



Vivre mieux
plus longtemps

20 REPORT 19



PRIVATE NON-PROFIT FOUNDATION SINCE 1898

www.pasteur-lille.fr

THE EDIT

IN 2019, OUR FOUNDATION CELEBRATED THE 120TH ANNIVERSARY OF THE OPENING OF ITS HISTORIC BUILDING!

120 years of innovation, research and fighting disease. 120 years of commitment and joint action. 120 years at the service of everyone's health. And, above all, 120 years of loyalty to the ideas of Pasteur and the wishes of the pioneers of the institute: Pasteur, Calmette, Guérin.

It is this history, peppered with doubts, efforts, major discoveries and successes that provides the foundation on which the future of Institut Pasteur de Lille is being built through its strategic project.

The evaluation of the research teams by the High Council for the Evaluation of Research

and Higher Education (HCERES) highlighted the excellence of the teams and the quality of the research carried out on the campus. In association with our partners - CNRS, INSERM, Lille university hospital, University of Lille - the 8 mixed research units are therefore developing their projects and organisation around the longevity project, which is the major objective of our foundation. Thanks to the renewed support of the French Ministry of Research, we can continue our projects on the issue of longevity and bear witness to the scientific standards of our foundation, confirmed by the 365 scientific publications of the research teams.

EDITO-

Convinced of the key importance of prevention in improving health, the teams at the Centre for Health and Longevity has developed new offers in 2019 for businesses and individuals. Through vaccination, the Longevity Course, health coaching, clinical studies and training, the disease prevention efforts are tackled on a cross-sector basis and must respond to the challenges of our society. As a result, the collaboration with associations and healthcare agents promotes and enhances our actions in the service of healthcare. All these advances in healthcare, all these innovations, all these fights against disease

would not be possible without the strong and ongoing support of the donors, patrons and companies that I would like to thank very warmly on behalf of all the researchers.

Together, let's speed up research and take action to promote tomorrow's health.

Many thanks for your commitment alongside our teams.



Prof. Xavier Nassif
Managing director

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2019 ACTIVITY REPORT

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HIGHLIGHTS

LONGEVITY OBJECTIVE

Speeding up research and acting for better health tomorrow

- The strategic project of Institut Pasteur de Lille
- International relations
- Results from the 3rd CPER-CTRL call for projects
- Launch of the 4th CPER-CTRL call for projects (phase 4)

SPEEDING UP RESEARCH FOR BETTER HEALTH TOMORROW

LONGEVITY: interdisciplinary teams for excellence in research

- The Campus Research Teams
- Technology platforms
- Biotechs

PREVENT TODAY IN ORDER TO AGE WELL TOMORROW

Centre for Health and Longevity: Innovation for Ageing Well

- Health checks and educational activities
- Research within the Centre for Health and Longevity
- Nutrition and Physical Activity Department
- The International Vaccination centre
- Development unit
- Microbiological Safety Unit

SUPPORT THE FOUNDATION, ADVANCE TOGETHER!

Institut Pasteur members working together!

- Donations, legacies and solidarity events
- Business patronage
- The Institut Pasteur de Lille museum

BUILD TOMORROW'S FOUNDATION

A Foundation at the service of the population

- Institut Pasteur core values
- Our CSR Commitments
- The Executive Board
- Scientific and Administrative Organisational Chart
- Employment/Resources

SCIENTIFIC PAPERS

PARTNERS AND SUPPORT

KEY EVENTS 2019

2019: 120 YEARS OF RESEARCH AND INNOVATION

1894 At the end of the 19th century, three quarters of the planet were decimated by infectious diseases such as **diphtheria, tuberculosis, cholera, smallpox** and **rabies**. The Nord-Pas de Calais region was not spared and the city of Lille had to face a major **diphtheria epidemic**. **Doctor Emile Roux**, who studied the disease with **Louis Pasteur** in Paris, discovered the toxin responsible for diphtheria. The decision to create the institute was approved by the municipal council of **9 November 1894**. **Albert Calmette** flew to Lille. An initial temporary laboratory was created at the Halle aux Sucres in the Vieux-Lille. The **production of the diphtheria serum** could begin.

20 NOV 1895 The **first stone of the building** is placed in the heart of the **Saint-Sauveur district**.

1898 The Foundation is a **non-profit organisation**, which is legally and financially independent of the Institut Pasteur in Paris.

9 APR 1899 Institut Pasteur de Lille formally opened at its current premises on Boulevard Louis XIV, on the same day as the statue of Louis Pasteur was unveiled on Place Philippe Lebon. This great day was conducted in the presence of ministers, official representatives of the French Academy, the Academy of Sciences and Medicine and Mrs Pasteur, without her husband, who had sadly died 4 years earlier.

This is how the history of Institut Pasteur de Lille began, originating in discoveries that would be significant for Humanity, following in the footsteps of Louis Pasteur and the example initiated by Albert Calmette.

1899



2019



INSTITUT PASTEUR DE LILLE, FROM ITS FOUNDATION TO TODAY

1894

Creation of Institut Pasteur de Lille to resolve a diphtheria epidemic

9 APR 1899

Opening of Institut Pasteur de Lille and unveiling of the statue of Louis Pasteur. In the presence of Albert Calmette, his wife, Mrs Pasteur, his children and grandchildren

1904

Opening of the first biological water purification station in La Madeleine, with a purification process applied by Albert Calmette

1945

Creation of the regional blood transfusion centre

1951

Implementation of the international vaccination centre intended for travellers, and approved by the WHO

1975

Installation of the Immunology and Parasitic Biology Department

1981

Creation of the health examination centre

1985

Creation of a nutrition department

1994

- Installation of a new team that will work on the **nuclear receptors** as therapeutic targets
- Creation of the high-field Nuclear Magnetic Resonance (NMR) centre
- Elucidation of the action mechanisms of PPAR α dependent fibrates on **lipoprotein metabolism**
- Discovery of a **genetic marker** for diagnosing **Alzheimer's disease**

1997

Discovery of a new genetic element which has been used since 2007 for the **molecular typing** of tuberculosis

1999

First trials of the bilharzia vaccine: Bilhvax

1898

The Foundation was recognised as a non-profit organisation of public interest by presidential decree

1901

Opening of the **Émile Roux dispensary**, the first French preventorium for the prevention of tuberculosis

1921

Discovery of the vaccine against tuberculosis: BCG (Bacillus Calmette and Guérin)

1948

First international BCG congress at Institut Pasteur in Lille

FROM 1966 TO 1970

Launch of a **tuberculosis prevention campaign** in the mining area where 200,000 children and adolescents were screened and vaccinated with BCG

1979

Identification and characterisation of **new oncogenes** and their involvement in cancer

1984

Installation of the Jean-Charles Fruchart laboratory: First team from Institut Pasteur de Lille to take an interest in **cardiovascular and metabolic diseases**

1986

Launch of a new **research objective on infection by the AIDS virus (HIV)** and on the immune response against the regulatory proteins of the virus in particular

1996

- Creation of the **Institute of Biology of Lille (IBL)** on the Pasteur Lille campus
- Discovery of a **biomarker** for lung, stomach and liver tumours, and leukaemia
- Discovery of two protective genes against **atherosclerosis**

1998

- Effects of **nuclear receptors** on inflammation and atherosclerosis
- Discovery of the role of PPARs in controlling inflammation during **atherosclerosis**. This discovery led to the **creation of Genfit**, a start-up initially hosted by Institut Pasteur de Lille

2005

Method for identifying a latent tuberculosis infection

2006

- Development of a **nasal whooping cough vaccine**, which can be used for inoculation from birth
- Discovery of the **first genes involved in** severe infantile

2009

- Creation of **EGID** (European Genomic Institute for Diabetes), the first research institute in France dedicated specifically to diabetes and its complications
- Identification of the **genetic determinants** involved in 13% of the forms of **Alzheimer's disease**

2011

- Identification of five new factors of genetic susceptibility to **Alzheimer's disease**
- **Sequencing** in record time of the **Escherichia coli** bacteria responsible for food poisoning

2013

Identification of **genes involved in the resistance of tuberculosis**

2016

- Signature of a **framework agreement** for an interdisciplinary partnership on digital sciences and health with the **INRIA**
- A new biological stethoscope for heart disease
- Creation of the first **mathematical model** to understand how the liver clock synchronises with the rhythm of meals

2018

- The discovery of a new **gene responsible for childhood obesity**
- Test-tubes containing the **original strains** of the vaccine against tuberculosis (BCG) to be opened at Institut Pasteur de Lille
- Design of a **new algorithm for detecting the resistance** of tuberculosis strains which are not detected by standard tests
- The biological clock as an important ally in the fight against inflammatory diseases
- Creation of the **Longevity Course**, an innovative course in preventive medicine, in partnership with the university hospital of Lille and the University of Lille
- Cardiac and immune chronobiology: **important role of Rev-erba** in cardiac chronobiology and circadian immunity

2000

- Development of the activities of the UMR1011 laboratory towards **metabolic diseases**
- New nuclear receptors such as FXR and LXR at the heart of pathophysiological processes leading to **cardio-metabolic diseases** such as obesity, diabetes and its cardiovascular complications
- The beginnings of the study of chronobiology in Lille
- Identification of the nuclear receptor Rev-erba as a target of PPAR α

2007

Identification of a new gene that may cause type 2 diabetes

2010

Discovery of a **biological marker of heart failure**, which can be used to identify the risk by way of a simple blood test

2012

- Involvement of **rare mutations** in common forms of type 2 diabetes and obesity
- Certification of the programme on **tumour dormancy** by the National Cancer Institute
- **Equipex** and **Labex** certification of the work of researchers of Lille

2015

- Creation of "**Centre Transdisciplinaire de Recherche sur la Longévité**"
- Creation of **METIS**: a website with health recommendations for international travellers

2017

- Installation of **Eurabio/Synlab**, a medical biology laboratory, on the Pasteur Lille campus
- Tuberculosis and resistance to antibiotics: discovery of a new **SMART-420**
- **Heart surgery**: Lille-based researchers discovered the impact of the time of day on the risk of heart complications
- An **edible mushroom** that is promising for the fight against human **genetic diseases**
- Creation of the **Centre for Health and Longevity**

2019

- 120 years since the opening of Institut Pasteur de Lille
- Launch of the great creative and collective challenge **#TousUnPeuChercheurs**



OBJECTIVE LONGEVITY

01

SPEEDING UP RESEARCH AND ACTING FOR BETTER HEALTH TOMORROW

Over the **past 60 years**, men and women have gained on average **a 14-year increase in life expectancy**. Life expectancy in a good state of health is increasing at a slower rate than life expectancy. When one knows that by **2060**, France will count **250,000** 100-year olds, the question of ageing well becomes essential.

