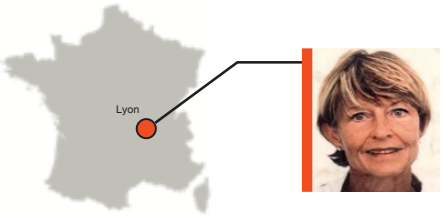

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OVERVIEW

AT A GLANCE

> Oncology
> Mesothelioma
> Coordinated by Prof. F.Galateau Sallé & Prof. S.Lantuejoul
> Centre Léon Bérard (Lyon) sponsorship
> Funded by INCa
> Key words: mesothelioma, biobanking, tumor banking, translational research

KEY FACTS & FIGURES

> Status: **19,000 included patients** until now (annual recruitment: actually 1,200 patients/year)
> No limit on expected number of included patients
> Follow-up period up to **10 years**
> National multicentric cohort
> **Biobank:** tumor, blood, cells, plasma, DNA/RNA
> Linked to CéPiDC, PMSI, RNIPP & PNSM, DO

The goals of Mesobank are to develop translational research for upgrading the molecular characterization of mesothelioma, to deciphering the preneoplastic stage as well as the mechanisms of aggressiveness and resistance to treatment of mesothelioma.

Positioning

> Until now, **this is the unique project worldwide** collecting clinical, biological, epidemiological, pathological and molecular data on mesothelioma with a such large scale follow-up. Mesobank is the largest cohort in the world in the mesothelioma field.

> The cohort is involved in several european and international projects, and aimed to be open to the scientific european and international communities for epidemiological and translational research

> Mesobank is closely working with the “Programme National de Surveillance des Mésothéliomes”(INVS) and takes part of BIOBANQUES Infrastructure.

LEADERSHIP

Dr. Françoise Galateau-Sallé, Professor of Pathology, Lyon, Centre Leon Bérard

Chairman of:

> The National Reference Center on pleural mesothelioma and rare peritoneal tumors MESOPATH

> The National Multicentric Mesothelioma Registry MESONAT

> The International Mesothelioma Panel IM@EC (International Mesothelioma Excellence Center)

> The Department of Pathology, Caen University Hospital

> The French Mesothelioma Panel for malignant pleural mesothelioma and rare peritoneal tumors

> The Biological Resource Center on mesothelioma (Inserm N°8-2005-2011)

> Pathological arm of the PNSM-InVS (French NIH)

Member of:

> The International Association for the Study of Lung Cancer (IASLC) providing expertise and core committee for the WHO's classification

> The panel of pathologists of TCGA

> The staging committee of the panel IASLC/TNM (tumor, node, and metastasis) classification

> The board of the ERS TASK Force on lung cancer and mesothelioma

> The French Association for Quality Assurance in Pathologic Anatomy and Cytology

Editorial Board

> Archiv of *Pathology*,Virchows Archiv

> *The European Journal of Pathology*

> Editorial Consultant of *European Society of Pathology*

> Reviewer for Archiv *Pathol Lab Med*, JTO, Lung Cancer

Pr Sylvie Lantuejoul, Professor of Pathology, Grenoble University Hospital

Expert for:

> The MESOPATH reference Center

> The Thymic reference Center

> The TENpath Center

Member of:

> The international board of pathologists for the lung cancer classification (IASLC) chaired by Prof. A Nicholson

> The International Mesothelioma Panel chaired Prof. F Galateau Sallé

> The board of the Lung Cancer group: sub group Bipathology

> The EORTC board

Editorial board and reviewing:

> European respiratory Journal, BMC Cancer, Lung Cancer, Histopathology, JTO, Lung Cancer, Archiv of Pathology and Lab Medecine

Current collaborations:

> Rob Michalides, The Netherlands Cancer Institute

> Joelle Roche, University of Poitiers and Harry A. Drabkin, Medical University of South Carolina

> Giulio Rossi, Department of Pathology, University of Modena and Reggio Emilia, Italy

> Andrew Nicholson & Mary Sheppard, Imperial College, London

> Margaret Burke, Department of Pathology, Royal Brompton, London

SCIENTIFIC NETWORK & MANAGEMENT

In France, the collaborative effort of the national program PNSM, the domestic network MESONAT, and the Center of Excellence MESOPATH made it possible to constitute a pole of research with international impact

> The **National Program for Mesothelioma Surveillance** (PNSM) consists of a system for epidemiological surveillance of the effects of asbestos and others (irradiation, other fibers etc.) on the health of the French population through a continuous follow-up of pleural mesotheliomas. This interdisciplinary program combines several teams having complementary skills

> The **national multicenter registry for pleural mesotheliomas** (MESONAT) represents, through its population coverage and its quality of exhaustive registration, one of the largest international system of registration of mesotheliomas

> The **Mesopath group** is a group of experts, specialists in histological and cytopathological diagnosis of mesotheliomas

> The **MESOPATH-IMEC** referral center gathers an international panel of 22 experts, specialists in the cytological and histopathological diagnosis of mesotheliomas

