New research challenges: biological samples of human origin

Pulmonary Biobank Consortium

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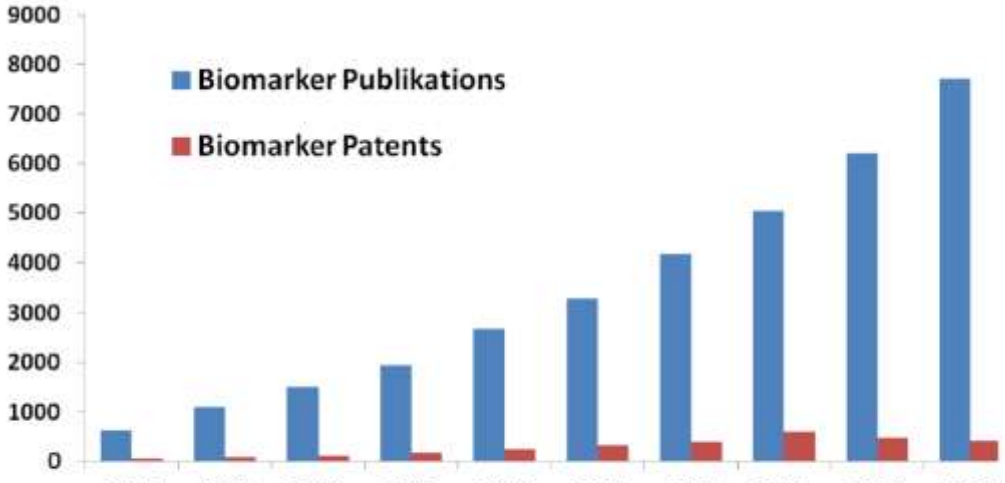
Introduction: Biomarkers

Scientific literature indicates that many studies report the discovery of different potential biomarkers.

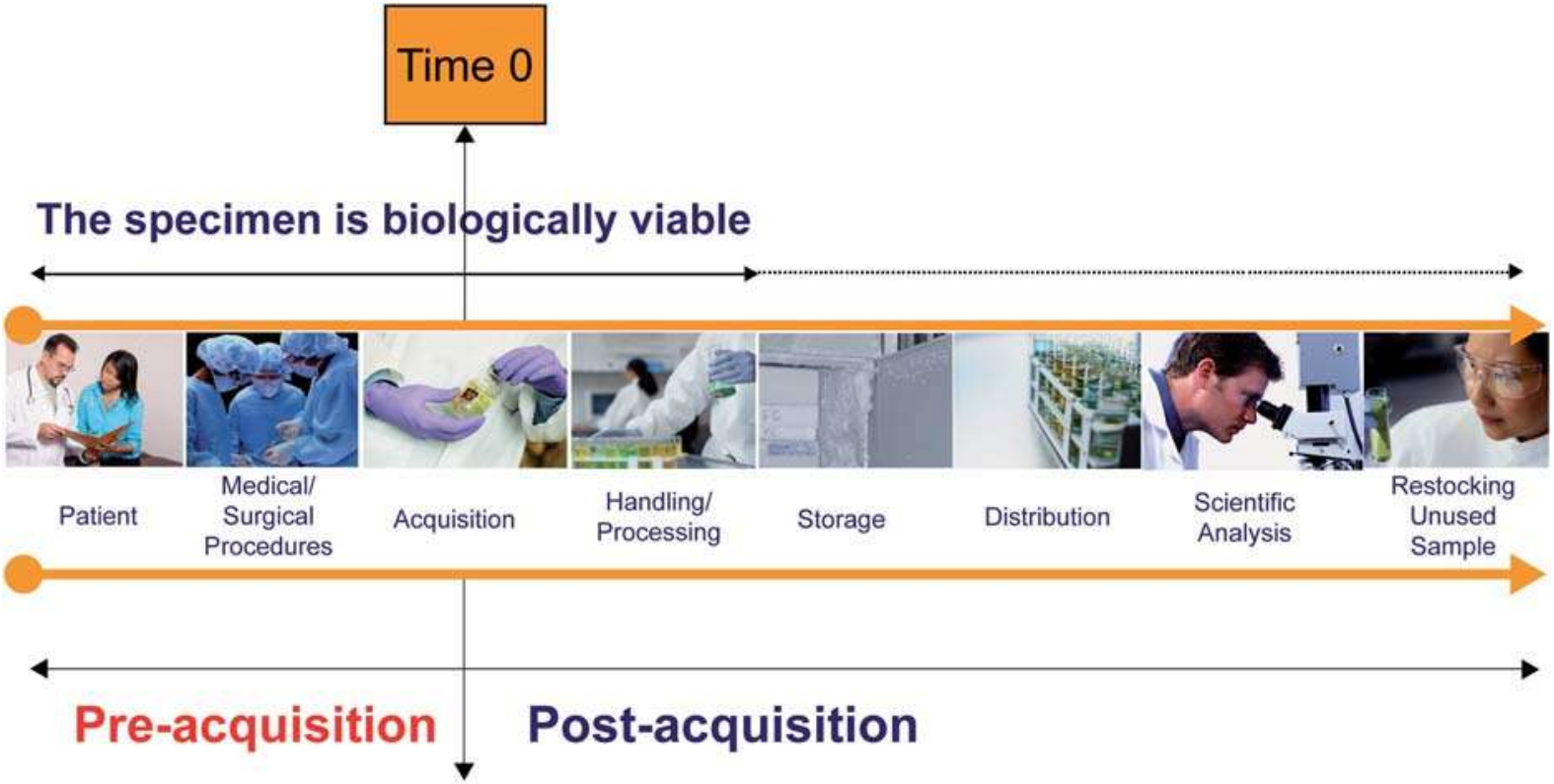


Year	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Biomarkers Publikation	625	1087	1478	1920	2661	3270	4168	5033	6208	7720
Biomarker Patents	50	74	95	180	238	320	396	593	471	407

But most of them can not be applied to clinical practice because they do not meet the criteria of high sensitivity and specificity (preanalytical factors)

Drucker and Krapfenbauer: Pitfalls and limitations in translation from biomarker discovery to clinical utility in predictive and personalised medicine. The EPMA Journal 2013 4:7.