But how are we ageing? And more specifically, can we live better longer? At age 60 , on average life expectancy is 20 years , ten of those in good health and the ten others with a gradual loss of autonomy. So, extending the period of life in good health is a challenge for research and public health.



CANCER

400,000

new cases detected in 2017.
1st cause of death

CARDIOVASCULAR DISEASES

140,000

deaths per year,

1,000,000

cases of heart failure

INFECTIOUS DISEASES

4 million

deaths worldwide

(HIV, tuberculosis, malaria, viral hepatitis, etc.)

480,000

case of **multidrug-resistant tuberculosis** every year

ALZHEIMER'S DISEASE

900,000

people in France are not diagnosed

DIABETES

3.3 million

of people with diabetes in France.

700,000

individuals unknowingly live with diabetes

ANTIBIOTIC RESISTANCE 2.0

700,000

deaths worldwide in 2019

12,500

in France

1st

cause of death by 2050

Having historically led the way in the fight against **infectious diseases**, Institut Pasteur de Lille now hosts some of the most well-known **international scientific experts** in the field of **antibiotic resistance 2.0**.

STRATEGIC PROJECT OF THE INSTITUTE

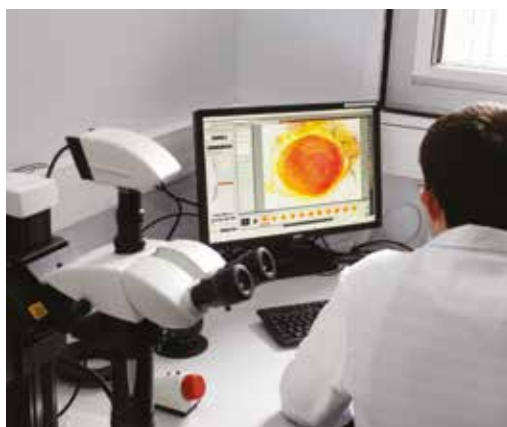
The Institut Pasteur de Lille was created in 1894 to respond to public health concerns at the end of the 19th century, including the fight against infectious diseases, through the research work on pathogens, the development of vaccines and serum and the promotion of preventive and hygienic measures. From the very beginning, Institut Pasteur de Lille has therefore organised its actions around the following three objectives: high-level fundamental research, disease prevention and the development of a healthcare offer aimed at the general public, that complies with the core values of Institut Pasteur.

The advances in research, vaccine development and the discovery of antibiotics and, more recently, antivirals, to which Institut Pasteur de Lille has contributed, have resulted in a considerable reduction in the prevalence of certain infectious diseases.

During the 20th century, new diseases linked to changing lifestyles and to the increase in life expectancy have developed with an epidemic progression, such as the cardiovascular diseases, diabetes and metabolic diseases, cancers and neuro-degenerative diseases. At the same time, economic and industrial changes in societies have also given rise to the emergence of other diseases linked to several rapid changes in the environment (long-distance travel, intensification of livestock farming, pollution, climate change) such as antibiotic resistant infections, emerging infectious diseases and respiratory ailments. Even more serious are the frequent combinations of genetic, environmental, nutritional

and behavioural determinants or "stressors" simultaneously affecting several organs, which have a generalised impact on the state of health of the general public, the quality of life of our fellow citizens and require complex and costly treatments.

In the last two decades, the life sciences have also been deeply affected by the rapid growth of the storage and computing capacities of computers, at the same time as the sequencing capacities of the improvement of imaging technologies (molecular, cellular, *in vivo*) and the automation and miniaturisation of the many search operations were producing data in exponentially growing volumes. As a result of these parallel developments, if they are integrated within laboratories, our descriptions of living things can be refined and more complex mechanisms can be understood.



POSITIONING AND STRUCTURING OF THE PROJECT

To understand the significant changes in health needs, and fully exploit the rapid development of scientific methods, Institut Pasteur de Lille has decided to organise its activities within an interdisciplinary and multi-sector campus, whose central focus is to understand the primary pathophysiological mechanisms of the most impactful diseases, in order to design and develop diversified health products for sustainable healthcare: treatments, diagnostic assessments, vaccines and innovative disease prevention protocols.

WHAT'S MORE, INSTITUT PASTEUR DE LILLE HAS SET ITSELF TWO PRIORITIES:

- ▶ **Degenerative diseases associated with life styles, the extension of life time, and changes in the environment:**
 - Diabetes and its complications
 - Cardiovascular and respiratory diseases
 - Neurodegenerative diseases
 - Senescence, fibrosis and cancer
- ▶ **Infectious diseases, in the context of antibiotic resistance**

These two objectives have strong scientific and methodological interconnections because both are linked to the functioning and ageing of innate and adaptive immunity, and of the microbiota. They can also be associated with effective disease prevention methods.

THE STRATEGY OF INSTITUT PASTEUR DE LILLE CAN BE BROKEN DOWN INTO 4 INTERDEPENDENT OPERATIONAL OBJECTIVES

1

Outlining an interdisciplinary research platform in pursuit of excellence with a holistic approach to the organisation, by encouraging collaborations between academic disciplines on the one hand and research units on the other, with the aim of identifying the earliest stages of the pathophysiological mechanisms of diseases, on which curative or preventive action will theoretically be more effective. Maintaining the highest level of scientific investigation thanks to the most recent means of observation and analysis will be sought.

2

Developing one's inter-sector ecosystem by bringing together academic

and industrial laboratories to facilitate the transformation of scientific results into innovative healthcare products (drugs, diagnostic assessments and vaccines, disease prevention protocols).

3

Conducting assessed healthcare measures, with a progressive deployment from the Hauts-de-France to all of France. These actions will be implemented by building intensified exchanges between research activities on the mechanisms of resilience and resistance to stressors on the one hand and disease prevention activities on the other. These exchanges naturally go both ways: from the fundamental research (including human and social sciences) to the disease prevention actions evaluated on the population on the one hand and from the observation of the

population according to the mechanistic hypotheses on the other hand. Regarding this third point, the experience of Institut Pasteur de Lille is unique in France, and has no equivalent in the academic or hospital infrastructures.

4

Passing on "evidence-based" knowledge by participating in the "life-long" training offer, internally (career development) as well as in partnership with the University of Lille and the I-site (ULNE) and the international network of Institut Pasteur, and by communicating directly to the public through conferences, and by exploiting all available channels and technologies, to facilitate personalised communication for individual coaching in particular.

There are eight founding research units of Institut Pasteur de Lille. The 34 teams that make them up gather together the initial scientific capital (researchers, expertise, methods and results) in line with the two topical priorities of the institute. These teams were highly rated during the 2019 assessment wave of HCERES and the Specialised Scientific Commissions of Inserm. Within Institut Pasteur de Lille, they form the Interdisciplinary Research Centre for Longevity (CTRL). This Interdisciplinary Research Centre for Longevity

implements a wide variety of complementary heuristic approaches, used to create numerous links between epidemiological research (from the many cohorts of "control subjects" and patients which they have formed), mechanistic and drug discovery (thanks to the many cell and animal models of diseases they have developed) and disease prevention strategies (thanks to the unique disease prevention infrastructure that hosts 15,000 men and women each year).

- 01 RISK FACTORS AND MOLECULAR DETERMINANTS OF DISEASES LINKED TO AGEING**
- 02 INTEGRATIVE GENOMICS AND MODELLING OF METABOLIC DISEASES**
- 03 NUCLEAR RECEPTORS, CARDIOVASCULAR DISEASES AND DIABETES**
- 04 TRANSLATIONAL RESEARCH ON DIABETES**
- 05 "CENTRE D'INFECTION ET D'IMMUNITÉ DE LILLE" (LILLE INFECTION AND IMMUNITY CENTRE)**
- 06 HETEROGENEITY, PLASTICITY AND RESISTANCE TO CANCER THERAPIES**
- 07 IMPACT OF THE CHEMICAL ENVIRONMENT ON HUMAN HEALTH**
- 08 MEDICINES AND MOLECULES FOR ACTING ON LIVING SYSTEMS**

It works with the Centre for Health and Longevity which receives the public and designs, implements and evaluates all the disease prevention activities, in collaboration with the hospitals of the Hauts-de-France region. Diabetes-related preventive measures are conducted within the National Centre for Precision Medicine, called "Précidiab", in collaboration with several hospitals in Hauts-de-France.

EXCELLENCE IN RESEARCH AT THE HEART OF THE PROJECT

- 12** In 2015, the Institut Pasteur de Lille created the Interdisciplinary Research Centre for Longevity where scientists are engaged in basic and applied sciences to find the means to promote healthy ageing by understanding, preventing and treating the diseases linked to ageing. Because sustained homeostasis at every level (e.g. genome, endoplasmic reticulum (ER), mitochondria, cell, organ, organism) is the determining factor in the internal stability of organisms over time, our ability to cope with a variety of potential endogenous or exogenous stressors is the key to the stability of our organism and to keeping it at its highest functional level.

Healthy ageing is possible by limiting exposure to preventable stressors and improving resistance and resilience to unavoidable stressors. One of the main objectives of our teams is therefore to identify the critical stress factors and their effects on the functions of cells, organs and organisms, as well as to understand the (patho)-physiological processes (sensors and effectors) triggered in response to stressors, especially during the prodromal phase when functional losses are too low to have a detectable effect on health. Theoretically, these early mechanisms are

the most effective targets for therapeutic or preventive intervention. It is these early alterations (vulnerabilities which are not yet pathological) that the Centre for Health and Longevity detects in "subjects" coming for consultation to offer them personalised disease prevention protocols in several areas (sensory, cognitive, metabolic, skeletal, muscular). Together, the teams at Institut Pasteur de Lille are studying the essential categories of genetic, infectious, nutritional, environmental and behavioural stressors. They characterise the structure, functions and their impact on



the molecular and cellular biology of various target systems (neurological, immune, metabolic, neurological, respiratory, etc.) as well as the integrated response of the organism as a whole through long-term *in vivo* studies. Regarding the latter, we know that the role of hormonal, metabolomic, immune and inflammatory responses is crucial. The importance of research in metabolism and immunology on the Campus is an important advantage. Regarding the study of cancerisation mechanisms, the institute will prioritise research into the processes that link primary stressors, senescence, fibrosis and cancer.

