UE Biopathologie et Biobanking

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www.biobank06.com

- Modalités de l' examen
  - Trois questions rédactionnelles de 45 min (coefficient 3/4)
  - 30 QCM (coefficient 1/4)
- Présence obligatoire (relevé de présence)
- Programme 2012
  - Cellules tumorales circulantes
  - Biobanque: pourquoi et comment ? (I)
  - **Biobanque: pourquoi et comment ? (II)**
  - Technique en biopathologie (I)
  - Techniques en biopathologie (II)
  - Techniques en biopathologie (III)
  - Pathologie moléculaire et médecine personnalisée
  - Microscopie électronique
  - Exemple de recherche translationnelle (I)
  - Exemple de recherche translationnelle (II)

UE Biobanking & Biopathology

Setting up criteria (including biospecimen quality controls) to evaluate the activity of a biobank

Toward an «impact factor» for biobanks ?

Paul Hofman
Laboratory of Clinical and Experimental Pathology & Human Biobank
www.biobank06.com

Nice Sophia Antipolis University, France

How to define a « good » biobank ? Which indicators ?

- Indicators showing that samples can be of good value for a research project
- Indicators of good research productivity
- Other indicators of strong interest

How to define a « good » biobank ? Which indicators ?

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Indicators showing that samples can be of good value for a research project

- Quality of the samples
  - Quality of DNA
  - Quality of RNA
  - Quantity of nucleic acids
  - Associated mirror sample for morphological control
  - Associated biological fluids to tissue samples
- Quality of associated clinical data
  - General data
  - Specific data for the pathology
  - Efficiency for updating the data (including the follow up of the patients)

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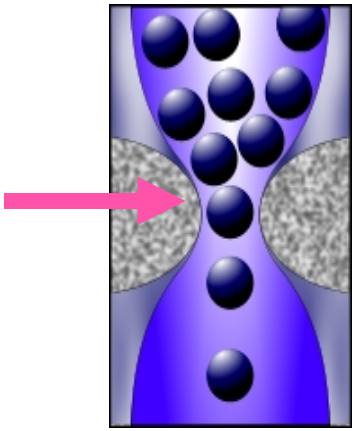
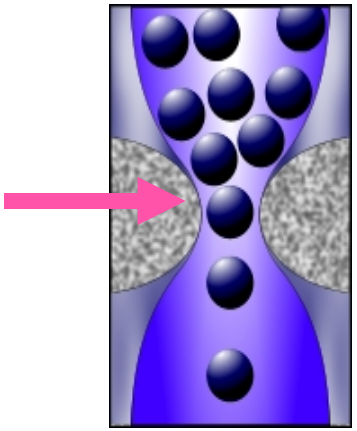
Parameters impacting the quality of samples



Bottle necks

- Pre analytical time
- Frozen procedure versus fixatives
- Sample size
- Percentage of tumor cells
- Area of necrosis
- Matched healthy sample available

Parameters impacting the quality of samples



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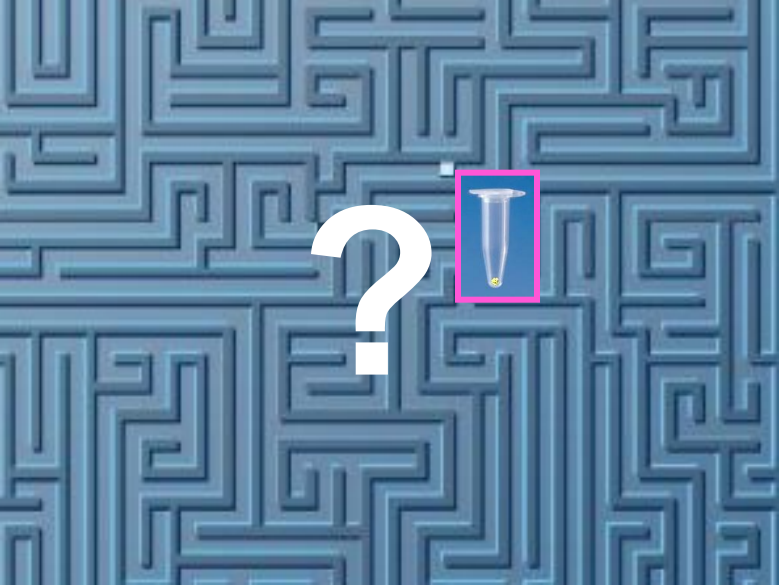


From the surgical room to the pathology laboratory and the biobank: How to get an « easy road » ?

Improving molecular medicine research, « omic » projects, and clinical practice

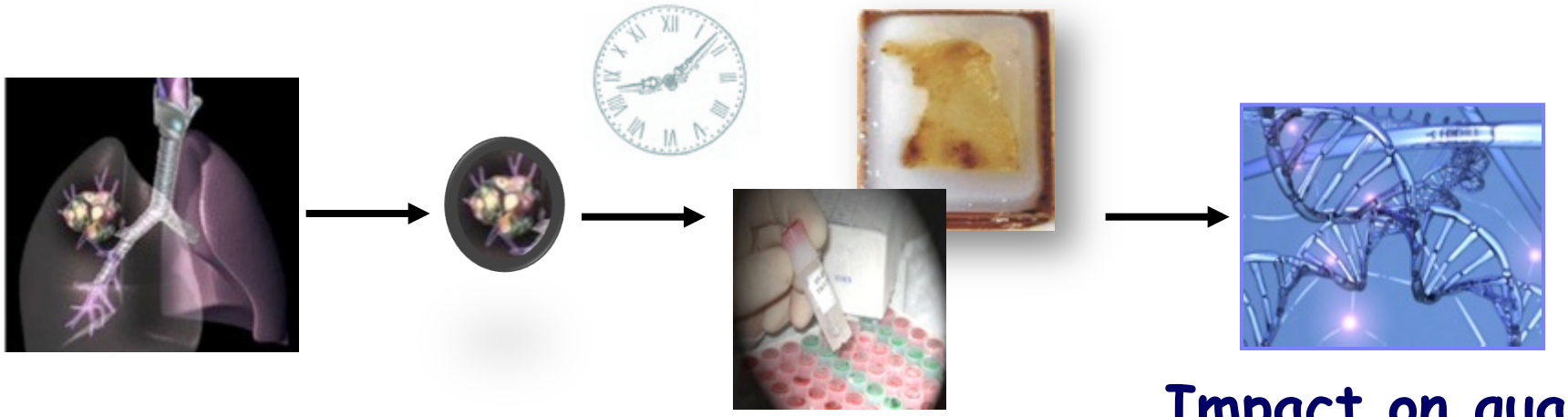
Archive frozen tissues &

Archive paraffin embedded tissues

But….

How to control the

Pre-Analytical Time Intervals (the « PATI ») ?



Impact on quality

Physicians Pathology Laboratory Biobanking

Differences in tissue preservation

Pre-Analytical Time Intervals

Surgery
Warm ischemia

Hospital
Organization
Cold ischemia

Transport to

Pathology department

Fixation

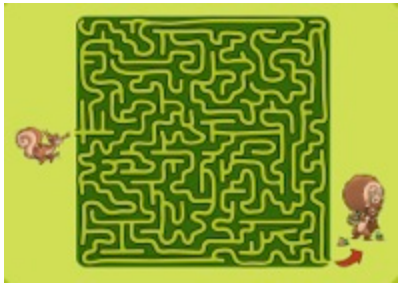
Grossing

Embedding

Archive

Formalin

New fixatives ?



How to avoid a labyrinth ?

