# missions

**The Institute Pasteur in Lille is a private foundation recognized of public utility since 1898.**
The mission of the Institute Pasteur de Lille is to **bring science to the benefit of public health** in order:

- **study** and **understand** **major diseases** to find solutions,
- **train** professionals and **support** companies to combat these diseases,
- **Prevent** their development through education and information to the general public.

To succeed its mission, the cross is essential, as the foundations associates it with the best partners in order to combine scientific excellence worldwide, the technology advanced, and the contact with patients and results of diffusion capacity of its work to the public.

## Major of the Lille Pasteur Institute research themes are:

- **Infectious** diseases, **inflammatory** and **parasitic** (**tuberculosis**, **asthma**, **Crohn's disease**, **malaria** ...)
- **Cancers** (aero-digestive tract, tumor dormancy mechanism ...)
- **Cardiovascular** and **metabolic** diseases (**obesity**, **diabetes**, **heart** failure ...)
- **Neurodegenerative** diseases (**Alzheimer**)

## Advances in Research

### *Infectious diseases, inflammatory and parasitic*

Asthma - Schistosomiasis - blastocystosis - COPD - Clostridium difficile - Pertussis -Crohn's disease - Hepatitis C - IBD - Malaria - Parasites of fish - Pneumocystosis - Lung diseases and respiratory tract - Toxoplasmosis - Tuberculosis

### *Cancers*

Cancers - Tumor Dormancy - Targeted therapy

### *Metabolic and cardiovascular diseases*

Atherosclerosis - Cardiovascular disease - Diabetes - Heart failure - Obesity - Metabolic Syndrome

***Neurodegenerative Diseases***

Alzheimer disease

***Other themes***

Plague - Contamination by bacteria and viruses - Contamination by heavy metals -Congenital malformations - Environmental Impact - Cell Research

# Infection and Immunity

## Center for Infection and Immunity of Lille (CIIL)

Director: Camille LOCHT
Institut Pasteur de Lille, Lille University

The CIIL is part of the Pasteur Institute of Lille and is composed of 11 research teams, 2 junior teams and 1 service facility on Transcriptomics and Genomics that investigate:

(i) **Biology** of the **Pathogen**,

(ii) **Strategies** of **Infection**

(iii) **Host Response** and **Inflammatory** Processes.

It gathers complementary expertise, covering a wide range of disciplines from epidemiology, over molecular and cellular virology, bacteriology and parasitology, to the immunological basis of infectious and non-infectious diseases and translation into clinical applications.

The **targeted** diseases include some of the **major infections** world-wide, such as **hepatitis C**, **tuberculosis** and **malaria**.

However, other diseases of Public Health concerns are also studied, including plague, whooping cough, **schistosomiasis**, **toxoplasmosis**, **pneumococcal pneumonia** and various other parasitic, fungal, respiratory and gastro-intestinal infections. Furthermore, deciphering the dialogue with the symbiotic microbiota might provide novel clues in our understanding of chronic **inflammatory diseases**, such as **inflammatory bowel** disease, **asthma** and **chronic** obstructive **pulmonary** disease.