The teams follow complementary heuristic approaches, ranging from observational sciences (structural biology, Genome Wide Association Study (GWAS), phenotyping, approaches associated with systems biology) to interventional life sciences (such as *in vitro* and *in vivo* pharmacology, microbiology, toxicology and chemical sciences (drug design, chemical biology, exploration of chemical diversity, development of new chemical syntheses, immunomodulation and vaccines). By working on models of the disease, the latter establish the causal role of the determinants identified by observational sciences.

The continued development of excellence for the benefit of Institut Pasteur de Lille project depends on the connection between the observational sciences and interventional activities on models

of disease and, ultimately, the human and social sciences. Indeed, they have radically different "business models". For example, genomics research requires a substantial initial investment to create and maintain cohorts, but then produces results on an ongoing basis. As for the "hypothesis driven", mechanistic and interventional studies needed to confirm the causal role of candidate genes or to further characterise biological or pathological processes, they can be very slow and require a lot of work. The institute should increasingly turn to strategies or technologies that are likely to bridge the "productivity" gap (such as high throughput technologies, non-mammalian intermediate models, organoids, etc.) Further downstream, the institute's project has already aroused the interest of several researchers in the field of human and social sciences (HSS) and their integration within the context of the project has begun. Visions on research objectives that are shared with disease prevention and the biomedical sciences is necessary to ensure effective collaboration.



In terms of academic disciplines, the strength of the Institut Pasteur de Lille campus resides in the close contacts that exist between biologists, chemists, physicists and specialists in scientific data and public health. The creation and maintenance of productive interfaces between disciplines is essential to the creation of new concepts, research tools and, ultimately, having an impact in society. The main challenge is to define a scientific question that is common to scientists from different disciplines and to avoid the usual customer/supplier relationship. Long-term relationships between chemists and biologists are particularly important in the field of drug discovery. All means of interpersonal, formal or informal cultural exchanges must be practised on the campus.

Translational research also feeds into basic research. Downstream from the study of biological processes, the research includes translational activities in the discovery and prevention plans of drugs and vaccines directly related to our basic

science activities. It should be noted that in several cases, translational projects on the discovery of vaccines and drugs have also facilitated new discoveries and the implementation of key fundamental programmes leading to articles in the most highly reputed journals. The same type of links will be established between the disease prevention research and HSS applications.

It is worth bearing in mind that the competitiveness of the researchers in the life sciences and healthcare is increasingly dependent on cohorts and advanced observation tools such as genomics, transcriptomics, proteomics as well as imaging, HCS/HTS, mass spectrometry, immunophenotyping, libraries of siRNA compounds, etc. on the one hand, and the processing of bio- and chemo-computer data on the other hand. The campus teams have access to all of these tools, through several Equipex platforms in particular.

KEY FACTORS OF SUCCESS OF THE PROJECT

As with any organisation that bases its work on research, the 4 key factors of lasting success are the attractiveness (and influence), the creativity (risk taking) and the willingness to translate discoveries into innovative health products and unite its ecosystem. It is with the aim of enhancing these factors of success that the foundation's project is directing the actions conducted on the existing capital.

- 01 Attractiveness:** increasing and renewing human potential.
- Academic excellence (increasing the influence of the 3 Labex and 2 Equipex of the campus);
 - International influence and exposure;
 - Attractive (i.e. competitive) environment for young researchers;
 - Attracting competitive funding (Horizon Europe, European Research Council (ERC), National Institute & Health (NIH), Bill & Melinda Gates Foundation, etc.)
 - Increasing scientific potential by adding to the institute's resources in HSS, including in the behavioural sciences and in health economics.

02 Creativity: the institute must cover the risk of the researcher, by promoting interdisciplinary research in particular. Indeed,

this presents an additional obstacle to the deepening of monodisciplinary research and a risk for careers and the team, which is often associated with a higher probability of breakthrough discoveries and is essential in translational research.

03 Willingness to translate discoveries into innovative and useful health products: marketing them will be a driver of economic growth for the institute, as has been the case twice in the past (CEREP, now Eurofins, and GENFIT).

04 Uniting: In addition to these elements related to the scientific integration of activities, Institut Pasteur de Lille must also unite all the stakeholders associated with its activities: healthcare players (CNAM, ARS, Ministry of Health, private social welfare players, hospitals, etc.), economic and industrial players.

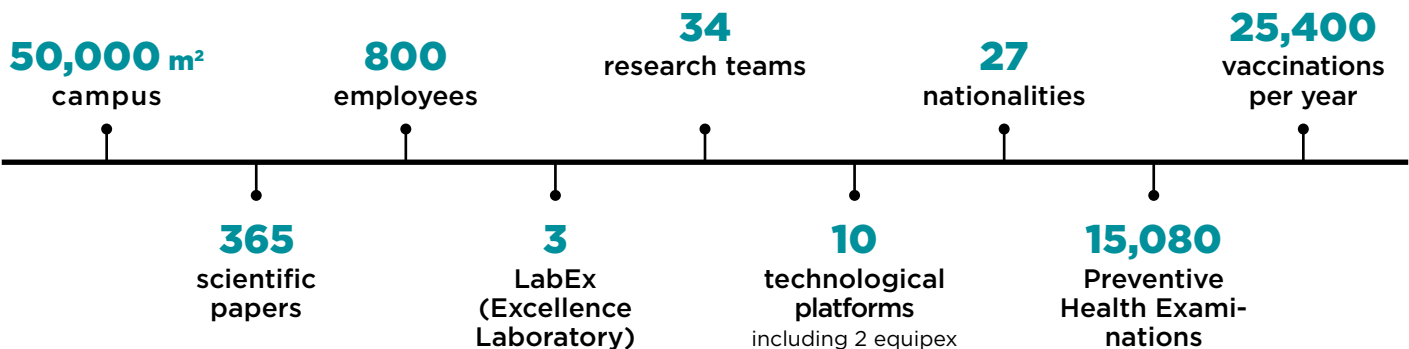
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Institut Pasteur de Lille supports its research teams (management, help with the preparation of files, accommodation, scientific staff, investment and maintenance in platforms) and stimulates interdisciplinary research by funding cross-sector activities between the teams from various disciplines (chemistry, biology, physics, medicine, disease prevention) but also by studying diffe-

rent organs or diseases, which present identical, comparable or interdependent pathophysiological mechanisms, e.g. fibrotic mechanisms. One of the priority interdisciplinary bridges is research on disease prevention, with the participation of researchers in the human sciences, biologists, doctors and paramedical staff.



KEY FIGURES



THE DNA OF INSTITUT PASTEUR DE LILLE

RESEARCH

661

researchers and technicians on campus
epidemiology / genetics / pharmacology /
biochemistry / chemistry

1 500

articles (over 5 years)

8

research units A/A+
working towards a common
goal

5,000

citations/year

TIES WITH THE ECONOMIC WORLD

44

active families
of patents

6

start ups

2

medicines
under development

PUBLIC HEALTH ACTIONS

15,000

consultations/year



15

INTERNATIONAL SCIENTIFIC COLLABORATIONS



Imperial College London
University of London
Harvard University
Helmholtz association
University of Oxford
University of Cambridge
Univ Oxford
University College London



Erasmus University
Rotterdam



University of Helsinki



Ghent University



Spain



National institutes of health
NIH USA
University of California
System
Boston University
Boston Univ
VA Boston healthcare
system
Washington State University



Helmholtz Center Munich



Italy



Estonia



Karolinska Institutet



Japan



Switzerland



INTERNATIONAL RELATIONS

Institut Pasteur de Lille is a leading research player and is developing relationships with organisations in different countries to share knowledge and speed up research.

Since November 2018, Institut Pasteur de Lille has been representing and coordinating the Europe region within the "Réseau International des Instituts Pasteur" (international network of Pasteur institutes) under a 3-year mandate.

In 2019, in coordination with the "Institut Pasteur Hellenique", the institute organised a meeting of the institutes of the RIIP Europe region in Athens from 4 to 5 September 2019. The 7 European institutes (Lille, Paris, Brussels, Saint Petersburg, Sofia, Rome and Athens), represented by their directors, scientific directors and researchers, presented the strategies, technological platforms and resources of each institute. Two major scientific topics were selected for the Europe region: **antimicrobial resistance** and **neurodegenerative**

diseases. The mission of Institut Pasteur de Lille is to make progress with these two topics within the network at the level of the Europe region. During this meeting, Jérôme Weinbach, European adviser to the health managing director at the Ministry of Solidarity and Health, made a speech presenting the health priorities of the European Commission within the framework of the future Horizon Europe programme.

From 12 to 15 November 2019, the directors of the 32 RIIP institutes met at the Pasteur Centre in Yaoundé in Cameroon to review the RIIP's activities and its outlook for the future. This meeting also involved discussions on the creation of new partnerships, regulations around the sharing of samples, as well as several scientific priorities of the network including antimicrobial resistance. Each RIIP region put forward a short and medium-term action plan on the topics that are specific to each region (antimicrobial resistance and neurodegenerative diseases for Europe).

COLLABORATING AT THE INTERNATIONAL LEVEL TO SPEED UP RESEARCH

A bilateral meeting was organised on 28 November 2019 between 2 close neighbours of the RIIP: Institut Pasteur de Lille and Sciensano, its Belgian counterpart resulting from the merger of the ISP (Scientific Institute of Public Health) and the CERVA (Centre for Veterinary and Agrochemical Study and Research). The objective of the meeting was to gain a better understanding of the strengths of each institute, highlight the complementary strengths and initiate interactions between the researchers of both institutes in the field of infectious diseases and antimicrobial

resistance. Researchers from Institut Pasteur de Lille met their Belgian counterparts to initiate various scientific collaborations.

A key formative event of the longevity project of Institut Pasteur de Lille was the 3rd International Symposium on Longevity, which was held in December to address the subject of "Fundamental science at the service of good health throughout life: disease prevention and treatment of age-related diseases". More than 130 international scientists participated in this event.



Le Réseau International des Instituts Pasteur

Une communauté humaine et scientifique mondiale unie par des valeurs et des missions communes au service de la santé.