Lifecycle of the biospecimen



*Helen M. Moore and **Jim Vaught**. Biospecimen Reporting for Improved Study Quality. Biopreservation and Biobanking 2011 9:1*

Standardisation of language

- MIABIS: Minimum Information About BIobank data Sharing

  BBMRI (Biobanking and Biomolecular Resources Research Infrastructure)

- STRATUM: Strategic Tissue Repository Alliances Through Unified Methods project

  UK Consortia of commercial and academic stakeholders

- SPREC: Standard Preanalytical Coding for Biospecimens: Defining the Sample PREanalytical Code

  International Society for Biological and Environmental Repositories (ISBER)

- BRISQ: Biospecimen reporting for improved study quality.

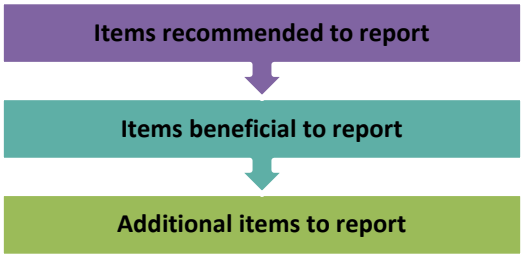
  NCI Biospecimen Research Network

- Biobank Data Standard: Collecting, storing and sharing data describing human biological material for research

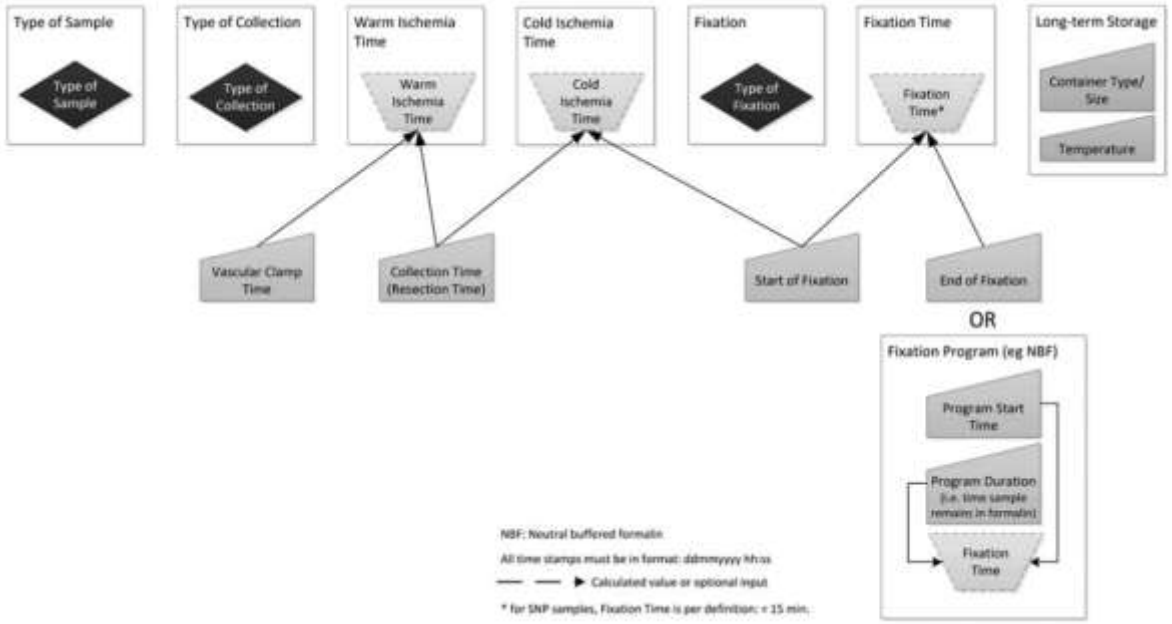
  NCRI Confederation of Cancer Biobanks

BRISQ and SPREC

BRISQ for documenting the elements of a human biological sample, priorizing information into three levels



SPREC identifies the main pre-analytical factors that may have an impact on the integrity of the clinical sample during its collection, processing and preservation.