# Units

## Parasitology
## Molecular microbiology
## Immunity and Inflammation
## Technological platforms

# Research activity

- Stanislas TOMAVO : Molecular and Cellular Biology of Toxoplasma gondii
- Raymond PIERCE : Molecular Signaling in the Control of Parasite Growth and Differentiation (MSCPGD)
  - Protein kinases of Schistosoma mansoni (Colette Dissous)
  - Schistosome histone modifying enzymes as drug targets (Ray Pierce, Emmanuel Roger, Stéphanie Caby)
  - Immunology and biology of malaria infection (Jamal Khalife, Christine Pierrot)
- Florent SEBBANE: Plague and Yersinia pestis
- Camille LOCHT: Bacterial respiratory infections : Pertussis and Tuberculosis
- Frank LAFONT: Cellular Microbiology of Infectious Pathogens
- Jean DUBUISSON: Molecular and Cellular Virology of Hepatitis C
- Mathias CHAMAILLARD: NODS-Like receptors in infection and immunity
- Francois TROTTEIN: Lung Infection and Innate Immunity (L3I)
  - Theme 1: Innate immune responses to respiratory infections
  - Theme 2: Susceptibility factors for secondary respiratory bacterial infections
  - Theme 3: Therapeutic strategies-Development of mucosal immune-stimulators
- Bruno POT: Lactic Acid Bacteria and Mucosal Immunity
- Sylviane PIED: Basic and clinical immunology of parasitic diseases
  - Malaria Immunophysiopatholog
    - Immune responses involved in protection against primary P.yoelii infection.
    - Immune responses associated with CM pathology induced by P. berghei ANKA.
    - Identification of genetic traits controlling host resistance to CM.
    - Studies on Pf-infected patients.
  - Clinical Immunology of Malaria and Schistosomiasis
    - Immuno-pharmacology of vaccine
    - Immuno-epidemiological studies on schistosomiasis and malaria
    - Clinical development of schistosomiasis vaccine
- Anne TSICOPOULOS : Pulmonary Immunity
  - Endothelial cells (EC): Proteoglycan endocan in sepsis, IL-33 in asthma and sepsis
  - Lymphoid cells: Aero contaminants, Obesity
- Yves LEMOINE: Transcriptomics and Applied genomics
- Priscille BRODIN: Chemical Genomics of Intracellular bacteria
  - Quantitative Imaging of the Mycobacterium tuberculosis fate within host cells: Reassessment of the current dogmas of mycobacterium trafficking and replication
  - Bacterial protein effectors as modulators of M. tuberculosis intracellular localization
  - Host cellular factors contributing to M. tuberculosis intracellular replication
  - Chemical modulators of M. tuberculosis intracellular persistence
- Eric VISCOGLIOSI: Biology and Diversity of Emerging Eukaryotic Pathogens
  - Parasitic protozoa: Blastocystis, Cryptosporidium and eukaryotic microbiota analysis
  - Pneumocystis intimate host-parasite interaction and pulmonary colonization
- Jean DUBUISSON: Molecular and Cellular Virology of Hepatitis C
- Lionel POULIN: Dendritic Cells in Infection and Immunity Laboratory (DCIIL)

# lille biology institute

The IBL research center was founded to reinforce **basic biology science** in the North / Pas-de-Calais area by, for example, group leaders and welcoming Permitting them to Develop highly competitive research.

Research programs Were **INIBTIALLY** Conducted in the fields of human **genetics**, **cellular biology**, **cancer**, **microbiology** and **biomolecule chemistry**.
IBL covers a total of 12,000 square meters with about 300 people: senior scientists, post-docs, PhD and master students, research assistants and technicians. The building possesses multiple core facilities Such As protein chemistry, biochemistry, molecular, cellular (confocal microscopy, atomic strength microscopy ...) and structural biology (radiocristallography), and genetics. Moreover, in close cooperation with the Pasteur Institute of Lille with qui IBL forms a Federal research institute (IFR 142), animal and NMR facilities are disponible to conduit research programs. Within the framework of a partnership with the universities of Lille I and Lille II (now merged in a PRES), the IBL Welcomes laboratories in Its numerous graduate and under-graduate students.

# Laboratories

## Cancer

### Genetic approaches, functional and structural cancers

Director: Yvan LAUNOIT

CNRS UMR 8161, Institute Pasteur de Lille, Lille University

#### Teams

1. Initiation of **Epithelial Cancer** - Corinne Abbadie
2. Functional studies of **tumor suppressor gene HIC1** (HIC) - Dominique Leprince
3. **VE-statin** / **EGFL7** functions During vascular development - Fabrice Soncin
4. Cancer **Biology** and **Chemistry** - Oleg Melnyk
5. **Signaling** - **Apoptosis** and Cancer - David Tulasne
6. **Virus**, Cancer & **transcript**: Immunoregulation of **virus-induced** cancer - Yvan Launoit and Nadira Delhem
7. **Virus**, Cancer & **transcription**: **ETS** Proteins and associated diseases - Yvan Launoit and Martine Duterque