Réseau International
des Instituts Pasteur

32
INSTITUTS MEMBRES

25
PAYS

23 000
PERSONNES



AMÉRIQUE
Fiocruz (Rio de Janeiro)
INRS-Institut Armand-Frappier (Laval)
Institut Pasteur de la Guayane (Pointe-à-Pitre)
Institut Pasteur de Montevideo

EUROPE
Institut Pasteur d'Italie - Fondation Cenci Bolognietti (Rome)
Institut Pasteur hellénique (Athènes)

Institut Pasteur de Lille
Institut Pasteur (Paris)
Institut Pasteur de Saint-Petersbourg
Sciensano (Bruxelles)
Institut Stephan Angeloff (Sofia)

MAGHREB-IRAN
Institut Pasteur d'Algérie (Alger)
Institut Pasteur d'Iran (Téhéran)
Institut Pasteur du Maroc (Casablanca)
Institut Pasteur de Tunisie

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Present in 25 countries across all the continents, the International Network of Instituts Pasteurs (RIIP) groups 32 institutions united by common missions and values for the benefit of the general public. Notably installed at the heart of

numerous endemic disease zones, the RIIP has, on multiple occasions, demonstrated its major role as a sentry in the face of infectious emergencies.

DRIVEN BY THE ETHICS AND RESPECT
FOR INSTITUT PASTEUR'S CORE VALUES,
THE INTERNATIONAL NETWORK OF
INSTITUTS PASTEURS ENDEAVOURS TO
IMPROVE HUMAN HEALTH.

RESULTS OF THE 3RD COLLABORATIVE AND EXPLORATORY CPER-CTRL CALL FOR PROJECTS 2018

In order to support interdisciplinary projects on longevity, Institut Pasteur de Lille is coordinating the CPER-CTRL programme for the 2016-2020 period (State-Region plan contract - Interdisciplinary Centre for Research on Longevity) funded by the state, the Hauts-de-France Region, the Métropole Européenne

de Lille (MEL) and the ERDF fund. The CPER-CTRL calls for projects aim to promote cooperation between teams in the region on new issues related to longevity as well as the emergence of new teams.

Following the 3rd CPER-CTRL call for projects launched in December 2018, 25 projects have been received and 11 projects were selected for funding after evaluation by independent experts and by the International Scientific Council (CSI).

EXPLORATION PROJECTS (€50K)

PROJECT NAME	APPLICANTS	PROJECT TITLE
CIRCASTHMA	Anne TSICOPOULOS/CIIL Hélène DUEZ/UMR1011	Circadian clock of the lymphoid cells of the lungs and severity of asthma
VIROPEX	Yves ROUILLE/CIIL Yasmine SEBTI/UMR1011	Study of the interaction between peroxisomes and hepatitis C virus replication complexes: impact on cell metabolism and oxidative stress

COLLABORATIVE PROJECTS (€200K)

PROJECT NAME	APPLICANTS	PROJECT TITLE
LivFib	Jérôme EECKHOUTE/UMR1011 Laurent DUBUQUOY/U1286	Transcriptional control of the hepatic stellate cell activation associated with hepatic fibrosis
ProActiv-2	Ruben Hartkoorn Alain Baulard/CIIL Nicolas Willand/U1177 Elisabeth Pradel/U1286	Activation of Pro-Antibiotic-2
SynapseScreen	Devrim KILINC/U1167 Sophie HALLIEZ/U1172	Medium-throughput screening based on co-cultures of neurons in microfluidic chambers for physiologically relevant synaptic toxicity
MELODY	Jean-Sébastien ANNICOTTE/ UMR8199 Benoît POURCET/UMR1011	Role of E2F1 in the loss of β cell function linked to inflammation during ageing

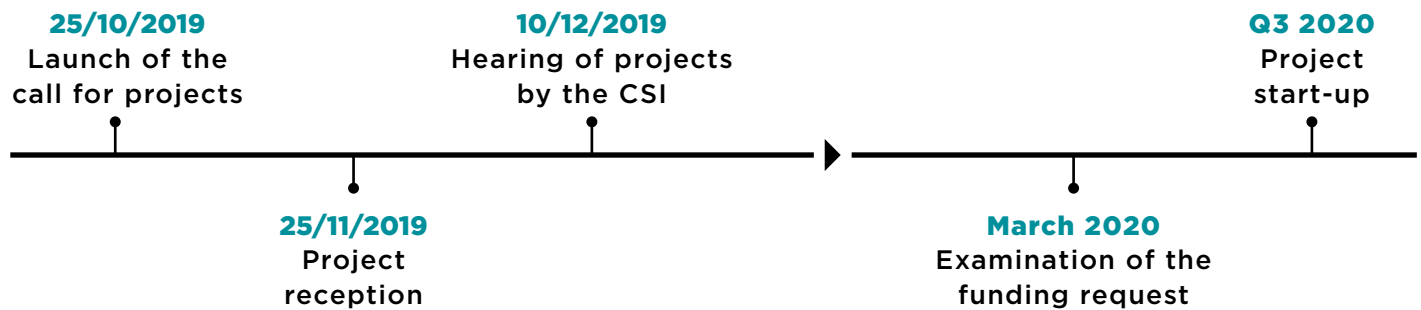
COLLABORATIVE PROJECTS (€90K)

PROJECT NAME	APPLICANTS	PROJECT TITLE
COMMONLY	Muriel Pichavant/CIIL Florence Pinet/U1167	Smoking and obesity: multi-organ impact of metabolic reprogramming in longevity
DESTRESS-Flu	Isabelle WOLOWCZUK/CIIL Steve LANCEL/U1167	Consequences of the induction of endoplasmic reticulum stress in white adipose tissue during infection with the influenza virus on the severity of infection in the elderly
ClockMuscleAging	Alicia MAYEUF-LOUCHART/ UMR1011 Pierre DOURLIN/U1167	Circadian regulation of muscle regeneration during ageing: a complementary approach in mice and drosophila
IDE-NASH	Rebecca DEPRez-POULAIN/ U1177 Nathalie HENNUYER/UMR1011	Modulation of the UPR response by IDE: consequences on inflammation, steatosis and ageing in NASH
FATeNASH	Réjane PAUMELLE/UMR1011 Albin POURTIER/UMR8161 Guillaume LASAILLY/U1286	Role of FAT10 in hepatocyte senescence: impact in the development of NASH

LAUNCH OF THE 4TH CPER-CTRL (PHASE 4) CALL FOR PROJECTS

In October 2019, Institut Pasteur de Lille launched the **4th CPER-CTRL call for research projects**. Each project submitted must be presented by 2 teams from different units and be part of one

of the 2 objectives of the Longevity research project. This call for projects is for the funding of collaborative projects and exploratory projects.



CPER-CTRL FINANCING



AN INTERNATIONAL SCIENTIFIC COUNCIL

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**SPEEDING UP
RESEARCH FOR
BETTER HEALTH
TOMORROW**

02

LONGEVITY: INTERDISCIPLINARY TEAMS FOR EXCELLENCE IN RESEARCH

Institut Pasteur de Lille hosts a centre for research on longevity divided into eight units¹, with multidisciplinary, cross-sector skills. This inter-disciplinary research programme which mobilises all Institut Pasteur de Lille teams aims to identify and characterise the genetic, environmental, metabolic, and infectious factors which contribute to lowering the functional performance of cells and the organism, which is what we call ageing. This then makes it possible to prevent exposure to these factors, or to reduce their impact by stimulating the resilience of cells and the organism with the assistance of innovative prevention strategies or treatment.

- 01 Risk factors and molecular determinants of diseases linked to ageing**
- 02 Integrative genomics and modelling of metabolic diseases**
- 03 Nuclear receptors, cardiovascular diseases and diabetes**
- 04 Translational research on diabetes**
- 05 Centre d'Infection et d'Immunité de Lille (Lille infection and immunity centre)**
- 06 Heterogeneity, Plasticity and Resistance to Cancer Therapies²**
- 07 Impact of the chemical environment on human health**
- 08 Medicines and molecules for acting on living systems**

Over the past ten years, these teams have endeavoured, together with their research partners, to get structured around excellence laboratories and facilities financed as part of the "PIA" (investment programme for the future), including:

- a LabEx dedicated to Alzheimer's disease (DISTALZ)
- a LabEx dedicated to studying diabetes (EGID)
- a research centre on infection and immunity (CIIL) involved in the ParaFrap LabEx
- an EquipEx dedicated to cellular imaging pharmacological screening (IMAGINEX BIOMED)
- an EquipEx dedicated to genomics (LIGAN-PM)

Institut Pasteur de Lille's campus boasts an exceptional concentration of high level facilities and technology platforms to serve all the researchers in the regional scientific community. It also has the largest molecule library in Europe – the chemical library – where thousands of tests are conducted every year, helping in the discovery of new prescription drugs.

¹On 1st January 2020

²On 1st January 2020, thereby replacing the Mechanisms of Tumorigenesis and Target Therapies (M3T) unit

RISK FACTORS AND MOLECULAR DETERMINANTS OF AGING-RELATED DISEASES

This unit focuses on the fight against age-related diseases, such as cardiovascular and neurodegenerative diseases. Prof Philippe Amouyel coordinates the DISTALZ laboratory of excellence, dedicated to Alzheimer's disease.

Three teams interact on the "epidemiology and public health of age-related diseases", the "molecular determinants of heart failure and ventricular remodelling", and on the "molecular

determinants of Alzheimer's disease and cognitive disorders". Each of these teams gained international recognition in the field of age-related diseases with a great openness to the general public in terms of disease prevention for successfully extending the life expectancy of everyone in good health.

PROF PHILIPPE AMOUYEL

MD PhD, University Hospital (CHU) of Lille
UMR1167 - Labex DISTALZ University of
Lille, Inserm, University Hospital of Lille,
Faculty of Medicine, Institut Pasteur de Lille.

DISSECTING THE RISK FACTORS TO EXTEND THE LIFE EXPECTANCY OF EVERYONE IN GOOD HEALTH

This team, led by Dr Aline Meirhaeghe, analyses the role of cardiovascular risk factors in the onset and progression of cardiac and cerebrovascular accidents and intellectual function disorders. Our work is based largely on recording all cases of cardiac and cerebrovascular accidents that occur in the region of Lille and its surroundings.