Lehmann et al. and Fotini Betsou. ***2012*** *10:4*

Impact of *anatomical site* on RNA quality

TABLE 1. AVERAGE RIN VALUES OF SELECTED TISSUE FROM THE ERASMUS MC TISSUE BANK*

Tissue type	*Average RIN*	*Standard deviation*	N	*N with RIN <6.5*	*Tissue type*	*Average RIN*	*Standard deviation*	N	*N with RIN <6.5*
Abdomen	7.80		1		Penis	7.60		1	
Adnex	6.90		1		Peritoneum	7.80	0.42	2	
Adrenal gland	8.03	0.76	3		Prostate	7.95	0.21	2	
Bladder	8.07	0.60	3		Rectum	7.77	1.81	3	1
Breast	8.45	0.07	2		Skin	4.95	3.46	2	1
Cervix	9.10		1		Soft Tissue	8.00	0.42	5	
Colon	7.44	0.80	5		Spleen	5.70		1	1
Esophagus	7.83	1.01	3		Stomach	7.60	1.13	3	1
Ethmoid	8.80		1		Testis	7.80	0.71	2	
Gall bladder	7.10		1		Thorax	7.90		1	
Kidney	8.17	0.25	3		Thymus	8.05	0.78	2	
Larynx	8.77	0.21	3		Thyroid	8.20	0.26	3	
Liver	8.09	0.76	7		Tongue	7.40		1	
Lung	6.99	0.60	7	1	Tonsil	7.03	1.52	3	1
Lymph node	7.75	1.00	6		Tuba	7.75	0.35	2	
Nose	8.30		1		Ureter	7.90		1	
Ovary	5.33	2.78	3	2	Uterus	5.50	4.38	2	1
Pancreas	7.97	0.29	3		Vulva	8.05	0.35	2	
Parotid	8.90		1						

TABLE 2. AVERAGE RIN VALUES OF SELECTED TISSUE FROM THE CANCER INSTITUTE ARCHIVE COLLECTION

Tissue type	*Average RIN*	*Standard deviation*	N
Breast	8.20		1
Colon	8.20	1.27	2
Larynx	8.15	1.48	2
Liver	8.23	0.71	4
Lung	8.50		1
Lymph node	7.63	0.92	15
Mouth	7.70		1
Omentum	6.20		1
Ovary	7.25	0.35	2
Pancreas	8.30		1
Penis	7.40		1
Rectum	7.70	1.13	2
Salivary gland	8.67	0.38	3
Thymus	6.90		1
Thyroid	8.80		1
Tonsil	6.90		1

Marcel Kap. 2014

Anatomical site can influence the RNA quality and integrity due to cellular content

Effect of centre of analysis*

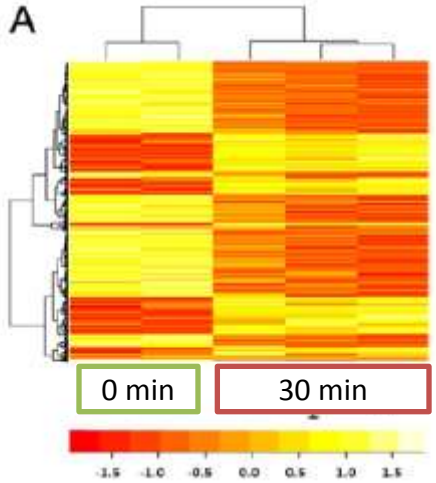
Table 3 RNA integrity and Yield Results for 18 human peripheral tissues compared to brain

Tissue (n)	RIN (±SD)	RIN range (% <6.5)	Yield (ng/mg)	Yield range (ng/mg)
Adrenal (23/24)	7.2 ± 1.8	3.0–9.0 (33)	946.2 ± 668.2	50–2363
Cervix (11/16)	6.4 ± 1.8	2.4–8.3 (50)	156.9 ± 144.0	0–578
Esophagus (18/18)	7.1 ± 2.3	2.4–8.5 (37.5)	455.0 ± 399.4	23–767
Heart (23/26)	7.6 ± 2.0	2.6–9.0 (26.9)	174.9 ± 136.2	1–488
Jejunum (21/21)	6.4 ± 1.5	2.5–8.8 (33)	1010.9 ± 734.2	107–1935
Kidney (26/26)	7.0 ± 1.5	4.6–9.1 (30.8)	868.8 ± 511.5	59–2914
Liver (29/30)	7.2 ± 2.2	1.1–9.4 (23.3)	2288.3 ± 1204.5	17–4701
Lymph node (21/21)	7.6 ± 1.4	3.6–9.2 (14.3)	1709.5 ± 773.0	684–2895
Lung (15/15)	6.5 ± 2.2	1.6–8.9 (33)	410.3 ± 358.6	77–1159
Ovary (15/17)	5.9 ± 6.6	2.4–9.1 (52.9)	546.4 ± 496.4	67–1795
Pancreas (25/26)	6.5 ± 1.6	3.9–9.1 (46.1)	2225.9 ± 2152.2	14–6840
Prostate (15/19)	5.7 ± 1.9	2.2–8.3 (63.1)	251.0 ± 617.3	12–2773
Colon (23/24)	6.7 ± 1.0	4.7–8.3 (37.5)	737.2 ± 422.7	41–1370
Skin (17/22)	6.2 ± 1.8	2.4–8.2 (54.4)	89.6 ± 75.4	0.1–347
Stomach (20/20)	6.0 ± 1.7	2.4–8.0 (45)	1420.4 ± 938.9	9.7–3275
Submandibular (20/21)	7.8 ± 1.4	2.8–9.2 (9.5)	2082.1 ± 1054.5	4 –3498
Testis (16/18)	7.5 ± 2.0	3.0–9.4 (33)	342.2 ± 343.5	25–528
Thyroid (23/25)	7.0 ± 1.5	2.4–8.8 (28)	400.2 ± 277.0	9–803
Brain (401/223)	8.6 + 1.2	2.4–10 (5.4)	379.8 + 200	0–966.8

n number of samples with RIN/Total number of samples, *RIN* RNA integrity number

Douglas G. 2016

Impact of *ischemia time* on RNA quality



Delaying tissue harvest for an average of **30 minutes** from the operating theater had a significant impact on gene expression, with approximately **25% of genes** differing between *immediately placed in RNA Later* and *after 30 minutes of ischemia time*.