Sec-Hrs

Sec-Hrs-Days

Hrs-Days

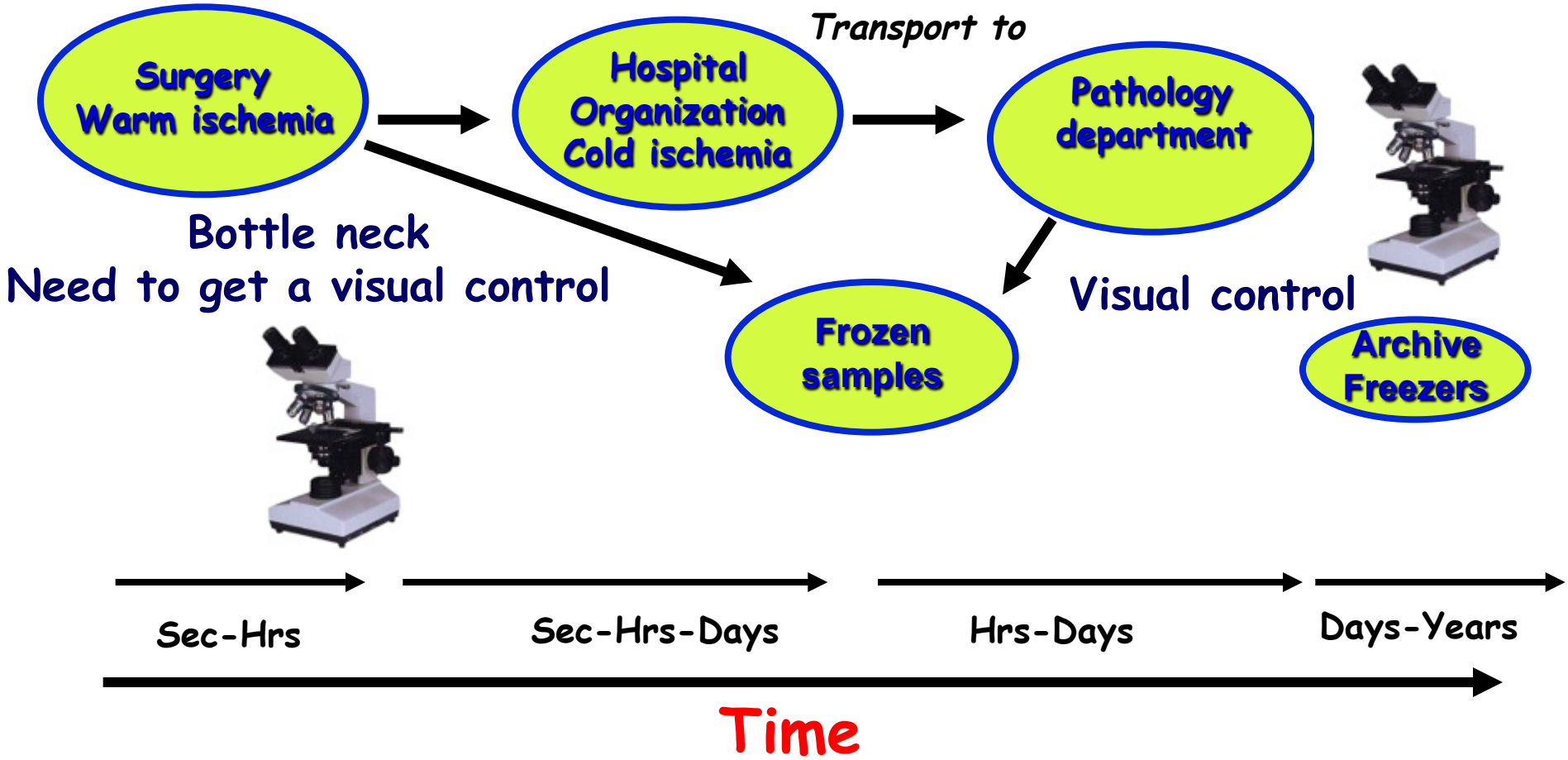
Days-Years

Time

Physicians Pathology Laboratory Biobanking

Differences in tissue preservation

Pre-Analytical Time Intervals

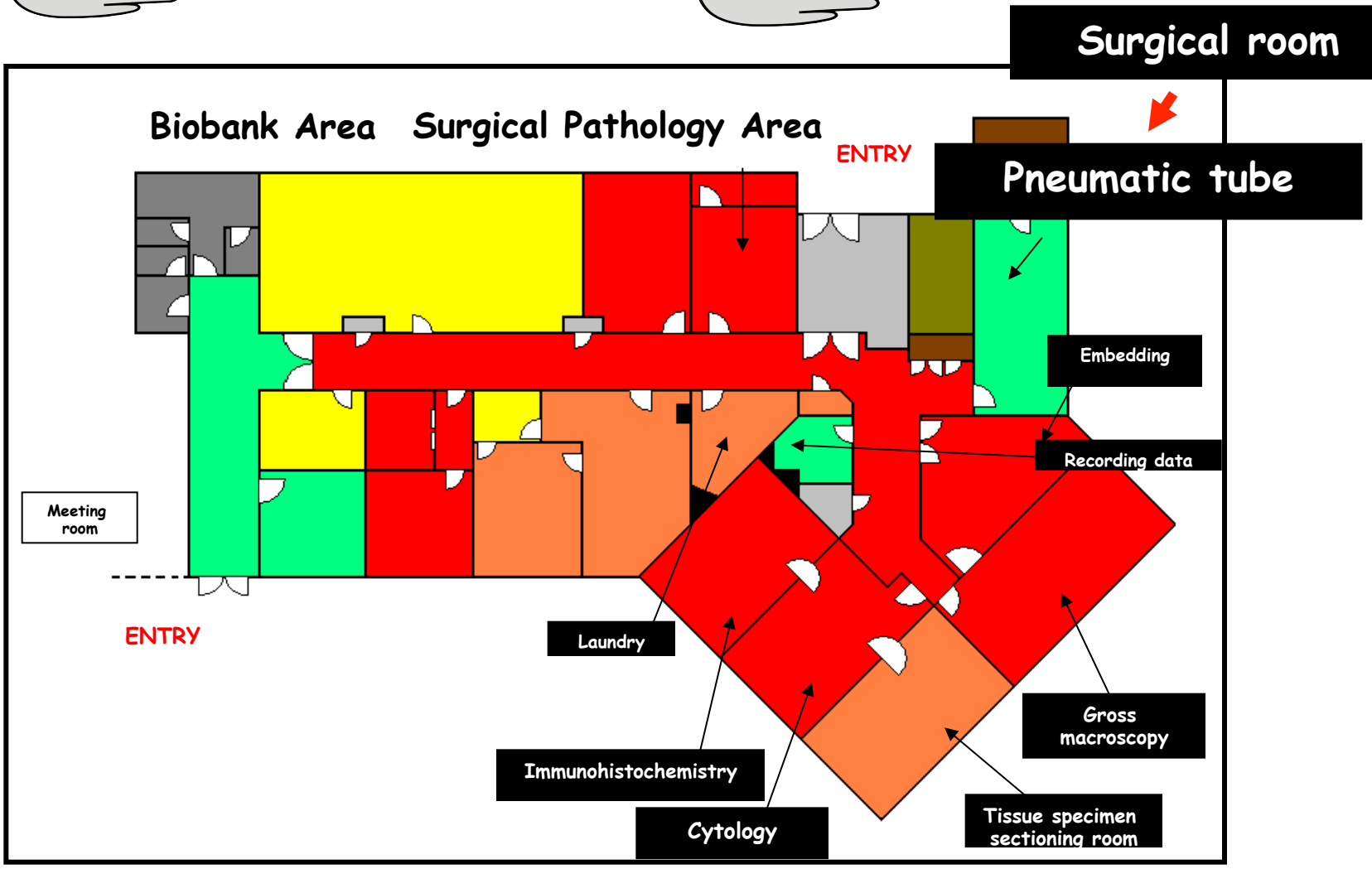


The best and simple system: A pneumatic tube

RFID technology

Cold ischemia time control

Biobank Pathology Laboratory Surgery



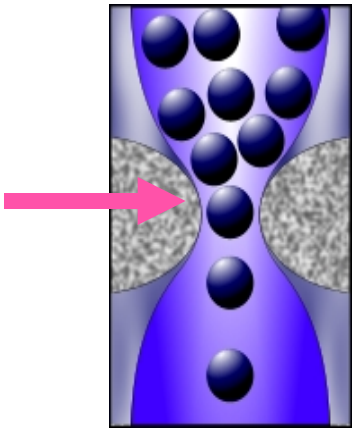
Integrative pathology model

LPCE BIOBANK
Quality Management Tissue

Optimization of the process

www.biobank06.com

Parameters impacting the quality of samples



Bottle necks

- Pre analytical time
- **Frozen procedure versus fixatives**
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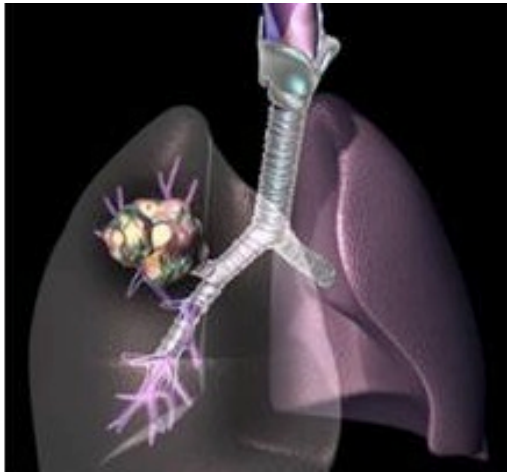
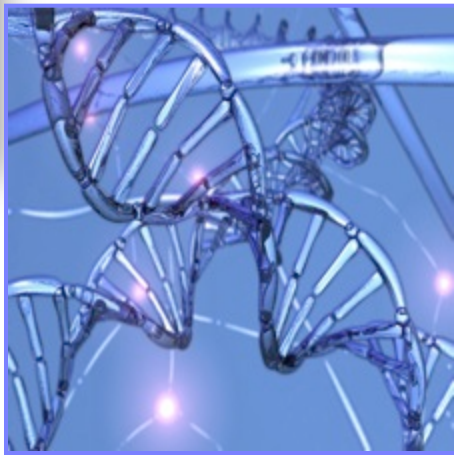