DETECTION OF CARDIAC AGEING IN ORDER TO ANTICIPATE IT MORE EFFECTIVELY

After a heart attack, the heart is often no longer able to eject enough blood to meet the body's need for oxygen, which causes heart failure. Dr Florence Pinet, who leads this team, is looking for the early markers of heart failure. She developed bedside clinical research protocols that she used to discover early biological markers of left

ventricular remodelling associated with heart failure to ultimately prevent this accelerated ageing of the heart.

DECIPHERING THE GENOME TO BETTER UNDERSTAND ALZHEIMER'S DISEASE AND FIGHT IT MORE EFFECTIVELY

Alzheimer's disease is a disorder of the brain that develops over several decades. The team led by Dr Jean-Charles Lambert is interested in studying the susceptibility we all have for Alzheimer's disease. In this way, we have identified the majority of genes involved in the onset of this disease. Our research should result in the development of new avenues of treatment and prevention.



KEY EVENTS

1 Heart diseases and cerebrovascular diseases are inextricably linked.

Using data from the Lille registers of ischemic heart diseases and strokes, we compared different indicators of these diseases in men and women aged from 35 to 74 between 2008 and 2014. We found that the heart attack rates exceeded the stroke rates, especially in men. The death rate was 2.2 times higher for heart attacks than for strokes, regardless of the age and sex of the patients. The same was true of the fatality rate (percentage of people who die after a heart attack or stroke) which was 1.5 times higher for heart attacks than for strokes (Meirhaeghe et al Bull Epidemiol Hebd. 2019)

2 Heart failure remains one of the leading causes of death worldwide.

We identified the proteins in our blood that could predict premature death, within 3 years, among the patients with heart failure hospitalised at the Lille University Hospital. The patient's blood proteins were analysed using nanotechnologies (SOMAscan Slow Off-rate Modified Aptamer technique). This was used to identify 203 proteins that were modulated differently between the patients who died from cardiovascular death and those who were alive 3 years after the onset of their heart failure. We finally selected six proteins: C3 complement, cathepsin S, MAPK5, MMP1 and MMP7 to predict the risk of early death in these patients (Cuvelliez et al, 2019).

3 To characterise individual susceptibility to Alzheimer's disease, we need to compare the genomes of several thousand patients and controls.

This is the thinking behind our decision to increase the size of our samples by 25% (nearly 100,000 individuals in total) in 2019. This resulted in our discovery of five new genes supporting the involvement of APP metabolism and the Tau proteins that make up disease lesions in the brain (Kunkle et al, Nat Genet, 2019). We are also continuing to expand our working samples with the European project EADB (European Alzheimer Disease Biobank), which we coordinate and which doubles the number of subjects studied and the ADES (Alzheimer Disease Exome Sequencing) project on the analysis of exomes of nearly 12,000 patients and 10,000 controls. Thanks to this unique access to the largest genomic study in the world, we will be able to identify new avenues in the fight against this disease more quickly.



INTEGRATIVE (EPI)-GENOMICS AND MODELLING OF METABOLIC DISEASES

UMR8199 included two teams:

1 | "Genetic and Epigenetic of diabetes and obesity" co-directed by **Philippe Froguel** and Amélie Bonnefond, and 2 | "Molecular bases and modelling of metabolic diseases" directed by Jean-Sébastien Annicotte. It counts 63 individuals, researchers,

teachers, docs/post-docs, engineers, and technicians. The unit is at the origin of LabEx-EGID and of EquipEx-LIGAN-PM, the genomic platform for personalised medicine.

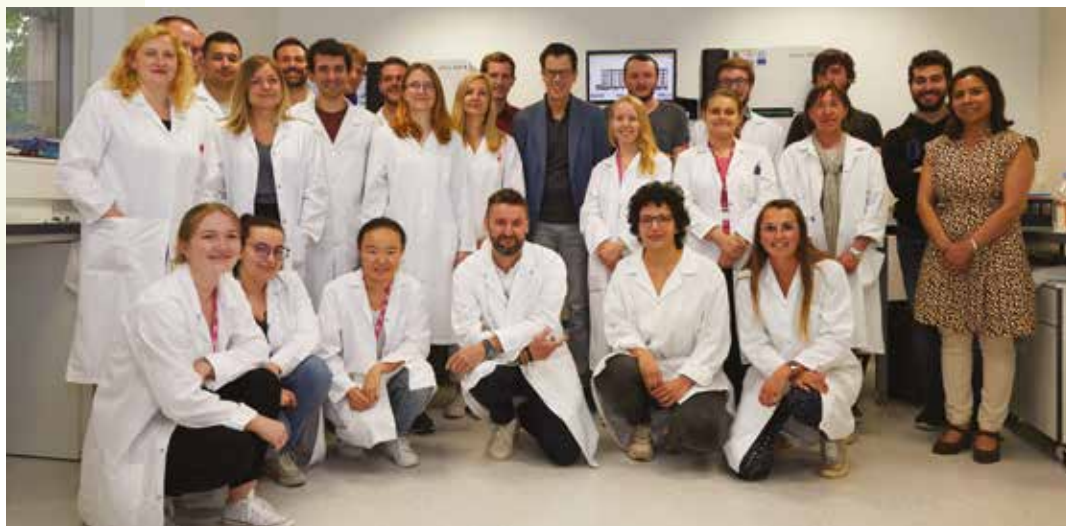
PROF PHILIPPE FROGUEL

PU-PH - Lille University, Lille University Hospital, LabEx, UMR8199, EGID, CNRS, Institut Pasteur de Lille, Lille University

UMR8199 aims to understand the genetic and pathophysiological mechanisms at the origin of diabetes and obesity in order to make progress towards personalised medicine for metabolic diseases.

The unit's research objectives are **to identify new genes implicated in diabetes and obesity, and to better diagnose forms of diabetes and obesity of genetic origin** which thus allows **personalised medicine** according to genetic sub-type. All projects also have as an objective to better stratify genetic and environmental risk factors, and the primary genetic causes, of metabolic diseases at different ages in life. Different "multi-omic" approaches were taken by means of our genomic platform which is unique in France (high-speed DNA and RNA sequencing, genotyping, and transcriptomic analysis by DNA chips, digital molecular counting using NanoString technology). Opening the LIGAN-PM platform to outside teams makes it possible to initiate collaborative research projects on other genetic diseases such as intellectual deficiencies associated, or not, with obesity, Crohn's disease, breast and ovarian cancers (using exome sequencing). The unit is a partner to several EU-H2020 Innovative Medicines Initiative programmes : IMIDIA (Improving beta-cell function and identification of diagnostic biomarkers for treatment monitoring in Diabetes), DIRECT (Diabetes research on patient stratification) and

RHAPSODY (Risk assessment and progression of diabetes); as well as at the Research University Hospital (RHU). PreciNASH (PIA-ANR, coordinated by François Patou, UMR1190). In these projects, our teams have a key role in producing and analysing (epi)genomic, transcriptomic data, or derivative microbiomes, starting with large European cohorts of diabetic and/or obese patients and control populations (including human samples selected from pancreatic, hepatic, or muscular tissues). The environment's epigenetic effects (which modify genetic activity) on the metabolism and hepatic and renal complications of diabetes are studied, consequently epigenetic variations in pre-diabetic conditions such as gestational or premature diabetes (EPx-GDM and EPIPRETERM projects). Thanks to the UMR8199's organisation, which is divided up between two teams, **new pathways can be identified leading to metabolic diseases**, after which cellular or animal models can be established in order to conduct in-depth studies leading to the development of **new diagnostic and therapeutic strategies**. Beyond that, the goal of the European Genomic Institute for Diabetes (EGID) is to offer optimal conditions for translational research on diabetes to truly ameliorate treatment of diabetics and their life.



KEY EVENTS

1 Genetic factors play an important role in the development of obesity with a heritability of about 70%. About 5% of obese patients in France have a "rare" form of obesity known as monogenic. We discovered a new form of monogenic obesity which has the unique characteristic of leading to diabetes and early hypertension, opening up diagnostic and therapeutic perspectives. Loss-of-function mutations in MRAP2 are pathogenic in hyperphagic obesity with hyperglycaemia and hypertension. *Nat Med.* 2019 Nov; 25 (11): 1733-1738. Baron et al.

2 Common obesity is very polygenic, a feature which was established in 2007 by the Lille team: currently nearly 400 genes contribute modestly to the risk of obesity. We show that the most common obesity genes are preferentially expressed in the brain. The surprise of this study is the lack of preferential expression of common obesity genes in the part of the brain that controls hunger, i.e. the hypothalamus. On the other hand, we find an enrichment of these genes in regions of the brain involved in the reward and addictions mechanisms. *The expression of genes in top obesity-associated loci is enriched in insula and substantia nigra brain regions involved in addiction and reward.* Ndiaye et al.

3 Our UMR managed the Lille application that brought together the University of Lille, Institut Pasteur de Lille, Inserm and the CNRS for the contest of the Future Investment Programme of University Hospital Institutes 2. An international panel of judges selected our PreciDIAB project which, thanks to funding from the state and local authorities (Métropole Européenne de Lille and Hauts-de-France region) obtained €23m for a period of 5 years with the objective of developing personalised medicine for diabetics within the framework of the new National Centre for Precision Medicine (PreciDIAB).

4 In collaboration with AptamiR, a biotechnology company recently established in the Lille agglomeration in the Eurasanté incubator, the MetaboMIR industrial chair project entitled "**Identification of new therapeutic targets and their mode of action for the treatment of obesity, type 2 diabetes and non-alcoholic fatty liver disease**", funded by the Métropole Européenne de Lille and I-SITE, aims to identify and validate new therapeutic targets with good potential for technological transfer and their modes of action in order to ultimately generate new treatments against certain metabolic diseases in humans, including diabetes, obesity and "NFALD/NASH" non-alcoholic fatty liver disease.

5 Our goal was to identify genomic sites where the genotype significantly affects the expression of genes located nearby within the genome. Our study identified novel genes for type 2 diabetes (T2DM) and eQTLs that have not yet been studied in the context of beta cell biology: their study will explain the pathophysiology of T2DM more effectively. *Laser capture microdissection of human pancreatic islets reveals novel eQTLs associated with type 2 diabetes.* *Mol Metab.* 2019 Jun; 24: 98-107 Khamis et al.



NUCLEAR RECEPTORS, METABOLIC AND CARDIOVASCULAR DISEASES

UMR1011 studies the pathophysiological mechanisms at the molecular and cellular level, in preclinical models and in humans, at the origin of obesity, type-2 diabetes and its cardiovascular (atherosclerosis, heart failure, valvular diseases) and hepatic complications (NASH).