#### Platforms

- Peptide CSB platform
- Bio-Imaging Center Lille Nord de France (BICeL)

### Genetic Toxicology Laboratory

Director: Fabrice Nesslany

Institut Pasteur de Lille, Lille University

#### Services

- **Screening**
- **Regulatory testing under GLP standards**
- **Cosmetology specific tests**
- **Validation / Development**

# Cardiovascular, metabolic and neurodegenerative

## Risk factors and molecular determinants of age-related diseases

Director: Philippe Amouyel

Inserm U 1167, Institute Pasteur de Lille, Lille University

**The aim of unit:**

consists in the acquisition of knowledge about the impact of **environmental factors** and **genetic susceptibility**, and their **interactions** in the **development**, **evolution** and **management** of diseases related to **aging** in humans.

Two main areas are studied:

- **cardiovascular**
- **neurodegenerative** diseases.

This research is addressed through the integration, within the unit, an expertise in epidemiology and a master of molecular biology tools for the epidemiological approach, incorporating recent advances in **Genomics** at high speed, **transcriptomics**, **proteomics** and **bioinformatics**.

**Research programs**

is organized around three themes supported by teams working in close constant contact both at the technical concepts:

1. **Team 1: Public health and epidemiology of cardiovascular** diseases.
2. **Team 2: Search the molecular determinants of cardiovascular diseases with proteomic analysis and candidate gene approaches**
3. **Team 3: Search molecular determinants of neurodegenerative diseases by transcriptomics and candidate gene approaches**

The work produced by these three teams are closely related. The expected results fall into three main directions, built to open new concepts in the approach to age-related diseases, their prevention and treatment, and thus meet the INSERM missions in Public Health, and Pathophysiology Therapeutic:

- The analysis of trends in cardiovascular disease and the dissemination of the use of protein markers in population will understand the impact of these conditions and develop more targeted prevention policies.
- The identification of gene-environment interactions and original candidate genes will discover new pathophysiological mechanisms and suggest targets for new treatments.
- The close links at the molecular level between vascular risk and neurodegenerative risk should lead to the establishment of new disease classification concepts.

# Genetics of Metabolic Diseases

## Integrative Genomics and modeling of metabolic diseases

Director: Froguel

CNRS UMR 8199, INSERM, Institut Pasteur de Lille, Lille University, Egid

- Genomics and Epigenomics of metabolic diseases
- Modeling and molecular basis of diabetes and obesity

## LABORATORY»

- AERES report
- Know-how»
  - Bio-bank (included more than 200,000 biological samples. Its mission is to receive, extract, quantify, maintain and manage the samples.)
  - Bio-informatics
  - Bio-statistics
  - Genomic platforms
  - Informatics

## RESEARCH»

- Next-generation sequencing
- Monogenic Diabetes
- Tryptophan metabolism
  - Inflammation and deregulated tryptophan metabolism in human obesity
- hiPSC-based type 2 diabetes models
  - Model the type 2 diabetes using human induced pluripotent stem cells
  - Application: Transcription factors and genetic susceptibility to type 2 diabetes.

- Statistical genetics
- Genetics and epigenetics of type 2 diabetes
- Obesity
- Molecular basis and modelization of Diabetes and Obesity
- Parvovirus oncolytic H-1

### Nuclear receptors, cardiovascular disease and diabetes

Director Bart STAELS
Insem U 1011, Institut Pasteur de Lille, Lille University, Egid

This unit studies the biological and molecular mechanisms controlling the development and progression of **type 2 diabetes** and its **cardiovascular** complications, to develop preventive and **therapeutic** strategies. We are studying the **regulation** of **genes** involved in these diseases and the consequences of deregulation, with particular interest for **specific transcription factors**, **nuclear receptors** that constitute potential therapeutic targets.

In recent years, they have significantly contributed to:

- Demonstrate the **involvement** of nuclear receptors in **disturbances** in metabolism and energy balance: characteristics disruptions type 2 diabetes
- Demonstrate the **regulatory** role of the nuclear receptors in **inflammatory** processes in **adipose** tissue and the vascular wall;
- Better understand the molecular mechanisms by which nuclear receptors modulate the **progression** of type 2 diabetes.