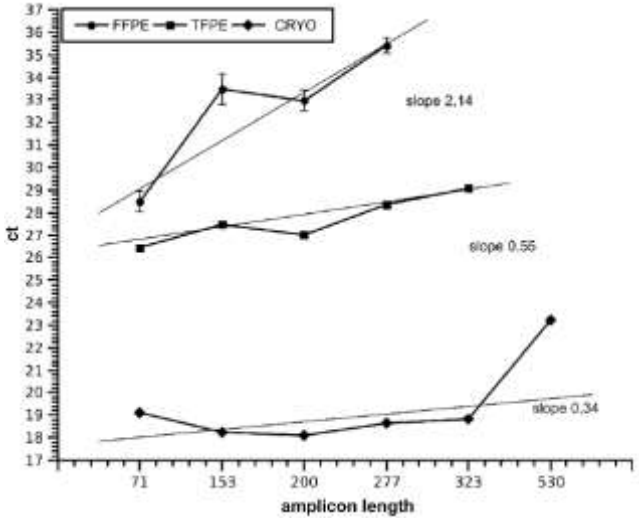
Freidin et al, 2012

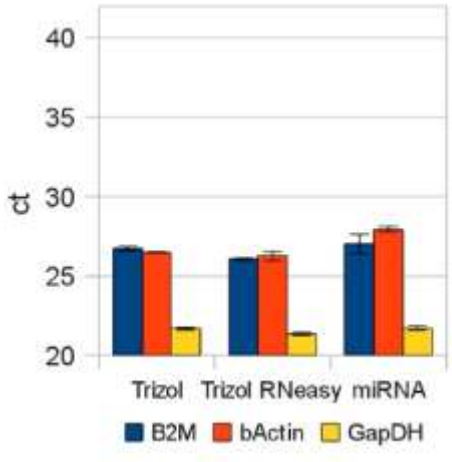
Table 1 Comparison between the cold ischemia times and quality of total RNA in all samples

Samples	Cold ischemia times						*p* value
	Up to 30′			At 45′			
	Intact	Degraded	Partly degraded	Intact	Degraded	Partly degraded	
Thyroid	16 (80 %)	3 (15 %)	1 (5 %)	6 (30 %)	7 (35 %)	7 (35 %)	0.006
Colorectal	11 (55 %)	6 (30 %)	3 (15 %)	4 (20 %)	14 (70 %)	2 (10 %)	0.030
Breast	14 (70 %)	4 (20 %)	2 (10 %)	8 (40 %)	10 (50 %)	2 (10 %)	0.131
Lung	7 (36.9 %)	7 (36.8 %)	5 (26.3 %)	6 (30 %)	9 (45 %)	5 (25 %)	0.919
Stomach	15 (79 %)	4 (21 %)	0 (0 %)	12 (60 %)	7 (35 %)	1 (5 %)	0.384
Total	63 (31.8 %)	24 (12.1 %)	11 (5.6 %)	36 (18.2 %)	47 (23.7 %)	17 (8.6 %)	<0.001