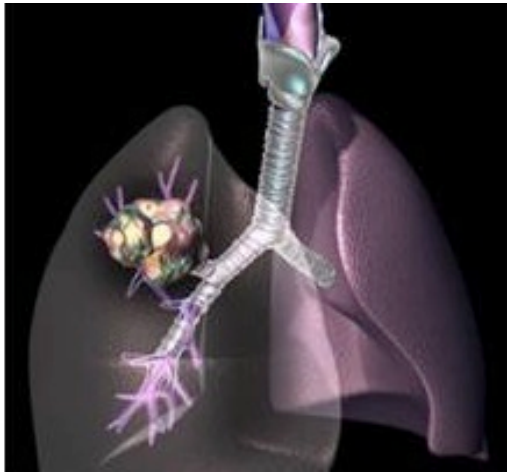
FFPE sample



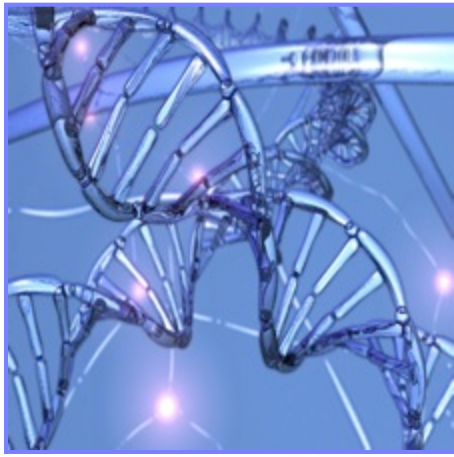
DNA
and miRNA

Frozen sample

RNA and miRNA



FFPE sample



DNA and miRNA

Frozen sample

RNA and miRNA

Frozen sample procedure

Drawbacks

- Different times of cold ischemia
- Morphological control in a mirror sample
- Quite expensive equipment (nitrogen tanks, freezers) and safety environment

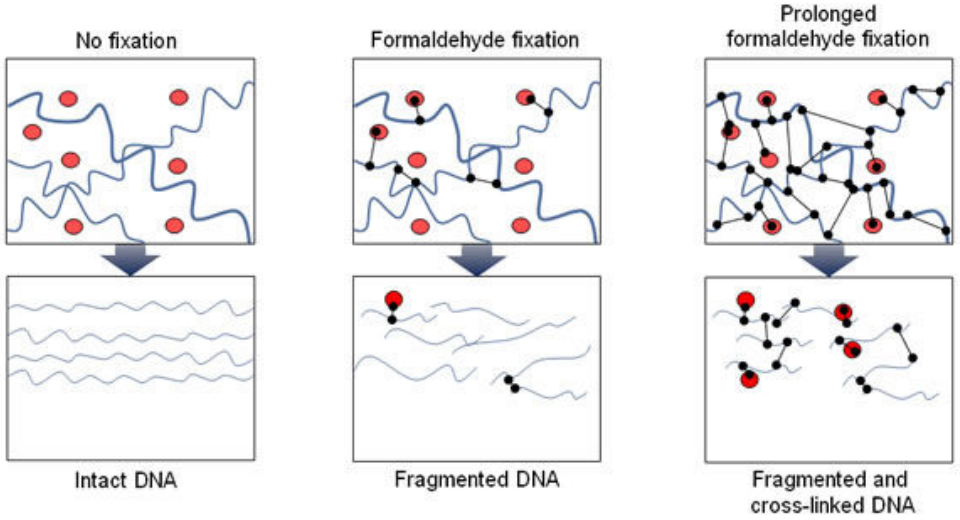
Usefulness & Advantages

- An easy and fast way for DNA & RNA extraction
- DNA & RNA of very good quality

Formalin-fixed paraffin embbeded sample procedure

Drawbacks

- Variability for fixative time period
  - DNA fragmentation
- Quality control is difficult and take quite a long time
- RNA of very low quality



Usefulness & Advantages

- Available in all surgical pathology laboratories
- An easy way for morphological control before DNA extraction

Indicators showing that samples can be of good value for research

- Quality of the samples
  - Quality of DNA
  - Quality of RNA
  - Quantity of nucleic acids
  - Associated mirror sample for morphological control
  - Associated biological fluids
- Quality of associated clinical data
  - General data
  - Specific data for the pathology
  - Efficiency for updating the data (including the follow up of the patients)

DNA extraction

- Depending of sample conditionment:
  - Frozen tissue or
  - FFPE

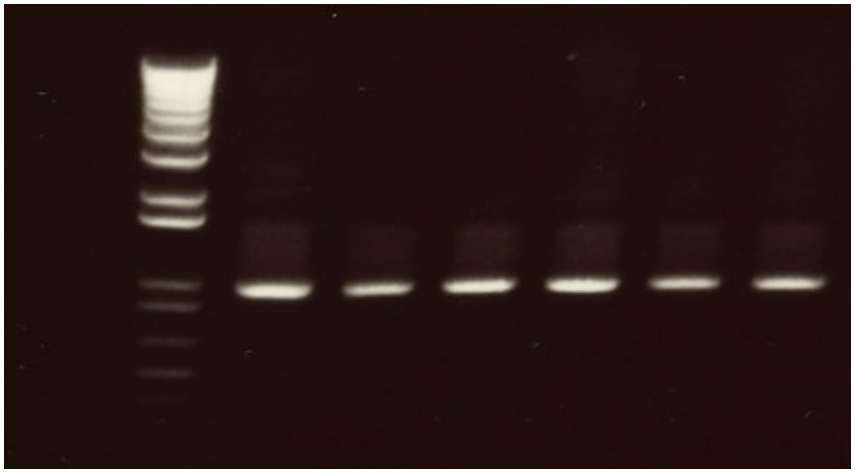
- Hand made method (lysis buffer & protease)
- Kits (ex Qiagen)
- Automated method



→ If tiny material available: Hand made method
If large material available: Automated method

DNA quality

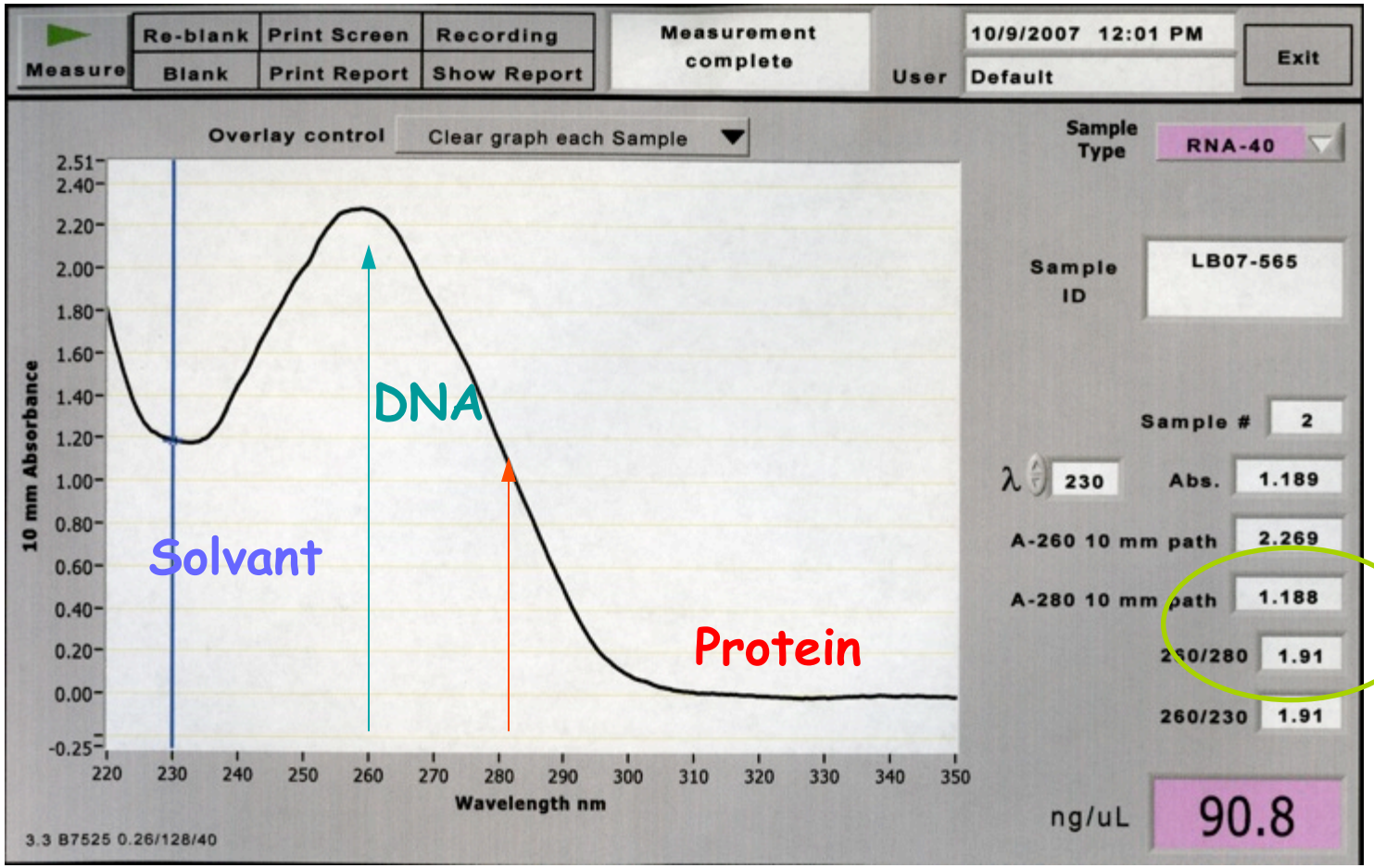
- PCR using a gene control
- Gene control must be selected according to the sample
  - FFPE: <350 pb (S26 gene)
  - Frozen sample: > 350 pb (GAPDH gene)



