen den Biobanken und die Koordination von Projekten und Ressourcen.

**BioMaterialBank Heidelberg (BMBH)**  
Das BMBH ist eine spezialisierte Biobank für die Sammlung, Charakterisierung, Lagerung und Distribution von biologischen Materialien. Es ist ein Mitglied des Deutschen Biobanknetzwerks (DBN) und des Nationalen Zentrums für Tumorerkrankungen (NCT) Heidelberg.

**Universitätsklinikum Heidelberg**

Patienteinformation  
**BioMaterialBank Heidelberg (BMBH)**

**BMBH**  
BioMaterialBank Heidelberg

ORIGINAL ARTICLE

**Structural requirements of research tissue banks from standardized project surveillance**

E. Herpel · N. Koleganova · B. Schreiber · B. Walter · Kalle · P. Schirmacher

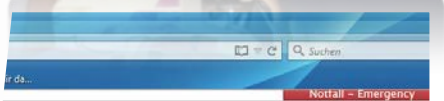
Verchows Arch  
DOI 10.1007/s00261-015-1825-5

ANNUAL REVIEW ISSUE



**Challenges for quality management in implementation, maintenance, and sustainability of research tissue biobanks**

S. Schmitt · K. Kymast · P. Schirmacher · E. Herpel<sup>1,2</sup>



**Disclaimer**  
**Gewebebank**  
**Informationen für Patienten**  
**Informationen zur Transparenz gemäß Ethikrat**

Rechtsform, Datenschutz, Aufsichtsbehörden, Zuständigkeiten, Ansprechpartner und vertiefende Informationen, Regeln und Zwecke, Aktivitäten der Biobank, Maßnahmen zur Qualitätssicherung

**Technologieplattform**  
Tissue-Micro-Arrays, Immunhistologische Färbungen, Extraktionsverfahren, Referenz- und Trainingsleistungen

**Mitarbeiter/Beirat**  
**Kontakt**  
**Downloads**  
**Links**  
**AG der Gewebekbanken der Comprehensive Cancer Centers**  
**Nationales Centrum für Tumorerkrankungen (NCT)**  
**Aktivitäten der Gewebekbank**

Kongresse und Workshops  
Publikationen  
Eingeladene Seminare  
Veranstaltungen  
Drittmittelanträge  
Internationale Aktivitäten  
Nationale Aktivitäten  
**Qualitätsmanagement**

**NCT-Gewebebank**

Die Gewebekbank ist eine Einrichtung des Nationalen Zentrums für Tumorerkrankungen (NCT) Heidelberg unter der Schirmherrschaft der Medizinischen Fakultät der Universität Heidelberg und des Deutschen Krebsforschungszentrums (DKFZ).

Zweck der Gewebekbank ist das Sammeln, Charakterisieren, Registrieren, Archivieren und Aufbereiten von Geweben und Gewebsextrakten (z. B. in Tissue-Micro-Arrays) in hoher Qualität für wissenschaftliche Untersuchungen im Rahmen der Tumorforschung.

Die Gewebekbank unterstützt biomedizinische, wissenschaftliche Projekte der Medizinischen Fakultät der Universität Heidelberg, des Deutschen Krebsforschungszentrums, der Thoraxklinik Heidelberg-Rohrbach, der Orthopädischen Universitätsklinik Heidelberg und aller sonstigen Einrichtungen, die Mitglied des NCT Heidelberg sind oder zur Gewebekbank des NCT beitragen.

Daher besteht für Mitarbeiter der oben genannten Gruppen die Möglichkeit, Gewebeprobe und Paraffinschnitte von Multi-Tissue-Arrays aus der Gewebekbank unter Darstellung des Verwendungszweckes zu erhalten, um diese im Rahmen von wissenschaftlichen Fragestellungen untersuchen zu können.

Entsprechende Anträge finden Sie unter Downloads.

**DAKKS**  
Deutsche Akkreditierungsstelle  
D-15189-01-00

**Nationales Centrum für Tumorerkrankungen (NCT)**

Original Article  
Verchows Arch  
December 2010, Volume 457, Issue 6, pp 741-747  
First online: 27 October 2010

**Quality management and accreditation of research tissue banks: experience of the National Center for Tumor Diseases (NCT) Heidelberg**

Esther Herpel · Christoph Röcken · Heike Manke · Peter Schirmacher · Christa Flechtenmacher

Seitenanfang Ruprecht-Karls-Universität

# Conclusion

## 10 biobanking issues for successful translational oncology

1. Align your biobank upon your objectives and local circumstances
2. Note the legal requirements and ethical aspects
3. Take care for clear data management
4. Build a "living" quality management
5. Ensure transparency and clear structures
6. Protect your samples and data
7. Be open to new scientific developments
8. Be willing to share
9. Provide sustainability
10. Do good things and talk about it