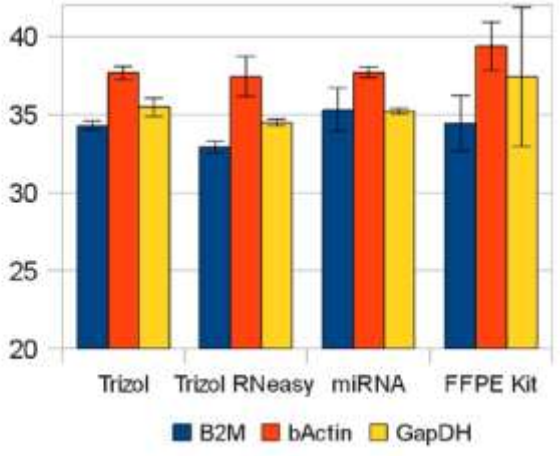
Viana et al. 2013

Impact of different preservation conditions on gene expression





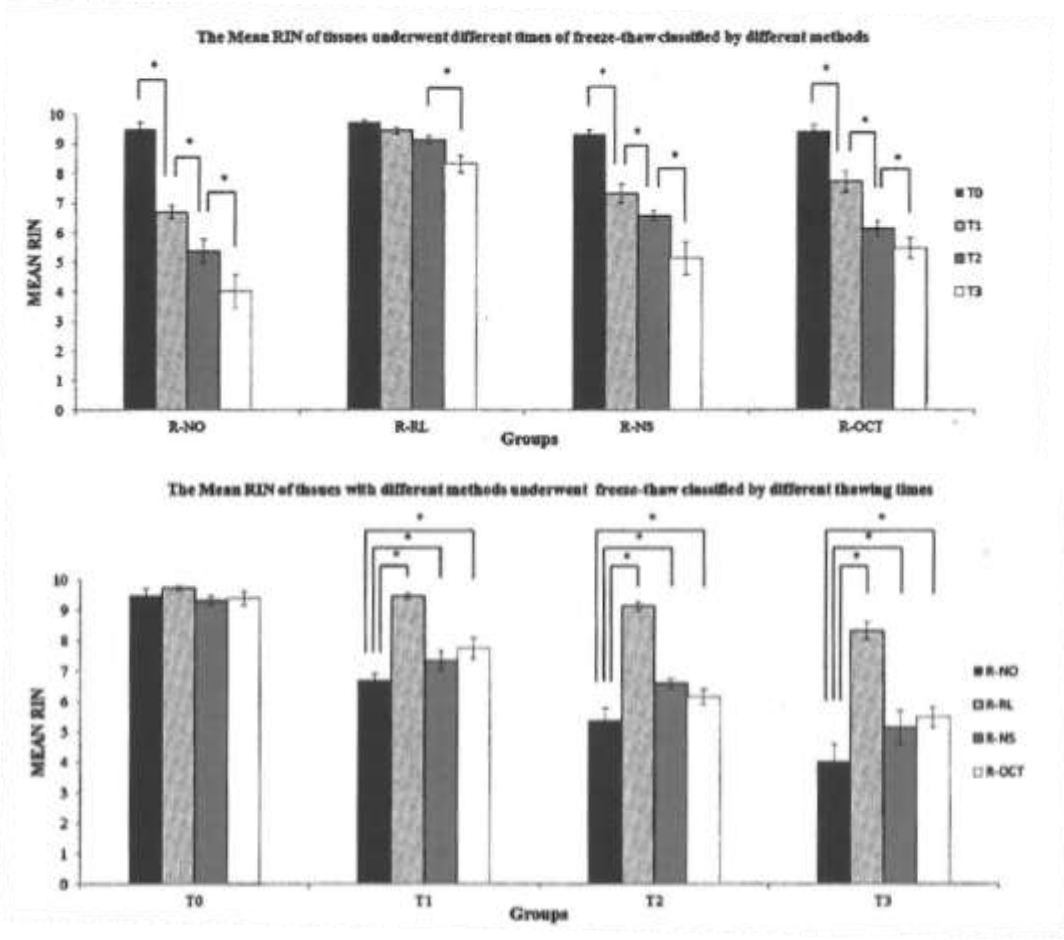
Snap Frozen



FFPE

It was observed a generally lower efficiency of qRT-PCR using cDNA generated from RNA extracted from *fixed* samples versus *snap frozen*

Kashofer et al. 2013



Different preservation conditions lead to differential quality of biospecimens.

Freezing-thaw cycles have a clearly detrimental effect on the sample integrity

Wang et al. 2015

OPTIMARK Project

1. Identify the **most relevant pre-analytical variables** in tissue samples that affect the biomarker validation with potential clinical utility.

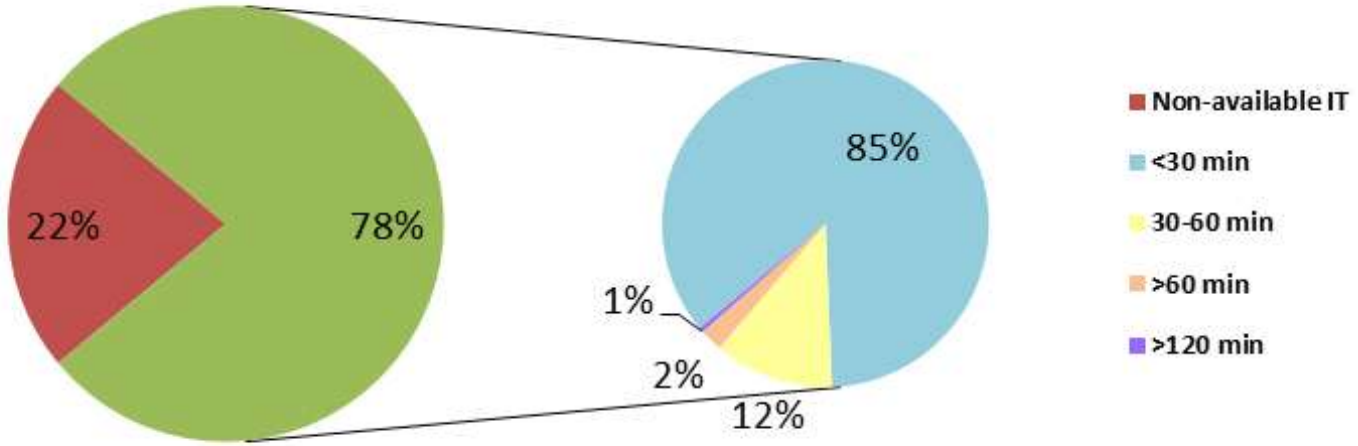
2. Develop and **validate a standardized procedure** to determine the usefulness of the samples for the current analytical techniques under investigation, including samples for which there is no prior control of their pre-analytical factors.

3. To make available to the scientific and biotechnology community **collections of well-characterized** samples, and with control of their pre-analytical variables in order to evaluate the sensitivity of the biomarkers under development to these factors.

4. To determine and **recommend** essential improvements in sample collection in routine clinical practice, when necessary in targeted therapies for the evaluation of biomarkers sensitive to pre-analytical factors.

Ischemia Time analysis

Among others, in PBC, cold ischemia time has been recorded in 78% out of **1.187 registered cases** and 85% of whom is less than 30 minutes.



Available samples

Sample type	Cases	Total samples
Non-tumor lung tissue	1.839	46.107
Tumor lung tissue	259	1.062
Whole blood	976	3.589
Plasma	1.108	8.900
Serum	1.176	8.370
Leucocytes	404	1.121
Urine	390	2.557
DNA	22	62
Fat	29	-
	>2.500	**71.768**