- DNA gel migration

DNA quantification (spectrophotometer)

- Analysis of 260/280 & 260/230 ratios
  - Potential proteins and/or solvants contamination



Indicators showing that samples can be of good value for a research project

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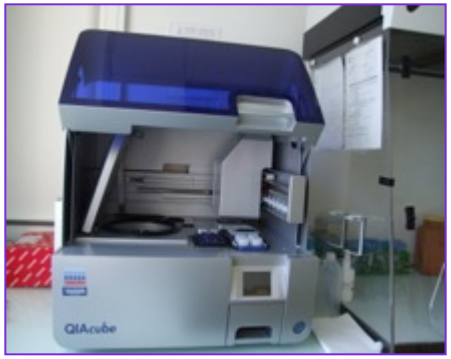
  - Quality of RNA
  - Quantity of nucleic acids
  - Associated mirror sample for morphological control
  - Associated biological fluids
- Quality of associated clinical data
  - General data
  - Specific data for the pathology
  - Efficiency for updating the data (including the follow up of the patients)

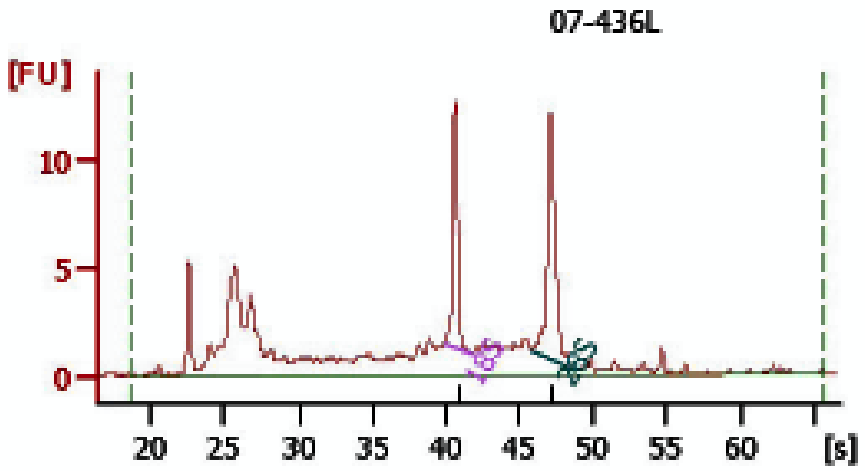
RNA extraction

- Quality of sample
- **Frozen tissue**
- Hand made (Trizol)
- Different kits (ex Qiagen)
- Automated method




→ If tiny material available: Hand made method
If large material available: Automated method

RNA quality & quantity
(Bioanalyser Agilent)



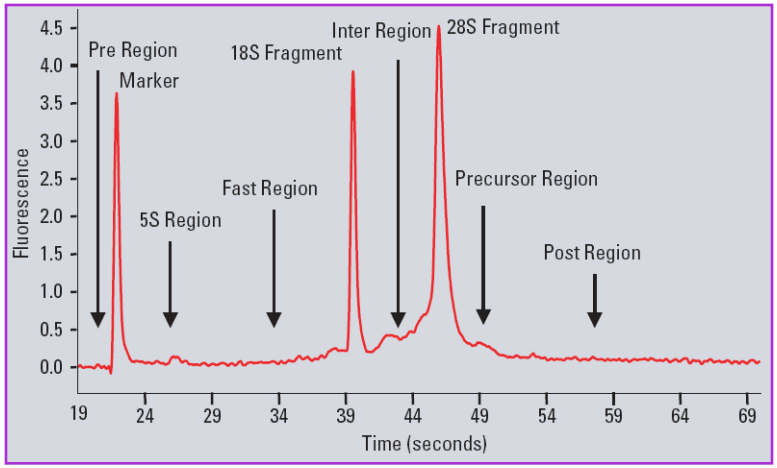
Overall Results for sample 6 : **07-436L**

RNA Area:	117.4
RNA Concentration:	112 ng/µl
rRNA Ratio [28s / 18s]:	1.5
RNA Integrity Number (RIN):	7.3 (B.02.03)
Result Flagging Color:	
Result Flagging Label:	RIN: 7.30

Fragment table for sample 6 : **07-436L**

Name	Start Time [s]	End Time [s]	Area	% of total Area
18S	39.95	41.71	10.4	8.9
28S	45.76	48.72	15.8	13.4

- RNA Integrity number (RIN) ≥ 7



Storage of nucleic acid collections

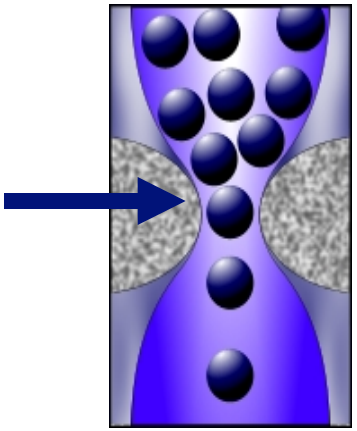
LPCE BIOBANK
Quality Management Tissue

- -80°C & -150°C freezers

Frozen samples

Tumoral tissue	Matched healthy tissue	THYROID / LUNG / HEAD & NECK / SKIN
1R mg	1R mg	
1R mg	1R mg	N° Biobank LB11 -
2R mg	2R mg	N° Pathology Lab LH11 -
3R mg	3R mg	Name :
4R mg	4R mg	Surname :
RFID : mg	RFID : mg	Date :
		Artery clamping : min Cold ischemia : min
Technician name :		Surgical Pathologist name:

Parameters impacting the quality of samples



Bottle necks

- Pre analytical time
- Frozen procedure versus fixatives
- **Sample size**
- Percentage of tumor cells
- Area of necrosis
- Matched healthy sample available