These networks are closely interconnected with Mesobank

Mesobank scientific committee is gathered around following expertises:

> **Epidemiology:** Marcel Goldberg, Danièle Luce, Anabelle Gilg Soit Ilg, Simone Mathoulin Pellissier

> **Lung cancer:** Etienne Leymarié, Denis Moro-Sibilot, Maurice Peyrol

> **Mesothelioma:** Arnaud Scherpereel, Françoise Le Pimpec Barthes, Isabelle Monet

> **Molecular genetics:** Lynette Fernandez Cuesta, Marie Claude Jaurand, Pierre Saintigny, Pierre Hainaut

PROJECT DESCRIPTION

SCIENTIFIC OBJECTIVES

The objectives of Mesobank are:

> Promote and optimize the databases of the **tumor banks** in the 10 biological resource centers supported by the INCa and integrate them in a single multicentric database with **national visibility**

> Develop ambitious collaborative projects exploiting the material collected and aiming at **discovering and validating new markers of early detection**

> Facilitate the development of high-impact projects in particular in **genomics** (exome sequencing)

INNOVATIVE SCIENTIFIC FEATURES

Mesobank is a platform constituted of **certified clinical dataset** associated to tumor paraffin embedded blocks, frozen tissue samples, blood/plasma/serum, effusion (pleural and ascites) and few cell lines

The originality of the cohort is based on the **standardized procedure of certification** of each cases included in the database and associated with the exact context of professional/environmental exposure, geographical location, clinical context and survival

Mesobank is a unique platform including more than 10,000 paraffin embedded blocks mainly histologically typed and subtyped with more than 10 immunohistochemichal markers tested notably using FISH and CGH array analyses

METHODOLOGY QUALITY

Quality control of data is an integral part of Mesobank and takes place at various stages: during data collection, data entry, and data checking. Twice a year, Mesobank database exchanges data with its interconnected databases to update its database

Mesobank has developed **suitable procedures for data quality control.** This includes an annually cross-checked of data from various interconnected databases constituting the Mesobank sources

Each patient included in the Mesobank is classified **according to the standardized procedure for case certification**

Quality controls are performed on **DNA & RNA** extractions from cryopreserved samples

DESIGN, METHODOLOGY & TIMELINE

Recruitment objectives: 19,000 Mesothelioma patients

Sites: 12 participating centers

Inclusion criteria: Patients newly diagnosed with a certified mesothelioma
All histological types, stages and grades are included. No selection on age or gender

Exclusion criteria: None

INCLUSION COLLECTION
Database: Administrative, demographic, cancer antecedents, tumor and treatments data

Biobank: Formalin-fixed, paraffin-embedded tumor samples & frozen samples

FOLLOW-UP: AT LEAST EVERY YEAR
Database: General practitioner name, disease specific physician name, data source, date of last follow-up, status at the date of the last follow-up, cause of death

DATABASE & BIOBANK CONTENTS

DATABASE

Mesobank is a multidisciplinary database part of several national network including:

> The FRANCIM network of French general and specialized registries
> The network of the Program of National Surveillance for Pleural and peritoneal Mesothelioma (PNSPM), the French NIH network of federally reportable disease («déclaration obligatoire de maladie»)
> The two databases of the clinical reference centers MESOCLIN (for pleura) and RENAPE (for peritoneal tumors)

Database comprises following items:

> **Administrative:** patient identification, ID number
> **Demographic:** date of birth, gender, place of birth, current residence, name and address of their physician(s), health insurance regimen
> **Cancer antecedents**
> **Tumor:** location, date of initial diagnosis, date of first sample, sample recording date, diagnostic method (clinic & biologic, paraclinic, cytology/histology), tumor morphology, WHO grade, tumor size, tumor stage, metastasis
> **Treatments:** date of first treatment, surgery, chemotherapy, radiotherapy, palliative
> **Follow-up:** general practitioner name, disease specific physician name, data source, date of last follow-up, status at the date of the last follow-up, cause of death

BIOBANK

Originality

> A standardized procedure of sample certification
> Epidemiological survey including a standardized questionnaire
> Enrollment of 19,000 patients with certified diagnosis linked to the Mesoclin national clinical reference center for pleural mesothelioma and RENAPE for peritoneal tumors allowing high quality annotations of clinical and therapeutic data and to the PNSM for occupational and environmental data
> Collection of more than 80 variables
> Mesobank is also part of the biobanques network

Scientific objectives

> Perform a molecular characterization of mesothelioma using new generation sequencing to allow a molecular classification of type and subtypes of mesothelioma and a classification according to survival (long/short)
> Decipher the precancerous stage of mesothelioma
> Investigate the mechanisms of disease aggressiveness and the resistance to treatment

Samples

> 11,800 formalin-fixed, paraffin-embedded samples
> Frozen samples: 15,883 tumoral tissues matched to 777 normal tissue; 10 to 20% matched to blood sample (in progression); 7,400 frozen cytological samples