The impact on the immune system of circadian

and epigenetic alterations. Therapeutic approaches centred on nuclear receptors are implemented.

PR BART STAELS

PU-PH - Lille University, Lille University Hospital, U1011, Inserm, Lille University, Institut Pasteur de Lille, Lille University Hospital

Metabolic pathologies such as obesity and type-2 diabetes and their cardiovascular complications are the primary cause of death not only in industrialised countries but also in developing countries. Using fundamental and translational approaches, UMR1011 studies the physio-pathological processes at the origin of these pathologies with a particular interest for the nuclear receptors which represent choice therapeutic targets.

Over the course of 2019, **major breakthroughs touched on the role of the Rev-erb α nuclear receptor, a major regulator of the circadian clock in controlling acute inflammatory reactions in mice (hepatitis) and cardiovascular**

complications further to myocardial surgery in humans. The receptor's molecular action mechanism at the hepatic level was also specified.

The contribution of other nuclear receptors and, more generally, transcription factors to hepatic functions was also highlighted (PPAR δ in septic shock, FXR, bile acid receptor, in the control of neoglucogenesis and diabetes). Finally, we have interpreted a new cellular mechanism for the formation of brown adipose tissue.

Unit 1011 published **over the course of 2019.**



KEY EVENTS

1 We have identified the transcriptional and immune signatures associated with the transition from benign steatosis to non-alcoholic steatohepatitis (NASH) in humans. We have shown an enrichment in genes related to inflammatory responses, antigen presentation and cytotoxic cells. We have identified alterations in immune blood populations. Lobular inflammation and the presence of "bloated" cells correlate with the accumulation of hepatic CD8 T lymphocytes. In addition, the progression of NASH in a mouse model caused by the diet induces a hepatic signature associated with the immune system and an accumulation of intrahepatic cDC and CD8 T-cells which could represent a therapeutic target in NASH.

2 Following a transcriptomic analysis carried out using valve interstitial cells (VIC) derived from healthy and fibrocalcified human aortic valves, we were able to identify an enzymatic target of interest and its signalling pathway (retinoic acid pathway) in aortic valve stenosis (AVS). We are studying the impact of the modulation of this pathway on the fibrocalcification of VICs and in an experimental model of a xenograft in sheep. We are continuing our work to characterise the Von Willebrand factor (VWF) as a biomarker for flow abnormalities in heart disease with high shear forces induced by AVS and have shown that VWF analysis is a key element in the clinical decision process, in addition to the usual clinical and imaging assessment.

3 We have shown that the innate responses of TLR-dependent dendritic cells (DCs) are exacerbated by high concentrations of fatty acids (FA). The FA inhibits TLR-induced glycolysis and disrupts the metabolism of the Krebs cycle. These changes increase the mitochondrial production of ROS (mtROS) and, consequently, the UPR (Unfolded Protein Response) leading to a unique transcriptome signature, with IL-23 as a characteristic marker. Specific inactivation of XBP1 within DC attenuates IL-23 expression and skin inflammation in a model of psoriasis. This international study therefore explains the mechanisms explaining the exacerbation of immuno-inflammatory pathologies such as psoriasis by a diet that is too rich in fat.

4 Statins are very widely used in the prevention of cardiovascular disease by correcting abnormally high levels of LDL-cholesterol. Their use increases the risk of developing type 2 diabetes, while the mechanism for this is not understood. By studying the hepatic transcriptome of a cohort of 910 patients treated or not treated with statins, it appeared that the increase in de novo lipogenesis is a mechanism that contributes to this process. This effect is observed regardless of the statin used and suggests that the dyslipidaemia observed in patients at high risk of developing type 2 diabetes should be treated with drugs of a different class.

5 Unlike white adipose tissue, the build-up of which is responsible for obesity, brown fat helps generate heat by burning calories. This tissue therefore represents an interesting target in the context of the development of therapies aimed at treating obesity and diabetes. In order to better understand how it works, we conducted a study aimed at characterising its formation during embryonic development. Our research revealed that the formation of lipid droplets requires an intermediate storage of glycogen, which is then degraded by glycophagy. This discovery could promote the development of new therapeutic strategies targeting the formation of glycogen in order to promote the formation of beneficial brown fat.



CENTER FOR INFECTION AND IMMUNITY OF LILLE (CIIL)

Microbial and parasitic infections as well as inflammatory diseases are major causes of mortality and morbidity. Their long-term impact on other conditions, such as cancer, cardiovascular, metabolic and neurodegenerative diseases, is considerable. The 14 CIIL teams develop multidisciplinary projects that combine fundamental, translational and clinical or field-based research on major public health topics: infectious diseases (tuberculosis, pneumococcal pneumonia, whooping cough, plague, hepatitis C and E, influenza, coronavirus, malaria, schistosomiasis, toxoplasmosis, cryptosporidiosis and blastocystosis) and chronic inflammatory diseases of non-infectious origin such as chronic

obstructive pulmonary disease and asthma which has a particularly high incidence in the Hauts-de-France region and which is on the increase in industrialised countries. The objectives of the CIIL are to dissect host-pathogen interactions as well as the mechanisms leading to chronic respiratory diseases and to develop innovative approaches in the diagnosis, treatment and prevention of these diseases while analysing their impact in the field.

DR CAMILLE LOCHT

Inserm research director UMR 8204 - U1019, CNRS, Inserm, University of Lille, Institut Pasteur de Lille

SINCE 1ST JANUARY 2020

DR JEAN DUBUISSON

Inserm research director UMR 8204 - U1019, CNRS, Inserm, University of Lille, Institut Pasteur de Lille

THE YEAR 2019 WAS MARKED BY:

The identification of new unexpected functions for the GTPase RAB11A protein of the parasite, called *Apicomplexa Toxoplasma gondii*, including its key role in the mobility/adhesion of the parasite to the host cell, which are two essential activities for the invasion of the host cell and, therefore, for the virulence of this parasite.

The discovery of a protein involved in host-parasite interactions in the context of schistosomiasis. This protein potentially plays a role in the reproduction and development of the invertebrate host of *Schistosoma mansoni*.

The demonstration of an autophagy pathway involved in the internalisation of Plasmodium microvesicles by astrocytes and of the pro-inflammatory response of the microglia, leading to the recruitment of cytotoxic lymphocytes in the brain and to the deterioration of the blood-brain barrier during cerebral malaria.

The demonstration that increased bacterial diversity is observed in the faecal microbiota of patients infected with *Blastocystis*, indicating that colonisation by this parasite is associated with a

favourable microbiota rather than dysbiosis.

The demonstration that the intestinal dysbiosis associated with an antibiotic treatment induces a deep immunosuppression of the pulmonary immune cells responsible for a susceptibility to infection, particularly in relation to *Pseudomonas aeruginosa*. This defect involves an alteration in the development of monocytes and macrophages in the bone marrow which can be corrected by a faecal microbiota transplant.

The creation of a mathematical model suggesting that the outbreaks of plague epidemics followed by lulls would be the result of a selection of strains of *Yersinia pestis* with variable flea transmission abilities.

The demonstration of the intrinsic antibacterial activity of nanoparticles composed of β -Cyclodextrins and the potentiality of their anti-infectious effect as a nano-carrier against tuberculosis.

Demonstration of an aberrant antiviral response of natural killer (NK) cells in severe asthma. More particularly, it has been shown that, following an infection by a rhinovirus, the NK cells exhibit a phenotype of exhaustion in the event of severe asthma. In addition, it seems to participate in the worsening of the exacerbation of virus-induced asthma in these patients.

Demonstrating the ability to map intracellular organelles and microorganisms by atomic force microscopy.

Demonstration that the C-terminal domain of the MERS coronavirus membrane protein contains a localisation signal in the trans-Golgi network. This subcellular location is important for viral assembly.

The launch of phase 2a and 2b clinical studies for the evaluation of the live attenuated vaccine, BPZE1, delivered intranasally against whooping cough. These trials are supported by ILIAD Biotechnologies (USA).



KEY EVENTS

1 Jean-Claude Sirard's team obtained funding for a European research programme of €10 million to combat respiratory infections.

The objective of this programme is to use a bacterial protein, called flagellin, to stimulate the immune system in order to combat the bacteria that infect the respiratory tract more effectively. Administered to the respiratory mucosa, flagellin prevents infection with pneumococcus, a bacterium responsible for community-acquired pneumonia, at an early stage of the disease which thereby decreases the spread of the infectious agent. This team also proved that the local administration of flagellin stimulates the innate immune defences in the airways. Combined with antibiotics, the effect of flagellin is curative in cases of declared pneumococcal infection or pneumococcal secondary infection in an influenza context. Administration by the respiratory route has the advantage of delivering the immunostimulating principle into the infected tissue thereby reducing the impact in other tissues and reducing the systematic undesirable effects.

2 Ruben Hartkoorn's team was awarded an ERC - European Research Council Consolidator Grants of €2 million for its "Bioinspired Clicked Siderophore Antibiotics" project or Antibioclicks.

Antibiotic resistance is one of the most serious threats to global health today. The danger is that it takes us back to the time when there were no common treatments for conditions like pneumonia and tuberculosis. It is therefore imperative to develop a new class of antibiotics. Resistance to antibiotics can result from several mechanisms: the production of an enzyme that modifies or destroys the antibiotic, the modification of the target of the antibiotic or the sealing of the membrane of the bacteria. The Antibioclicks project will use a new, recently discovered natural chemical reaction to vectorise antibiotics so that they are actively transported inside bacteria and then released so as to eliminate them. This type of strategy known as the "Trojan Horse" offers a new therapeutic perspective.

3 Jamal Khalife's team demonstrated the essential role of plasmodium-specific protein phosphatase 1 regulators in the growth and transmission of malaria in a mouse model of malaria.