Español | English

CIBER | INTRANET | CONTACTO

ciberes — Plataforma Biobanco Pulmonar

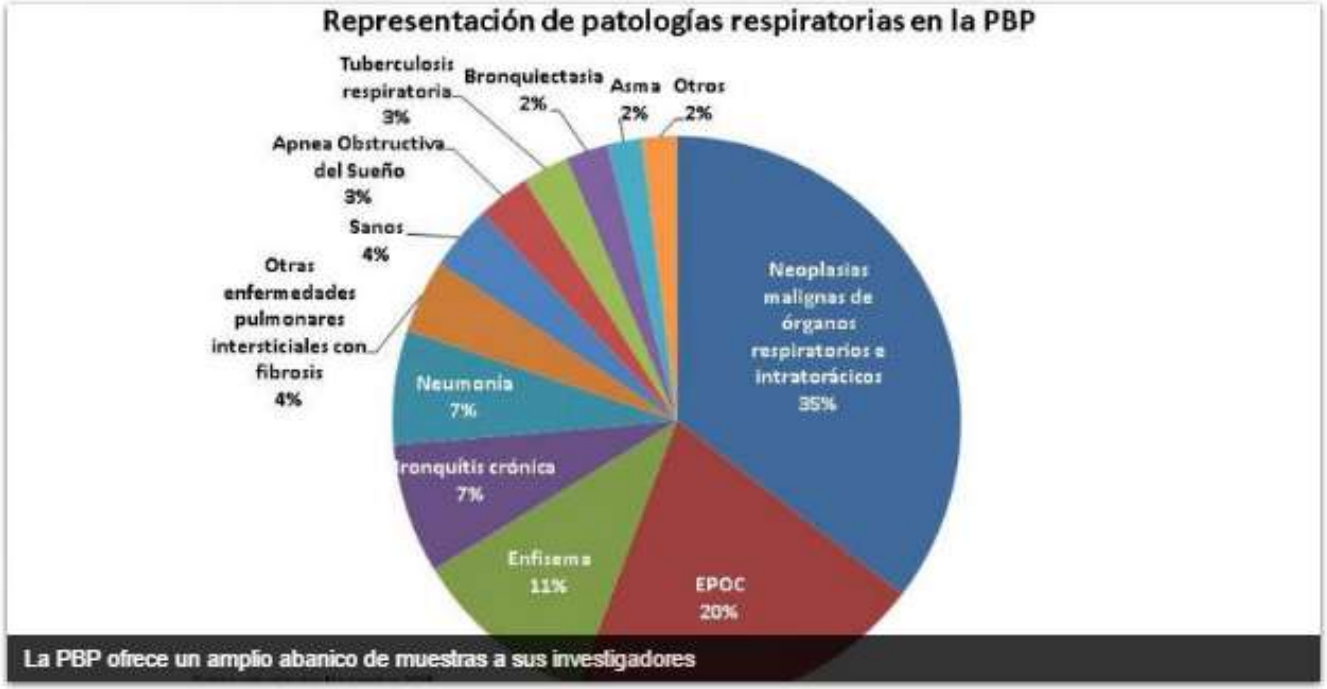
Unión Europea — FONDO EUROPEO DE DESARROLLO REGIONAL — FONDO SOCIAL EUROPEO

PLATAFORMA BIOBANCO PULMONAR | INVESTIGADORES | DONANTES | ACTIVIDAD | NOVEDADES

Bienvenido a la

Plataforma Biobanco Pulmonar (PBP)

Creada en 2008 por el Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES).



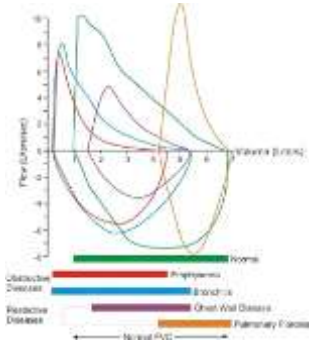
Sample registration system

Clinical information

Relevant respiratory data

homogeneous

systematically



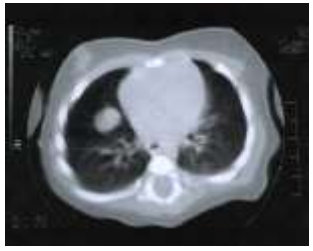
Smoking history

Respiratory function tests

Anthropometric measures

Expositions

Treatments



Hemogram

Clinical diagnosis

surgical indication

CT scan

Extraction

Blood

Plasma

Serum

Pulmonary resection

Lung tissue

Large population cohorts

Pathology	Cohort/Project
Lung cancer	Retrospective and prospective cohort
Obstructive sleep apnea	ISAAC, BioSAHOS
Idiopathic Pulmonary Fibrosis	FPI strategic project
Pulmonary Hypertension	REHAP register
Pulmonary thromboembolism	OSIRIS

- ✓ **Sample processing and storage armonization**
- ✓ **Phenotypic characterization of biospecimens in a integrated database**
- ✓ **Legal cover for future application**


Services available

Supply of:

- **Tissue and haemorerivative samples with strict quality criteria.**
- **Standardised clinical data.**
- **DICOM Images (Computerised Tomography).**

Sample processing (histological, cellular and molecular techniques).

Setting up new collections in multi-centre studies.

Centralized storage of sample collections.

Management of national and international shipments.

Control, monitoring and audits multi-center collections.

Establishing quality management systems.