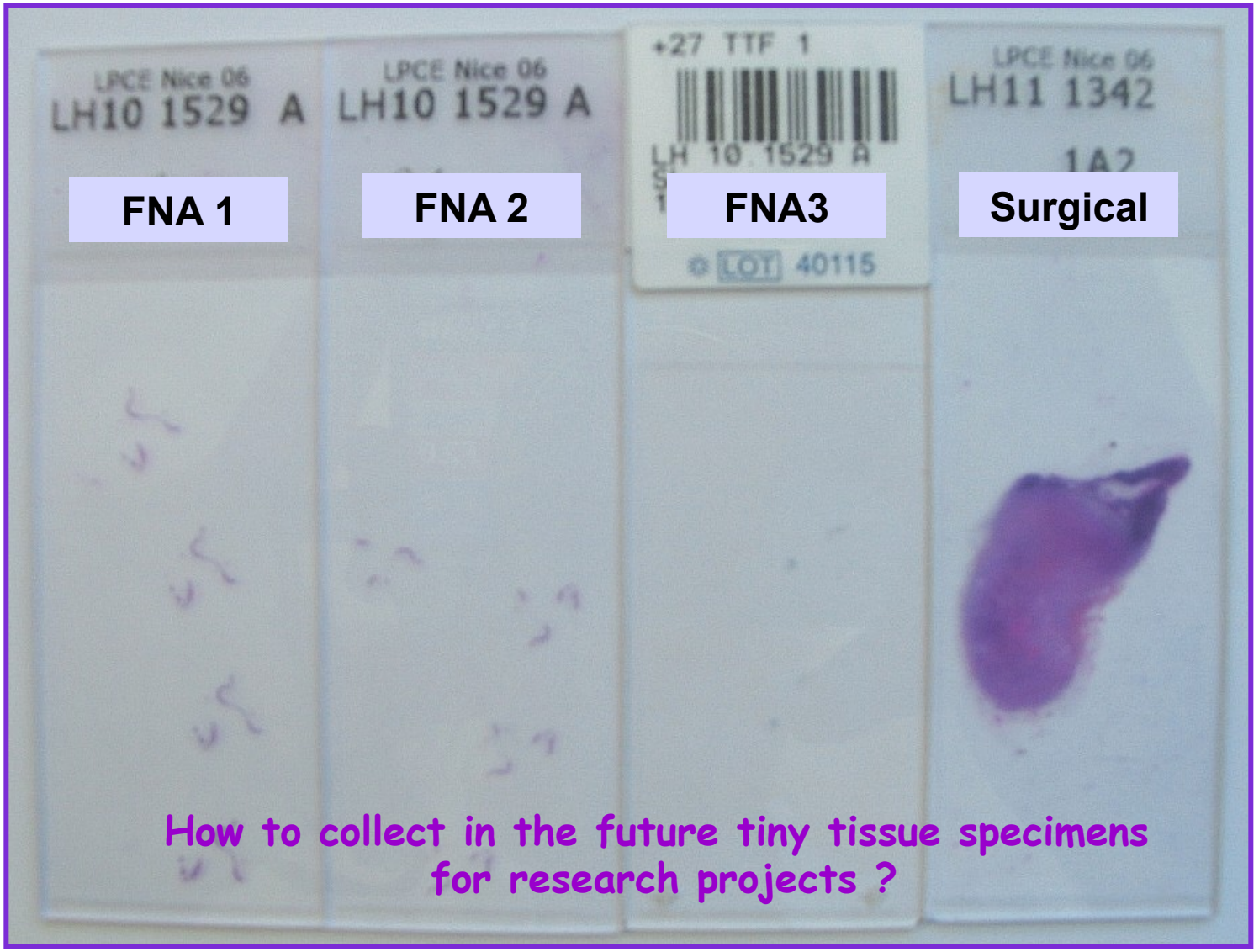
Tissue sampling
(& other biospecimen sampling)
« Time is moving »

Tissue sample available for biobanking will become **more and more smaller** in the futur

Fine needle aspiration

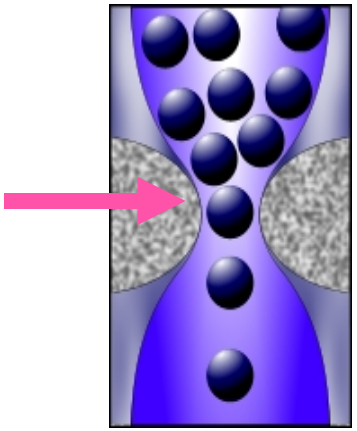
Transbronchial biopsie

Etc., Etc.



Large variabilty of the size (and wheight) of the different FFPE and frozen samples available for biobanking and research

Parameters impacting the quality of samples



Bottle necks

- Pre analytical time
- Frozen procedure versus fixatives
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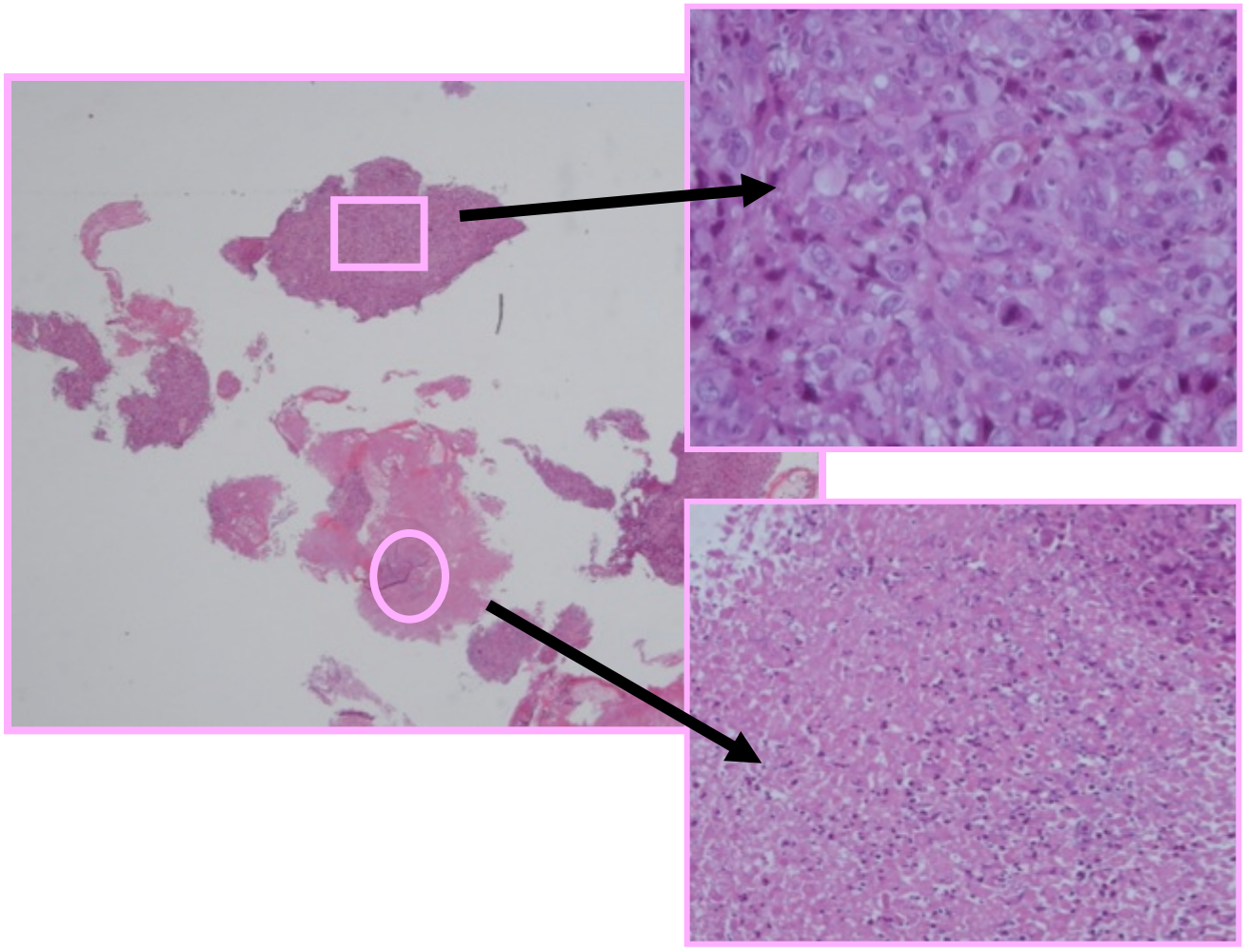
- **Percentage of tumor cells**
- Area of necrosis
- Matched healthy sample

Variability of the percentage of tumor cells

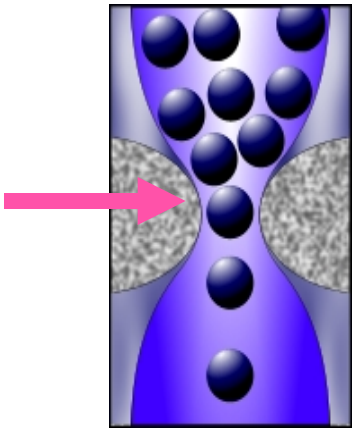
According to the tumor
According to the tumor area