The current state of the laboratory objectives are to understand the contribution of nuclear receptors - as **regulators of gene expression** - in the pathophysiology of type 2 diabetes, and to assess the **therapeutic potential of selective ligands** for these receptors in **prevention** and treatment of type 2 diabetes and its cardiovascular complications. Specifically,

The UMR 1011 is organized in four cross-functional teams with complementary technical and scientific skills:

1. Team 1 (Nuclear Receptors in the metabolic syndrome)
    a. Studying the metabolic functions of **RNs** (FXR, Rev-erbα, RORα) and their involvement as potential **therapeutic targets** in humans.
2. Team 2 (Molecular control functions of monocytes / macrophages in the cardiometabolic syndrome)
    a. focuses his project on the role of **PPAR gamma** in cells from **adipose tissue** of obese subjects studied in humans the role of **RNs** (PPAR and LXR) and protein **CDKN2Ap16** $^{INK4a}$ in the mechanisms of differentiation and functions of macrophages infiltrating the adipose tissue and atheroma.
3. Team 3 (Immuno-inflammation and cardiovascular diseases)
    a. Examines the **contribution** and **regulation** by RNs other immune cells in the **pathophysiology** of **atherosclerosis** with particular interest for **PPAR gamma**.
4. Team 4 (molecular analysis of gene regulation in the cardio-metabolic syndrome)
    a. Identifies the molecular mechanisms of regulation orchestrated by RNs, to discover new regulatory pathways and better define the therapeutic molecules.

The laboratory is one of the cofounders of EGID (European Genomic Institute for Diabetes), the first research institute in France specifically dedicated to diabetes and its complications.
Launched in 2009, this project was made possible by the complementary skills of the three founding teams:

- This laboratory, UMR 1011 "Nuclear receptors, cardiovascular disease and atherosclerosis"
- The Joint Research Unit 8199 "Genomics and metabolic diseases" headed by Professor Froguel (CNRS - Université Lille 2 - Pasteur Institute of Lille)
- Unit 859 "Diabetes Biotherapy" led by Professor François Pattou (Inserm - Lille 2 University - University Hospital of Lille).

# Chemistry and Pharmacology

## Drug discovery

Director: Benoît DEPREZ
Inserm U 1177 Pasteur Institute in Lille, Lille University

UMR1177: Drugs and Molecules for Living Systems

**Therapeutic Innovation: Discovery Across Boundaries**

The unit is dedicated to **drug design, discovery and selection**.

The Lab's mission is to design and study compounds that modulates selected molecular targets in a desired way to **treat infectious** and **metabolic** diseases. Our projects engage researchers across physical, chemical and biological sciences to trade ideas and knowledge and sincerely endeavor to validate new therapeutic concepts with drug prototypes and bring drugs candidates to the clinic.

Projects :

1. Developing **cutting edge** methods for **quantitative** **pharmacology** (High Content Screening, Pharmacokinetics)
2. Designing the **next generation** of **anti-TB** antibiotics: **ethionamide** boosters.
3. Deciphering the role(s) of **Insulin Degrading Enzyme** in diabetes with several families of modulators.
4. Modulating the molecular interplay between intestine, liver and muscles with **TGRb5** ligands to treat diabetes.
5. Blocking HCV cell entry as a potential therapy against hepatitis C.
6. Developing small chemical modulators of antigenic presentation.
7. **Malaria compounds** :
    a. **PDE** inhibitors
        i. **Phosphodiesterases**, « molecular morphing » and Malaria
    **b.** **PfAM1** inhibitors

# Bio Imaging Center

## BICeL

**FACILITIES**

- Atomic Force Microscopy
- Electron Microscopy
- Photonic Microscopy
- High-Content Screening
- Cytometry and Microscopy in flow

# Chemistry Systems Biology (CSB)

The CSB facility is particularly interested in developing **academic or industrial collaborations** for developing therapeutic peptides or proteins. This facility offers cutting edge expertise in two complementary areas:

- The first expertise is in **peptide** and **protein** total **synthesis** and **characterization**. The use of innovative native peptide ligation chemistry gives access to complex and original peptide scaffolds (cyclic, branched, polycyclic...), or to small proteins with an atom-by-atom control of their structure. The CSB facility make use of automated systems for the synthesis of the peptide/protein libraries and for their screening.
- The second and complementary expertise is the biological study of peptide and proteins using an **array** of **biochemical**, **biophysical**, **cellular** and **in vivo assays**.