Associated resources

> Resources equipment:
>> Pathological and molecular platform from the comprehensive cancer center of Lyon, the Centre Léon Bérard
>> Collaboration with the International Agency for Research on Cancer (IARC) in Lyon which hosts three centralized platforms for studies on genetics, biomarkers and carcinogenic mechanisms (next-generation sequencing (NGS), mass spectrometry platform, and the platform for the detection of multiple infectious agents)

TECHNICAL MODALITIES & SPECIFICATIONS

ORGANIZATION

- The biobank spreads over 10 biological resource centres (BRC) supported by INCa
- Each biological sample is identified by a patient-specific barcode

SPECIFICATIONS

- Date of the first sampling: 1972 (1998 PNSM)
- Solid tumor tissue bank is supervised by F. Galateau Sallé and mesothelioma cell lines are chaired by MC Jaurand
- Protocol for the biological sample collection is available
- Biobank IT management is performed through the Databiotec software which offers three essential features: stock management and sample location, printing barcode labels, and the management of pathological, biological and clinical data
- **Label of quality:** biobank gathers all samples with a **diagnosis, certified** according to collegial standardized procedure. Each BRC has entered into a quality program (double check, sample quality controls, traceability, temperature registry, etc) to be labelled NF S96-900 and IBiSA

BIOLOGICAL SAMPLE COLLECTION & ACCESS

Biological specimens	Status *	Origin	Quantity available	No. of aliquot	Expected percentage of sampled patients or No. of sampled subjects	Storage conditions
At baseline						
Cells	A	Blood	57 cell lines	8,000 aliquots of pleural cell effusions	100 %	-80°C
Serum	A	Blood	2 ml		100 %	-80°C
DNA	A	Blood	µg	340	100 %	-80°C
RNA	A	Blood	µg	100	100 %	-80°C
Paraffin Embedded tissue block	IT	Formalin fixed tumor	1 block	>11,000 blocks linked to healthy tissue	100 %	20°C
Paraffin Embedded tissue block	NA	Healthy tissue	1 to 10 block	3 480	100 %	20°C
Plasma	A	Tumor	na	na	410 patients	-80°C
Cryopreserved tissue	A	Tumor tissue	na	4,089	710 patients	- 80°C

* A=Affected, NA= Non-affected, IT=indication of grade of tumor + value

BIOBANK SAMPLE ACCESS MODALITIES

- An ethic **charter** specifies tumor sample collection, conservation, and utilization, for care and research purposes
- Biological samples **will be accessible** to public and/or private/industrial teams
- A **restriction access** will be applied for samples with small quantities of molecular extracts
- **Procedures for accessing biological samples** will be described in the **charter**. They include feasibility, financial, and scientific evaluations
- Biological samples can be transferred to public or private teams according to modalities defined in a contract. Project must be previously validated by Mesobank experts
- Biological samples can be transferred to foreign companies

BIOLOGICAL SAMPLE ANALYSES

- Samples analysis are performed through a collaboration with:
  - > The Léon Bérard Center which hosts on state-of-the-art technical equipment through its translational research platform
  - > The International Agency for Research on Cancer (IARC) in Lyon hosts three centralized platforms for studies on genetics, biomarkers and carcinogenic mechanisms
  - > A platform of high resolution sequencing (in progress)
- Tumors are also analyzed with FISH analysis and CGH array to characterize its histological sub-types

COST

- MESOBANK uses the calculation grid developed by an international expert group from biobanques infrastructure to evaluate the biospecimens cost

RESEARCH COLLABORATION OPPORTUNITIES

Phase IV Product approval Phase III Phase II Phase I Pre-clinical Proof of concept

Translational research

> Performed studies on mesothelioma tissues and cells to identify serum biomarkers such as mesothelin, osteopontin, or calretinin MUC1

> Better understanding of the molecular basis of mesothelioma to improve its early recognition

> Genome instability: oxidative stress, DNA damages and senescence in the genesis of mesothelioma

> Study immunity checkpoint alterations in mesothelioma

> Identify novel targets in mesothelioma and sensitivity to chemotherapy

Clinical development

> Identify prognostic markers and biomarkers of early mesothelioma detection

> **Pharmacogenomic:**

>> Mesothelin and osteopontin as diagnostic markers in patients with mesothelioma

>> Analysis of molecular biomarkers for cancer (methylation, mIR), immunohistochemical biomarkers and serum biomarkers (osteopontin, SRMP, VEGF etc.)

> **Patient stratification:**

>> Histomolecular characterization of mesothelioma in young and children

>> Molecular characterization of post irradiation mesothelioma

Outcomes research

> Epidemiology of pleural/peritoneal/other location mesothelioma in term of incidence and/or survival

> Etiology of mesothelioma in women, young adult and children

> Education and training in thoracic tumors' new WHO classification and digitalized platform for diagnostic certification in cancer, consultant cases and e-learning

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