100%
of tumor cells

5 %
of tumor cells

Parameters impacting the quality of samples



Bottle necks

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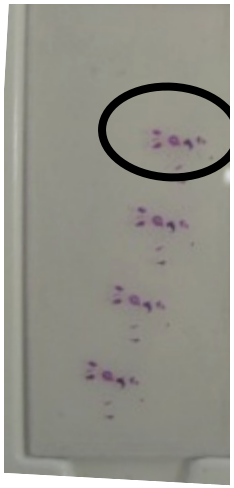
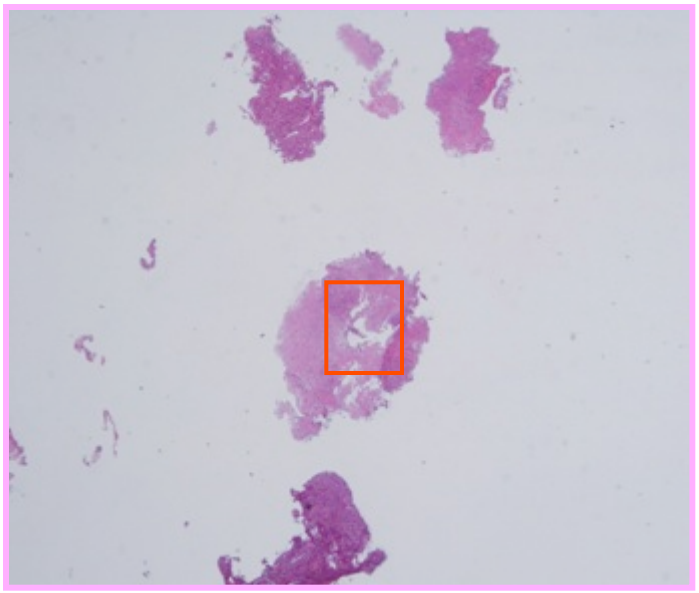
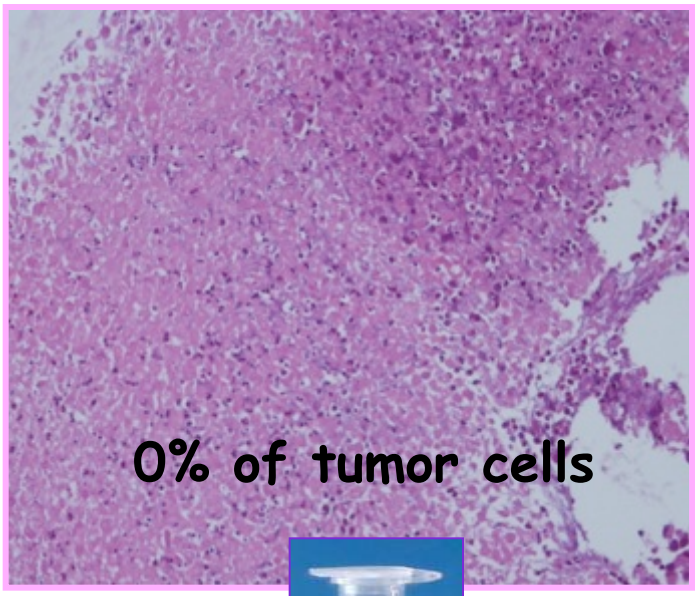
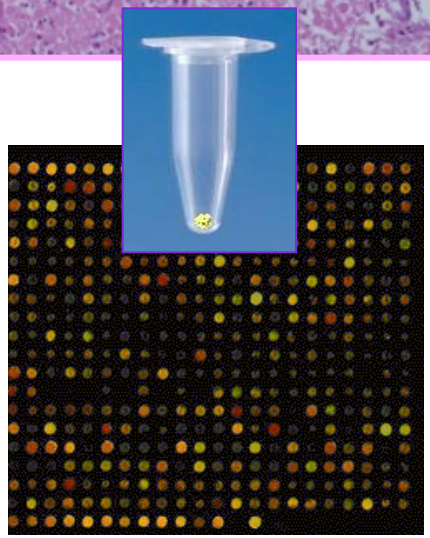
Large necrosis



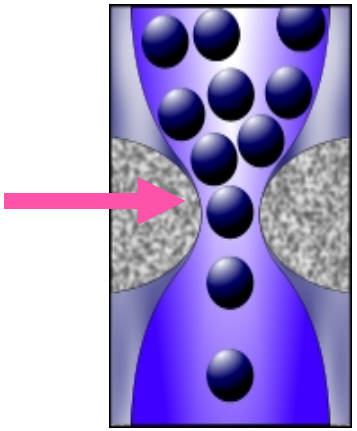




Lung specimen



Parameters impacting the quality of samples



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Biobank
Initial check list
(available for 6877 patients)