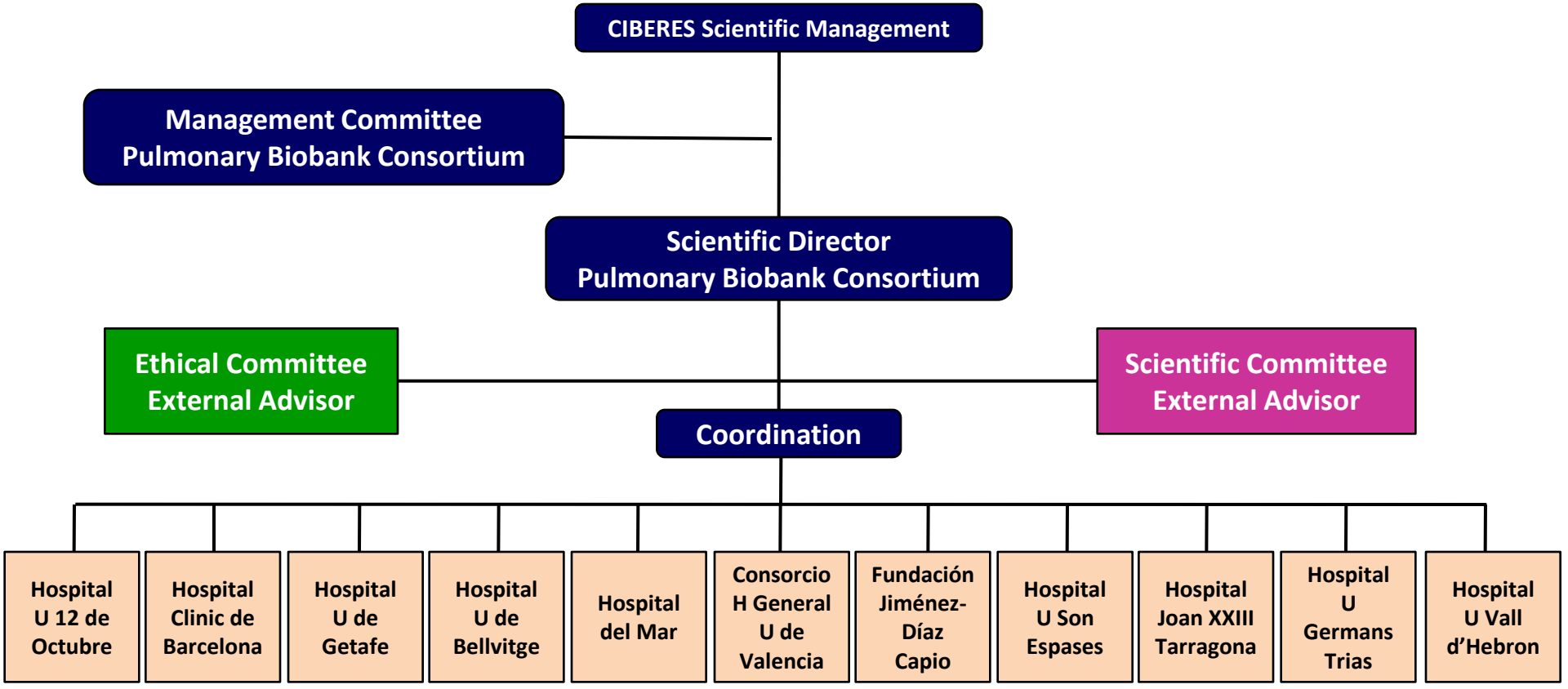
On-line platform for registration of standardized data.

Support on ehical-legal aspects.