EQUIPMENT AND RESERVATION

- Chemistry
- HPLC
- Lab Equipment
- Mass Spectrometry
- Molecular Interactions
- Peptide Synthesis

## Biotech of the Pasteur Institute of Lille

**Installed on the campus of the Pasteur Institute in Lille, biotechnology companies, market, and worldwide, analytical or diagnostic products directly from fundamental research in Lille.**

### Genoscreen

**Genoscreen** offers analytical services in genomics on all types of genomes and analysis and training in bioinformatics for both "academic" research teams for hospital or industrial research.
In recent years, own research programs, conducted in partnership with research units of the Pasteur Institute of Lille, INSERM and INRA have enabled the development of highly competitive applications in areas such as genetics Alzheimer's disease, microbial typing or molecular control of biodiversity.

### Lunginnov

**Lunginnov** produces **Endocan** a biomarker of the state of the blood vessels which can be used for the treatment of **cancers** and **septis**. The endothelial cell Endocan or specific molecule (**ESM-1**) was discovered in 1996 by Philippe Lassalle and his staff team Pulmonary Immunity of CIIL (CNRS, INSERM, Institut Pasteur de Lille

### X'Prochem

**X'ProChem** sells **proteins** synthesized from a chemical method. Innovative technology derived directly from academic research Oleg Melnyck laboratory.

### APTEEUS

**APTEEUS** has developed an **innovative** solution to individually take care of **patients** with **rare diseases**.
The technology APTEEUS can test **thousands** of molecules existing pharmacopoeia directly on **primary** cells from the **patient**.
APTEEUS has its administrative headquarters at the Faculty Pharmacy and has a laboratory on the campus of the Pasteur Institute in Lille.

## Technological platforms

**Cytometry and microscopy imaging**
BICEL
charge: Frank LAFONT
Access Platform site: http://www.bicel.org

**Transcriptomics and Applied Genomics**
Transcriptomics and Applied Genomics Group [TAG]
INSERM U 1019, CNRS UMR 8204, Institute Pasteur de Lille, Lille University
Head: David HOT
Access Platform site: http://www.pegase-biosciences.com

**Chemistry peptides**
Peptide Chemistry, Systems Biology
CNRS UMR 8161, Institut Pasteur de Lille, Lille University
Head Oleg MELNYK
Access Platform site: http://csb.ibl.fr

**HTS ADME and PK-screening lab**
INSERM U 1177 Institute Pasteur de Lille, Lille University
Head: Benoit Deprez
Access to laboratory site: http://www.deprezlab.fr

**Nuclear Magnetic Resonance**
Nuclear Magnetic Resonance
CNRS UMR 8576, Institut Pasteur de Lille, Lille University
in charge: Guy LIPPENS

**High Security Laboratory**
Institut Pasteur de Lille
in charge: Jean-Pierre DE CAVEL

**Genome Studies Laboratory**
Genomic Analysis Laboratory
Inserm U 744, Institut Pasteur de Lille, Lille
University: Philippe Amouyel and Nathalie FIEVET-Verrecas

**Metabolic Genomics and Diseases**
Ligand-PM (Lille Integrated Genomics Network for Advanced Medicine Personnalized)
CNRS UMR 8199, Institut Pasteur de Lille, Lille University
Head: Jérôme DELPLANQUE
Access to laboratory site: http://www-good.ibl.fr

**Proteomics and Analysis modified peptides**
Modified Peptides and Proteomics Platform (P3M)
Laboratory ParaFrap Excellency Lille Pasteur Institute, CNRS, University of Lille
Manager: Stan TOMAVO
Access Platform site: website under construction