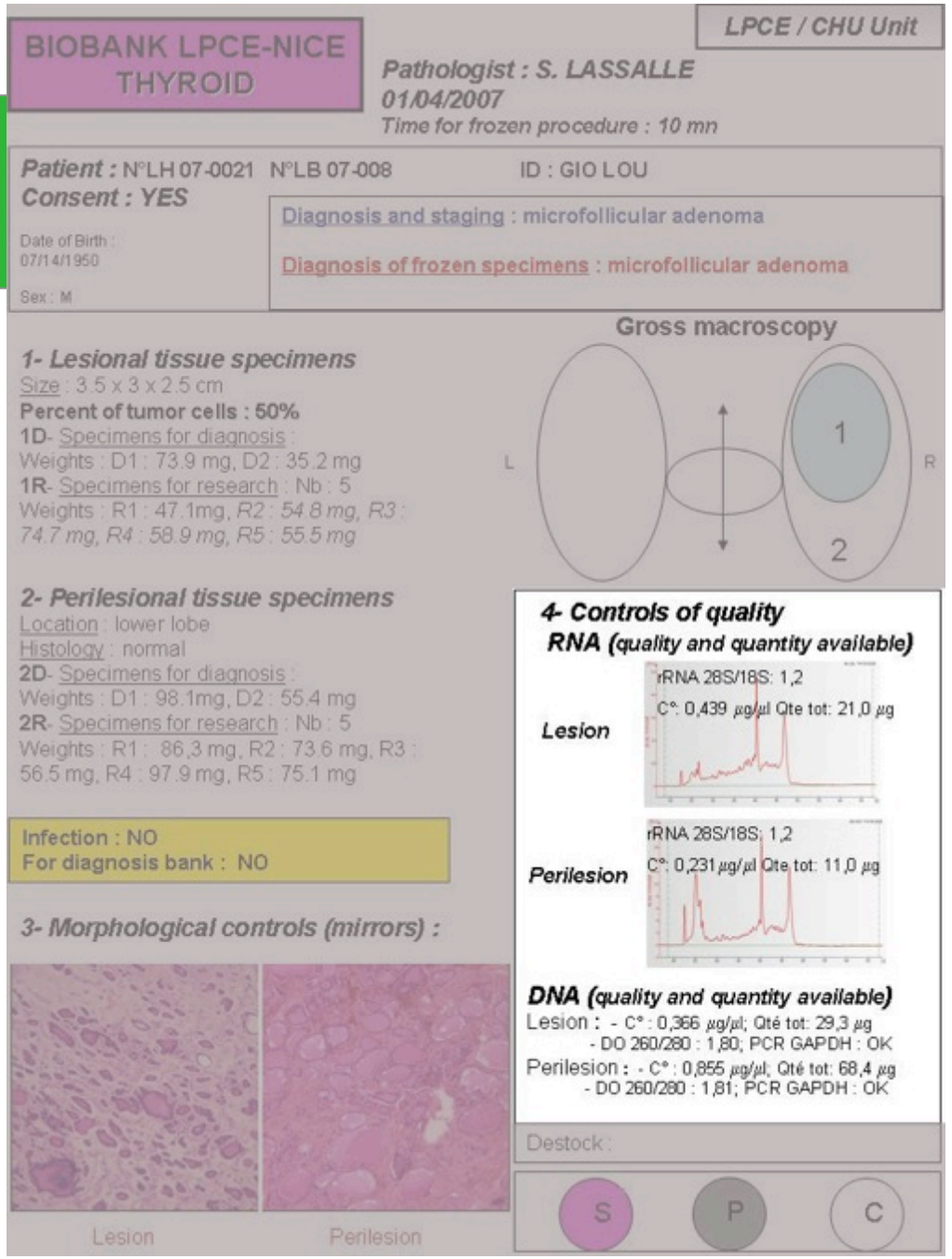
ID
Consent

Sample weights
Morphological control

DNA & RNA quality

Associated fluids

LPCE BIOBANK
Quality Management Tissue



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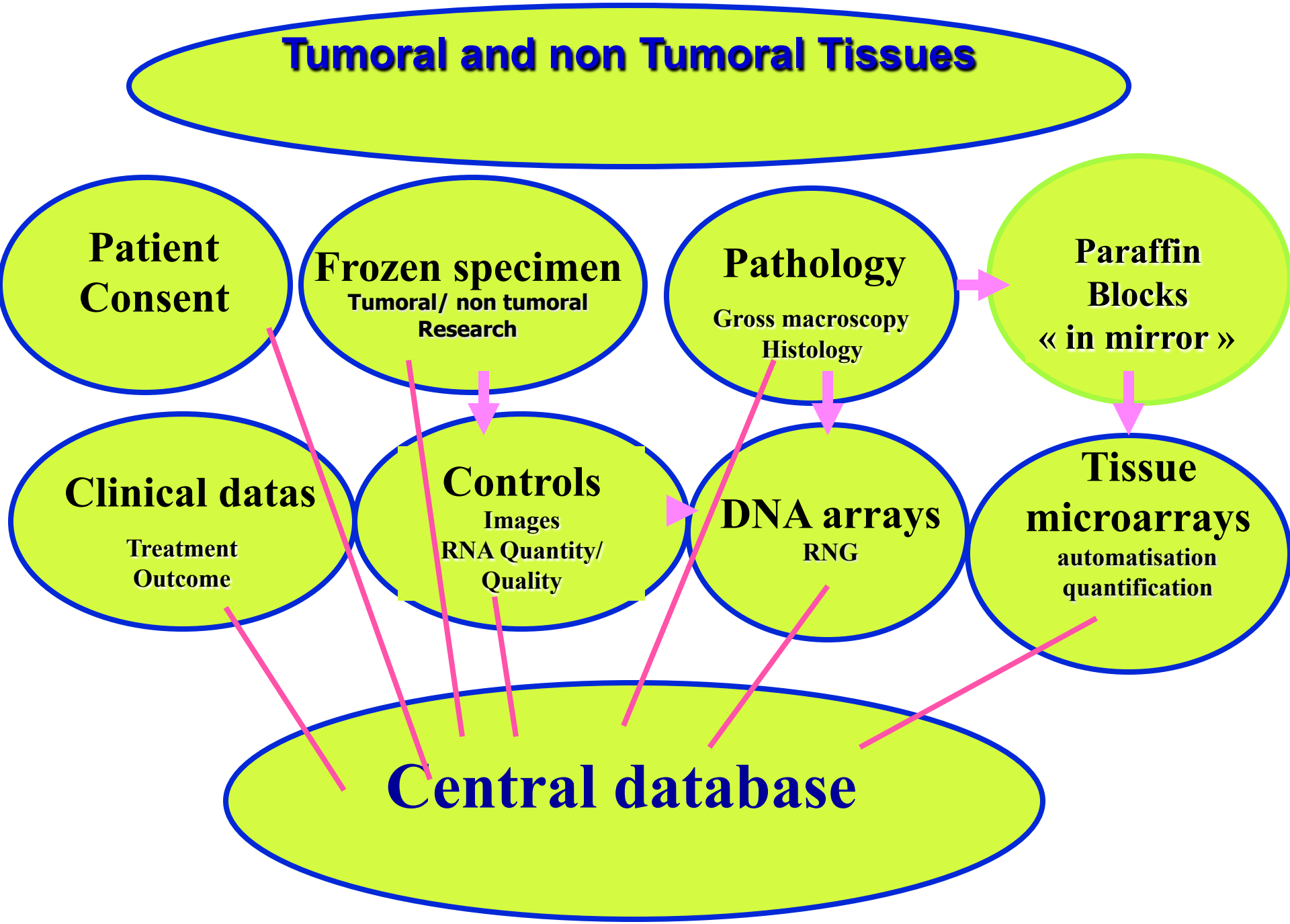
Tumoral and non Tumoral Tissues
Patient Consent
Frozen specimen
Tumoral/ non tumoral
Research
Pathology
Gross macroscopy
Histology
Paraffin Blocks
« in mirror »
Clinical datas
Treatment
Outcome
Controls
Images
RNA Quantity/
Quality
DNA arrays
RNG
Tissue microarrays
automatisation
quantification
Central database

How to define a « good » biobank ?

- Indicators showing that samples can be of good value for a research project
- Indicators of good research productivity
- Other indicators of strong interest

Indicators of good research productivity

- Number of publications
  - Biobank staff are authors
  - Biobank staff are contributors
  - Biobank staff are mentioned in the acknowledgment section or the biobank is cited in the article
- Impact factor of the journal
  - Cumulative impact factor by year
  - Cumulative impact factor by year and by collection
- Grants
  - Obtained by the users of the biobank
  - Obtained to support the biobank
- Patents
  - Based on research supported by the biobank
  - Others

How to define a « good » biobank ?

- Indicators showing that samples can be of good value for a research project
- Indicators of good research productivity
- Other indicators of strong interest

Other indicators of strong interest

- Ethical standards
- Certification and accreditation
- QC/QA processes in place within the resource
- Training/competence of biobank staff
- Educational training program (Academic program)
- Official recognition from Regional/National/ International Health Institutions
- Other important indicators of biobank efficiency

Other indicators of strong interest

- Ethical standards
- **Certification and accreditation**
- QC/QA processes in place within the resource
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- Official recognition from Regional/National/ International Health Institutions
- Other important indicators of biobank efficiency

Certification
NF S96-900 & ISO 9001

Accreditation
NF ISO 15189 &NF 17025

ISO 15189 is the international standard for medical laboratories (ISO 15189 Medical laboratories - **Particular requirements for quality and competence**).

ISO 17025 is the general standard for testing and calibration laboratories (ISO 17025 General **requirements for the competence of testing and calibration laboratories**).

Other indicators of strong interest

- Ethical standards
- Certification and accreditation
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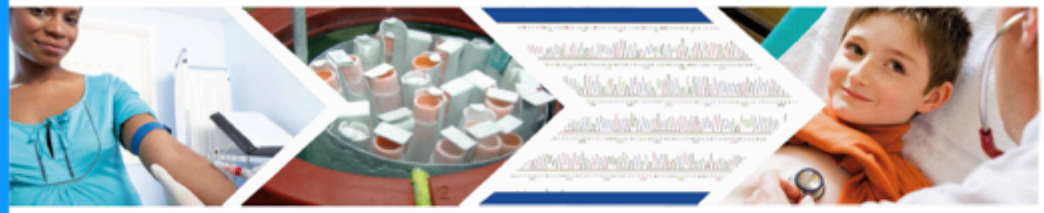


MANAGEMENT OF BIOLOGICAL RESOURCE CENTERS

BIOBANKS AND BIOSPECIMEN SCIENCES

MASTER LEVEL

How to get a senior manager for biobanking !

9 months hands on

Become a senior manager in a cross-disciplinary and transversal emerging international field

Be a part of public health and personalized medicine issues

Evolve in industrial, academic or hospital environments

in partnership with the biobank LPCE BIOBANK

Université Catholique de Lyon — Membre de Université de Lyon

Université Nice Sophia Antipolis

A team at your disposal

Isabelle HARDY
director of ESTBB
(Université Catholique de Lyon)

Paul HOFMAN
responsible of the Master
(Université de Nice Sophia Antipolis)

Emmanuelle GORMALLY
course manager
(Université Catholique de Lyon)

OBJECTIVES AND SKILLS

Scientific and technical coordination of BRC*

Ensure biospecimen security during storage and transport
Coordinate biospecimen flow
Annotate biospecimens
Process and analyse biospecimens

Ethic and legislation

Know the deontology and the rules that apply to biospecimens
Apply national and international BRC legislation

Technological transfer and innovation

Set up technological platforms
Monitor technological development
Harmonise biospecimen collection

Information management - Communication

Participate in the development and manage a database
Ensure biospecimen traceability
Make available collections
Advise collectors and users
Communicate on the BRC activities
Participate in BRC international networking

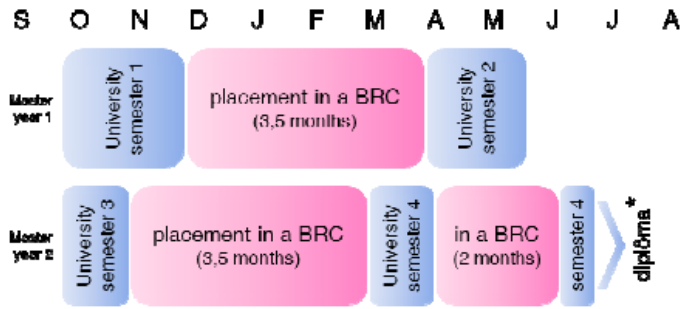
Management

Coordinate a team of laboratory assistants and bio-informaticians
Develop quality assurance and control
Develop and coordinate scientific and technological projects

JOB TITLES

Responsible for a BRC
In charge of platform development in a BRC (transport, transformation, storage, analyses, ...)
Responsible for sample annotations and databases
Adviser for collectors and users
In charge of monitoring technological, legislation, ethical, ..., development
Responsible of quality assurance and control

> 9 months hands on in a BRC over 2 years



** Master of the University of Nice Sophia-Antipolis (France)*

CURRICULUM

> Semesters 1 & 2 (Master year 1 level)

The different biospecimens and their analyses
Sampling and biospecimen conservation methods
Databases and data management for BRC
Quality applied to BRC
Insertion of BRC in the scientific community
Methodological tools : French/English languages, project management, inter-cultural communication