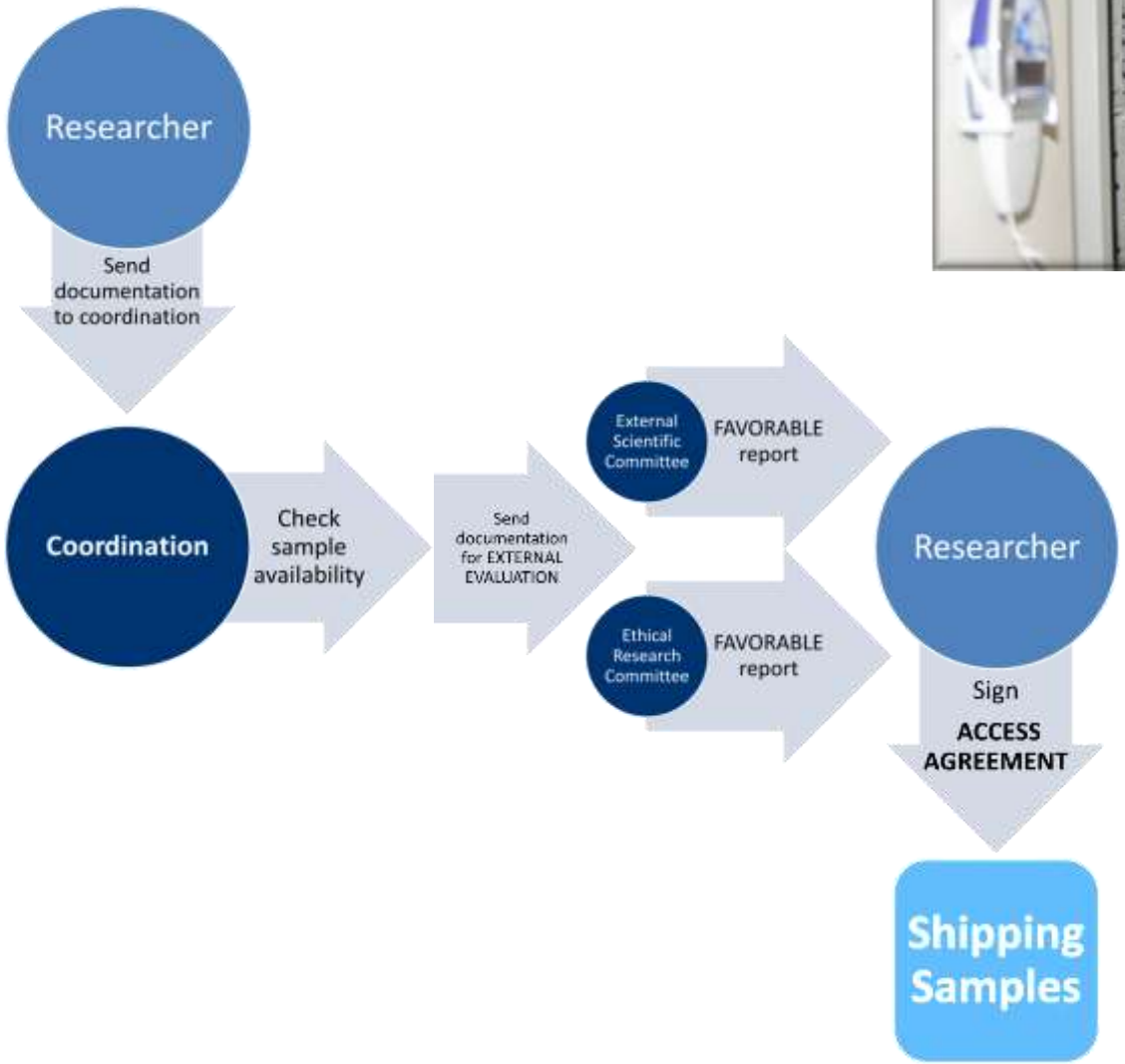
Cooperative groups

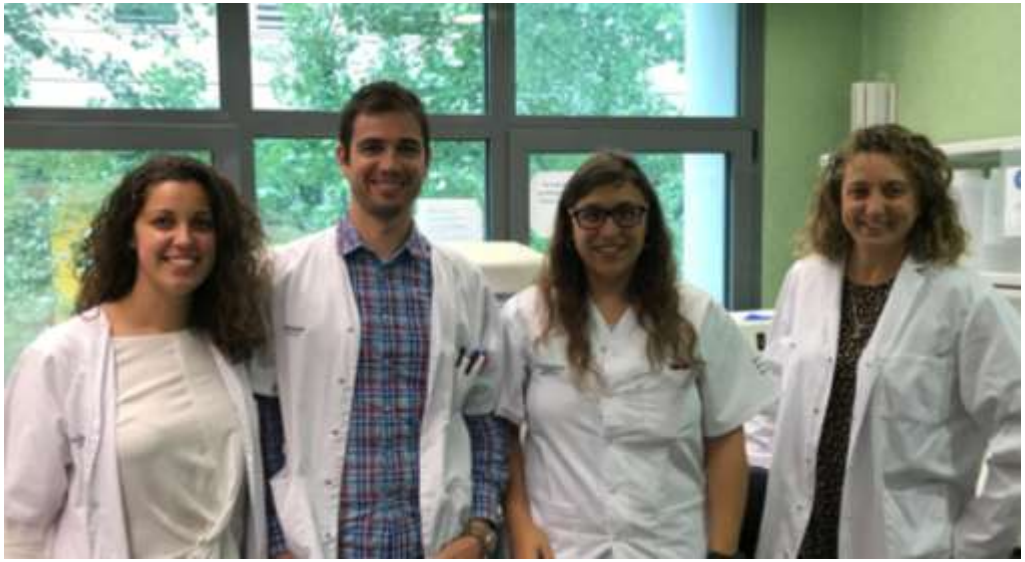
	Surgeons	Anatomical Pathology	Pneumologists	Laboratory	Local coordinator
Hospital U 12 Octubre	Carmen Marrón José Carlos Meneses	Ana Belén Enguita	Eva Maria Arias	José Luís Rodriguez Peralto	Antonio Pablo Gámez
Hospital Clinic Barcelona	Laureano Molins	Josep Ramírez	Joan Albert Barberà	Victor Ivo Peinado	Joan Albert Barberà
Hospital U Getafe	Beatriz de Olaiz Luis Jiménez Eduardo Camarero	José Antonio Aramburu	Andrés Esteban	Isabel Sánchez	Andrés Esteban
Hospital U Bellvitge	Ignacio Escobar Joan Moya	Roger Llatjos Enric Condom	Toni Rosell	Ana Montes	Maria Molina
Hospital del Mar	Joan Minguella	Lara Pijuan	Victor Curull	Carme Casadevall	Joaquim Gea
C H General U Valencia	Ricardo Guijarro	Miguel Martorell	Gustavo Juan	Sonia González	Julio Cortijo
F Jimenez Díaz Capio	Ignacio Muguruza José Zapatero	María Jesús Fernandez Aceñero	María Jesús Rodriguez Nieto	José Fernandez Marta Escribano	Germán Peces-Barba
Hospital Germans Trias i Pujol	Pedro López de Castro	María Teresa Fernandez	Alicia Marin	Edurne Pedrosa	Marian García
Hospital Joan XXIII Tarragona	Emili Canalís	Joan Francesc Garcia	Maria A. Bodí	Lluís Gallart	Juan José Sirvent
Hospital Son Espases	Ángel F Carvajal	Cristina Gómez	Francisco Borja Cosío	Cristina Villena	Jaume Sauleda
Hospital Vall Hebron	Joan Sole	Irene Sansano	Antonio Román	Susana Gómez	María Jesús Cruz

Organizational structure



Samples request





Coordination

CIBERES Pulmonary Biobank Consortium

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Magdalena A. Campaner, *Soporte coordinación*
Daniel Pons, *PhD Soporte coordinación*
Cristina Villena, *PhD Coordinadora*
Germán Peces-Barba, *Director Científico*

Con el soporte de la Plataforma Biobanco Pulmonar CIBERES (http://biobancopulmonar.ciberes.org/)