Malaria remains a parasitic disease which leads to nearly 500,000 deaths each year. This mosquito-borne infection mainly affects children in sub-Saharan Africa. Currently, in the absence of an effective vaccine, the main antimalarial treatments are therapeutic combinations based on artemisinin. However, with the emergence of resistance to these treatments, new therapeutic targets must be found. In order to better understand the specific mechanisms of the biology of the plasmodium parasite and to identify new strategies for controlling this infection, Jamal Khalife's research team has demonstrated that a specific plasmodium protein was able to interact with Protein Phosphatase 1 (PP1) and regulate its activity. The deletion of this protein has been found to reduce the virulence of the parasite during the asexual stages and completely

block development in mosquitoes. It has also been shown in these deficient parasites that the expression of proteins essential to the schizont and gametocyte stages was affected, as well as the phosphorylation of certain proteins. This study characterises for the first time a new molecular pathway through the control of PP1 by an essential and specific Plasmodium regulator, which may contribute to the discovery of new therapeutic targets to control malaria.

4 Dr Philip Supply of Camille Loch's team was involved in the launch of the clinical study of the new molecular diagnosis of antibiotic-resistant tuberculosis, called Deeplex-MycTB, developed with Genoscreen.

With 10 million new cases and 1.5 million deaths in 2018, tuberculosis is the number one infectious disease in the world. Nearly 400,000 new cases of multidrug-resistant tuberculosis have probably emerged in this year alone, of which only 30% were detected and treated, due to the lack of the quick and precise screening of resistance profiles. With the FIND foundation (Foundation for Innovative New Diagnostics, based in Geneva) and the financial support of UNITAID, a clinical study was launched to evaluate a new molecular diagnostic test of antibiotic-resistant tuberculosis, called Deeplex-MycTB, which was developed with Genoscreen. Based on next-generation DNA sequencing, this test can simultaneously identify the mycobacterial pathogens that cause tuberculosis, predict their resistance to 13 antibiotics or classes of antibiotics, and genotype them for epidemiological surveillance. The evaluation phases are planned over the next 2 years in India, South Africa, Georgia, Brazil and China, with the final objective of approving the test by the World Health Organisation (WHO) for its use by tuberculosis control programmes worldwide.

5 François Trottein's team (I2M, CIIL) has shown that intestinal dysbiosis during influenza infection contributes to secondary bacterial infections through an alteration in the production of short-chain fatty acids.

Severe influenza is associated with defects in innate pulmonary immunity, a phenomenon which leads to secondary bacterial superinfections. François Trottein's team put forward the hypothesis that a disruption of the intestinal microbiota during severe influenza could participate in this phenomenon. The team demonstrated that the influenza infection alters the composition and functionality of the gut microbiota. Indeed, the production of short-chain fatty acids (SCFA), which results mainly from the fermentation of dietary fibres by bacteria in the microbiota, is altered. The treatment of mice with flu using acetate (a major SCFA) strengthens the host's defences against *Streptococcus pneumoniae*. These results offer interesting prospects for the prevention and treatment of bacterial pneumonia, a major cause of death in the elderly or vulnerable.

MECHANISMS OF TUMORIGENESIS AND TARGETED THERAPIES

Despite major progress in their detection and treatment, cancers are still a feared disease, a major cause of morbidity and mortality. Research in cancerology at Institut Pasteur de Lille is part of a long tradition since the discovery of the first cancer genes, the oncogenes, in the 80s. For several years now, there has been a very strong dialogue between our research unit and the other fundamental or clinical research teams

in cancerology in the Lille agglomeration, in order to develop integrated research ranging from understanding the fundamental molecular mechanisms of tumorigenesis in search of new therapeutic targets.

PROF CORINNE ABBADIE

PU - Lille University, UMR 8161, CNRS, Inserm, Lille University, Institut Pasteur de Lille

ON 2 JANUARY 2020

Heterogeneity, Plasticity and Resistance to Cancer Therapies (CANTHER). Led by the **DR ISABELLE VAN SEUNINGEN**

CNRS Research Director - UMR 9020 CNRS - UMR1277 Inserm - Inserm, University of Lille, CNRS, Lille University Hospital, Institut Pasteur de Lille, Oscar Lambret Centre

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Our "Mechanisms of Tumorigenesis and Targeted Therapies" research unit is made up of about 60 researchers, engineers, technicians and thesis students arranged into 6 teams. Their primary task is to improve the knowledge of the precise molecular mechanisms which are responsible for the initial formation of a tumour, its growth and its escape from anti-tumoral immune defences, followed by the dissemination of tumoral cells, their attraction to certain organs and their metastatic implantation. It is therefore a fundamental research task, but whose challenges are naturally therapeutic: each piece of new knowledge makes it possible to propose a new therapeutic lead or to modify a treatment protocol.

Prof Corinne Abbadie's team works on understanding why cancers develop preferentially at an advanced age. The hypothesis is that certain molecular mechanisms which lead to cellular senescence could favour tumoral transformation. In support of this idea, many senescent cells are found in pre-cancerous lesions. Thus, the pharmacological inhibitors of certain proteins involved in the mechanisms of cellular senescence could be used to eliminate these senescent cells, thereby preventing the malignant evolution of pre-cancerous lesions.

Dr David Tulasne's team is studying mutations that activate oncogenes including receptors with tyrosine kinase activity or inhibit the expression of tumour suppressor genes. It is known, for example, that the MET receptor is mutated in certain lung cancers and that therapies against MET are effective in these patients. Unfortunately, resistances can develop. The team is concentrating on understanding these resistance mechanisms. Complementing this, the team is seeking to restore the expression of tumour suppressor genes like p53 with nonsense mutations. To achieve this, the team is implementing original strategies for inhibiting mRNA quality control mechanisms.

As for Dr Martine Duterque's team, it is interested in understanding why prostate cancer preferentially develops bone metastases. The TMPRSS2-ERG oncogene it is working on appears to be a major actor in regulating the gene's expression conferring a bone tropism to prostate cancer cells.

The cancerous cells present mutations which distinguishes them from others. As a result, they can be recognised by the immune system and eliminated. Nonetheless, during this malignant evolution, cancerous cells acquire the capacity to negatively regulate the immune response. These are the mechanisms studied by Prof Nadira Delhem's team with the aim of finding therapeutic targets which would restore or amplify the natural anti-tumoral immune responses.



KEY EVENTS

1 **Dominique Stehelin, co-discoverer of the 1st oncogene, Src, in 1976 and founder in 1979 of the first cancer research unit at Institut Pasteur in Lille, died in April 2019.** A project to enhance its archives has begun. Work has also begun to organise a scientific day in his honour.

2 **The task of uniting the various cancer research units in the Lille agglomeration has borne fruit with the evaluation and creation of the new "Heterogeneity, Plasticity and Resistance to Cancer Therapies" Canther research unit.** This unit, which will start on 1 January 2020, will be headed by Isabelle van Seuningen. It will include around 180 people from the grouping of three pre-existing laboratories, including the Institut's teams led by Prof Corinne Abbadie, Dr Dominique Leprince, Dr David Tulasne and Dr Martine Duterque.

3 **Lung cancer is characterised by the existence of mutations that cause tumour progression.** Thanks to a translational approach carried out in collaboration with the University Hospital of Lille, our work this year contributed to improving the selection of patients carrying MET receptor tyrosine kinase mutations. These patients may benefit from new targeted therapies directed against this receptor (Baldacci et al. Journal of Thoracic Oncology. 2019). Another key issue is the characterisation of the resistance mechanisms that hinder the effectiveness of these targeted therapies. By using patient cohorts, we revealed a new mechanism of resistance to treatment with MET inhibitors, involving the activation of the PI3K signalling pathway. These data can be used to consider new co-treatments to counteract this resistance (Jamme et al, Journal of Thoracic Oncology. In press).

4 **The MET receptor plays an important role in the homeostasis of epithelial organs, particularly thanks to its ability to regulate the survival/apoptosis balance.** However, in addition to its standard abilities to induce cell survival in response to its ligand, MET is capable of promoting apoptosis in the absence of ligand. This double capacity puts MET among the dependent receptors. By creating transgenic animal models, we have shown that the apoptotic abilities of MET are involved in the regulation of the survival/apoptosis balance in epithelial organs like the liver. This induction of apoptosis is based on an original mechanism since MET promotes calcium exchanges between the endoplasmic

reticulum and the mitochondria, thereby inducing the intrinsic pathway of apoptosis. These new data could provide a better understanding of the role of MET in tumorigenesis during which the survival/apoptosis balance is deregulated (Duplaquet et al, eLife. in press).

5 **Nonsense mutations disrupt the synthesis of the proteins and may be responsible for about 10% of the cases of genetic diseases, including cancers in which the nonsense mutations affect tumour suppressor genes.** Through screening, we identified 2,6-diaminopurine as a molecule capable of very efficiently correcting nonsense mutations in cell lines, in mouse models and in the cells of patients with cystic fibrosis. This molecule turns out to be not very toxic under the experimental conditions tested. We also demonstrated its mode of action which involves the inhibition of an enzyme that modifies certain transfer RNAs. 2,6-diaminopurine could therefore represent some genuine hope of treating patients whose genetic pathology is linked to the presence of a nonsense mutation (Trzaska et al. Nature Commun. In press).

6 **Many cancer patients are now cured by conventional treatments, however some of them unfortunately relapse years later.** An emerging hypothesis is that the relapse results are caused by the persistence of tumour cells that would have withstood the initial treatment and that would have remained dormant in the body for years before resuming their malignant growth. An underlying question is to understand the nature of this state of dormancy. We put forward the idea, argued in an article published in the Cancer Letters journal, that this state of dormancy could resemble, or correspond to, a state of premature cell senescence induced by the initial therapy (Pluquet et al, Cancer Letters, 2019 , 463, 50-58).



LABORATORY OF GENETIC TOXICOLOGY

The genetic toxicology laboratory is a centre of excellence in France. In particular, it conducts studies to assess the genotoxic and mutagenic potential but also the endocrine disruption potential of many categories of substances.

With a very wide field of competence (human health, animal health, cosmetics, food, chemicals, plants/vegetable, nanotechnologies, environment, etc.), the experts from the genetic toxicology laboratory have been cooperating with the pharmaceutical, cosmetics, food, chemical industries, etc.

The laboratory also participates in research programmes at a national and European level aimed at evaluating the genotoxic potential of atmospheric particles, manufactured nanoparticles, or even the endocrine disruption potential of the contaminants in our general environment, etc.