> Semesters 3 & 4 (Master year 2 level)

Clinical research and epidemiological methods
Management
Legislation of BRC
Bio-ethics of BRC
Insertion of BRC in the scientific community
Methodological tools : French/English languages, intercultural communication, career development

TEACHING METHODS

Lectures and laboratory classes
9 months of experience in a BRC in France or abroad (placement or apprenticeship)
Teaching seminars in French and English by world recognized experts
Project learning by transversal case studies
E-learning, BRC visits

Other indicators of strong interest

- Ethical standards
- Certification and accreditation
- QC/QA processes in place within the resource
- Training/competence of biobank staff
- Educational training program
- Official recognition from Regional/National/ International Health Institutions
- **Other important indicators of biobank efficiency**

Made by CHU de Nice

BIOBANK | LPCE
Quality Management Tissue

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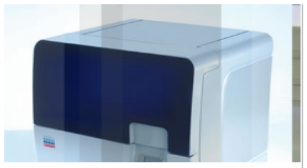
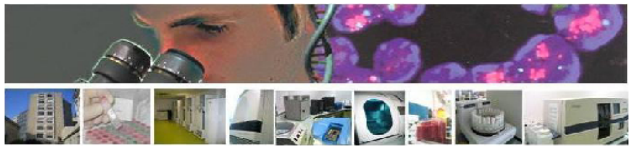


Biobank

- Home
- BioBank
- Valorization
- News

Research

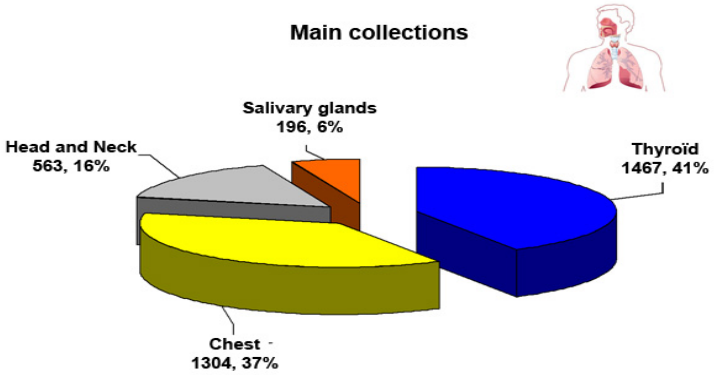


The biobank of the University of Nice Sophia Antipolis (Pasteur Hospital and Antoine Lacassagne Center for Clinical and Cancer Research) has been open on September 2004.

The Nice Biobank is located in the Department of Biopathology [laboratory of clinical and experimental pathology "LPCE" of the Nice Hospital (Pasteur Hospital), France. Since 2004, different non tumoral and tumoral targeted collections of various biological samples are systematically frozen [lung pathology, thyroid pathology, head and neck pathology, infectious pathology, breast pathology and gastro-intestinal pathology]. Since 2006, plasma, sera, nucleic acids and primary cultures are available in association with tissue specimens of the same cohort of patients.

Pr. Paul HOFMAN

« Marketing efficiency »



Type of pathology, nomber of patients, distribution

The Nice Biobank is certified "CRB" by INSERM since 2007 and by IBiSA since 2009. The human Biobank is certified (NF S 96-900) since the second march 2010.

Inserm — Institut national de la santé et de la recherche médicale
IBiSA — Infrastructures Biologie Santé et Agronomie
afaq NF S 96-900 Centre de ressource biologique — AFNOR CERTIFICATION
BBMRI — Biobanking and Biomolecular Resources Research Infrastructure
European, Middle Eastern & African Society for Biopreservation & Biobanking

http://www.biobank06.com

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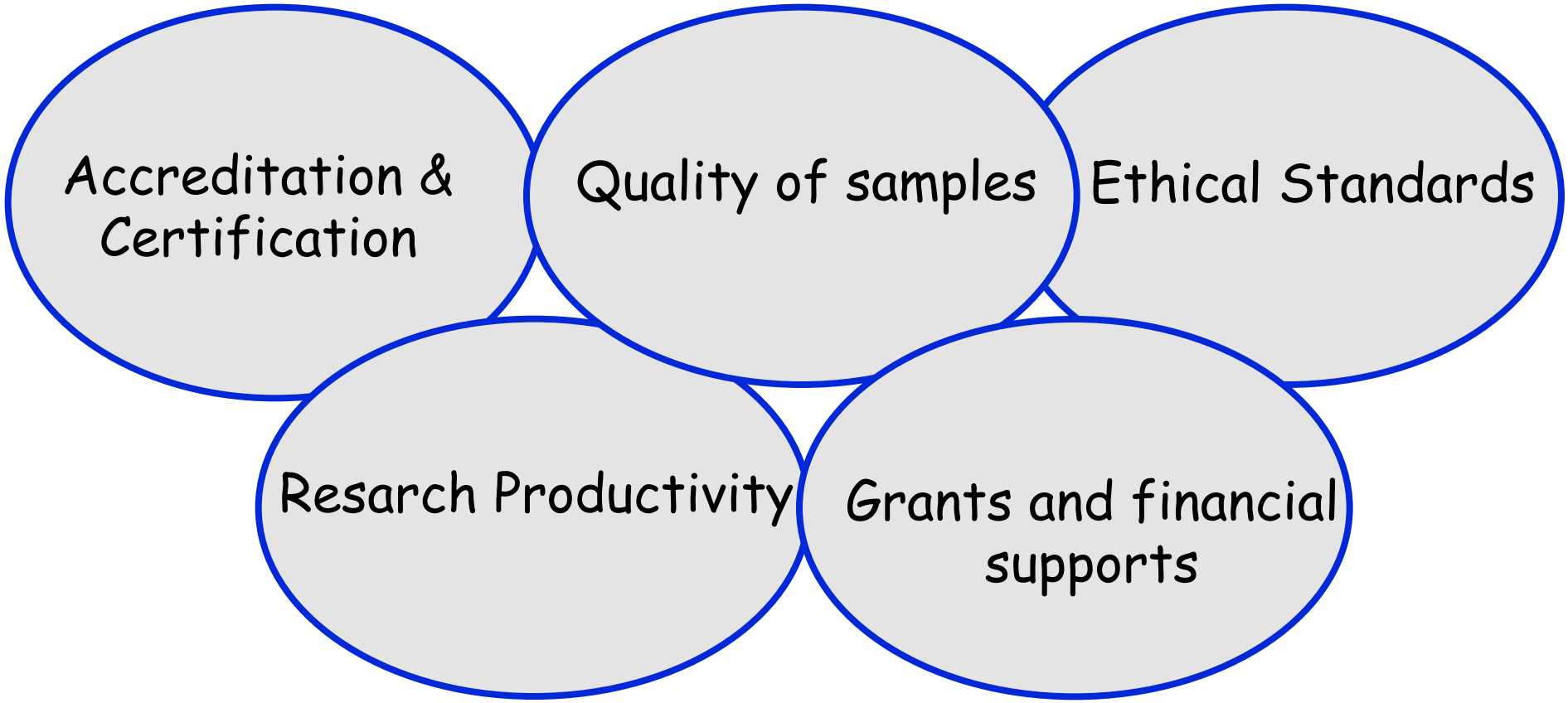
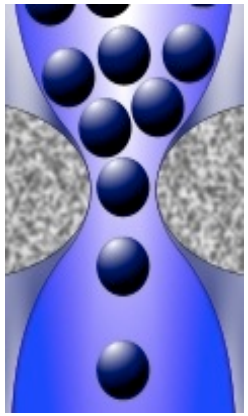
Criteria to get a high standing biobank

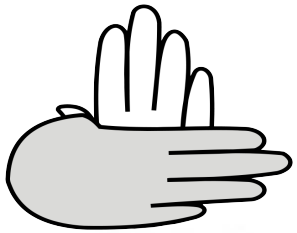


Toward a high Bioresource Research Impact factor

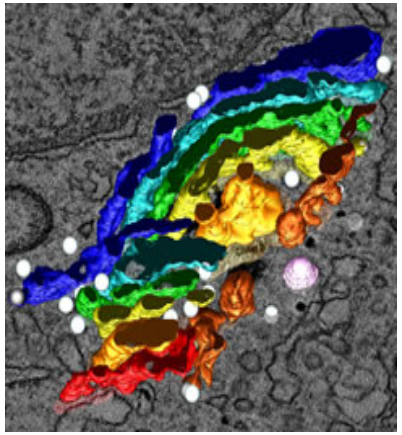
« The main bottle neck » ?



Biobanker



Surgical Pathologist



LPCE BIOBANK

Quality Management Tissue

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Biobank06 Team