DR FABRICE NESSLANY

Institut Pasteur de Lille research director

One of the main challenges is to replace the use of experimental animals with *in vitro* models. What's more, these models should make it possible to pursue the research into the characterisation of the most worrying airborne, chemical and particulate contaminants, whose desired effects are exacerbated, and the identification of the most sensitive populations. Indeed, the conditions leading to the damaging effects to human health from the particulate

and/or gaseous substances present in the atmosphere are not well defined and there are still many major uncertainties. It is clear that the specific role of each of the atmospheric contaminants in the overall toxicity of the mixtures, which make up the atmospheric aerosols, and in the potentiation of their effects has not been specifically studied.



KEY EVENTS

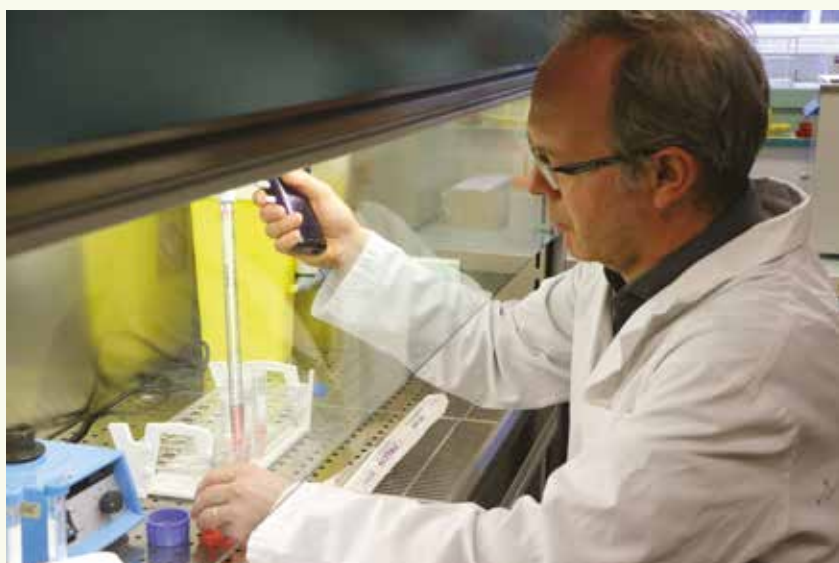
1 Start of 2 research programmes.
The first funded by ITMO Cancer/AVIESAN aims to **replace animal experiments by validating an *in vitro* model of 3D spheroid cultures of hepatocytes to assess chemical-induced hepatocarcinogenesis.**

FREEDOM - eEffect of dietary Exposure to Endocrine Disruptor Mixture"

The objective of the 2nd project is to **study the effects of mixtures representative of dietary exposure to substances with a potential for endocrine disruption (ED).** The main mixtures of potentially ED substances, to which consumers are exposed, will be researched. The qualitative and quantitative composition of the representative mixtures will be determined by modelling the exposures (according to the different types of diet). The effects of the selected mixtures on the action and synthesis of oestrogens, androgens and thyroid hormones will then be studied in *in vitro models*.

2 Organisation of the 3rd Day of regional meetings of the Health and Longevity Pollution Centre covering the topic of "inequalities, vulnerabilities and susceptibilities" linked to atmospheric pollution. During this new day of meetings, the focus was on management, prevention and regulation of atmospheric pollution measures in the HdF region with representatives of the Regional Health Agency, the Métropole Européenne de Lille and the city of Lille.

3 Optimisation of the use of reconstructed human skin models to replace the animal experiments with the aim of validating these models to highlight the genotoxic potential of chemical substances.



DRUGS AND MOLECULES FOR LIVING SYSTEMS

The laboratory's mission is to design and synthesise drug prototypes with an innovative mode of action, aimed at achieving clear therapeutic progress in indications where the medical need is poorly satisfied. This interdisciplinary molecular invention work is inspired by the most recent discoveries made on infectious diseases, metabolic diseases and cancer.

By discovering molecules, new therapeutic solutions can be offered and the involvement of the mechanisms highlighted by biologists in the pathophysiological processes can be validated.

BENOIT DEPREZ

PU - Lille University, U1177, Inserm, Institut Pasteur de Lille, Lille University, (Pharmacy faculty)

The design and optimisation of new drugs requires interdisciplinary expertise covering chemistry, physics, biology and in silico modelling. Indeed, the active ingredient of modern drugs, whether they are synthetic or biological in origin, is always defined at the molecular, or even the atomic, level. This particular molecular structure - perfected by the researchers of the unit - is the key to all the properties of the drug. It conditions its ability to cross the physical and chemical barriers between the different biophases (intestine, blood, tissues, brain, etc.) of the body, and to attain the set target. It is also key to its interaction with the intended

target and the achievement of the desired effect. Beyond the therapeutic goal, molecules also serve as valuable tools that help biologists better understand how the cell and living organisms work and verify that the proposed targets for treating diseases are relevant. Researchers are working on **antibiotic resistance, type 2 diabetes, certain forms of cancer and the recognition of intracellular antigens by the immune system.**



KEY EVENTS

1 **Launch of SmartLab, a private public laboratory between the unit and Bioversys.**

This laboratory is working on the discovery of drugs to fight antibiotic resistance.

In this scientific field, researchers from the unit, in collaboration with the Lille Centre for Infection and Immunity, discovered antibiotic molecules that implement a new mechanism to treat tuberculosis and infections caused by bacteria that are frequently resistant to antibiotics.

2 **The laboratory is participating in a major European research project for new "ERA4TB" anti-tuberculosis treatments,**

by getting its pharmacokinetics and bioanalysis teams involved.

3 **Using an original and optimised method (KTGS),**

we discovered powerful inhibitors of enzymes that modulate the presentation of antigens on the surface of cells and their recognition by the immune system.

4 **A drug candidate that works in synergy with current treatments for multiple myeloma**

has demonstrated its effectiveness *in vivo* and is opening up new perspectives for the treatment of this disease with a poor prognosis.

5 **A recent study shows that a molecule developed by the laboratory and targeting the TGR5 receptor in the digestive tract**

could **treat inflammatory bowel disease.**



THE CAMPUS RESEARCH TEAMS ON 1 JANUARY 2020



U1011

Director
Bart Staels

NUCLEAR RECEPTORS, METABOLIC AND CARDIOVASCULAR DISEASES

University of Lille - Inserm - Institut Pasteur de Lille - Lille University Hospital

- Nuclear receptors in the metabolic syndrome / **Group Leader: Bart Staels**
- Cardiac pathologies, blood flow abnormalities and haemostasis
Group Leaders: Sophie Susen / Eric Van Belle
- Immuno-metabolic dialogue in obesity and its comorbidities
Group Leader: David Dombrowicz
- Integrated transcriptional analysis of diseases of the liver
Group Leader: Philippe Lefebvre
- Nuclear receptors and circadian rhythms in pathophysiology
Group Leader: H       Duez



U1167

Director
Philippe Amouyel

RISK FACTORS AND MOLECULAR DETERMINANTS OF AGING-RELATED DISEASE

Lille University - Lille University Hospital - Inserm - Institut Pasteur de Lille

- Public health and molecular epidemiology of age-related diseases
Group Leader: Aline Meirhaeghe
- Molecular determinants of cardiac remodelling and heart failure
Group Leader: Florence Pinet
- Molecular determinants of Alzheimer's disease and cognitive disorders
Group Leader: Jean-Charles Lambert
- Integrative structural biology
Isabelle Landrieu
- Glycation: from inflammation to ageing
Eric Boulanger



U1177

Director
Beno  t D  prez

DRUGS AND MOLECULES FOR LIVING SYSTEMS

Lille University - Inserm - Institut Pasteur de Lille

- M2SV: Medicines and Molecules for acting on Living Systems



U1283 - UMR8199

Director
Philippe Froguel

METABOLIC FUNCTIONAL (EPI)GENOMICS AND MOLECULAR MECHANISMS INVOLVED IN TYPE 2 DIABETES AND RELATED DISEASES

University of Lille - Inserm - Institut Pasteur de Lille - CNRS - Lille University Hospital

- Metabolic functional (epi)genomics and their abnormalities in type 2 diabetes and related disorders | **Group leaders: Am  lie Bonnefond / Philippe Froguel**
- Molecular and cellular pathophysiology of metabolic diseases
Group Leaders: Jean-S  bastien Annicotte / R       Chambrey
- Administrative Department | **Group leader: Philippe Froguel**



U1019 - UMR9017

Director
Jean Dubuisson

CENTER FOR INFECTION AND IMMUNITY OF LILLE

Inserm - CNRS - Lille University - Institut Pasteur de Lille - Lille University Hospital

- Chemogenomic of Intracellular Mycobacterium | **Group Leader: Priscille Brodin**
- Molecular and cellular virology | **Group Leader: Jean Dubuisson**
- Opportunistic Infections, Immunity, Environment and Lung Diseases
Group Leader: Philippe Gosset
- Biology of Apicomplexa parasites: factors regulating growth, differentiation and virulence **Group Leader: Jamal Khalife**
- Cellular and physical microbiology of infection | **Group Leader: Frank Lafont**
- Biology and chemistry of Platyhelminthes | **Group Leader: Oleg Melnyk**
- Research on Mycobacteria and Bordetella | **Group Leader: Nathalie Mielcarek**
- Tropical Biomes and Immune-Pathophysiology | **Group Leader: Sylviane Pied**
- Plague and Yersinia pestis | **Group Leader: Florent Sebbane**
- Bacteria, Antibiotics and Immunity | **Group Leader: Jean-Claude Sirard**
- Influenza, Immunity and Metabolism | **Group Leader: François Trottein**
- Pulmonary immunity | **Group Leader: Anne Tsicopoulos**
- Ecology and Pathophysiology of Intestinal Protozoa | **Group Leader: Eric Viscogliosi**
- Chemical Biology of Antibiotics | **Group Leader: Ruben Hartkoorn**
- Administrative Department | **Group leader: Isabelle Aslani**

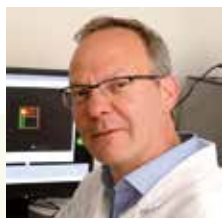


U1190

Director
François Pattou

TRANSLATIONAL RESEARCH ON DIABETES (RTD)

Lille University Hospital - University of Lille - Inserm - Institut Pasteur de Lille



IMPACT OF THE CHEMICAL ENVIRONMENT ON HEALTH

LABORATORY OF GENETIC TOXICOLOGY

Institut Pasteur de Lille

Group Leader: Fabrice Nesslany



UMR9020 - UMR1277

Director
Isabelle Van Seuning

CANCER HETEROGENEITY, PLASTICITY AND RESISTANCE TO THERAPIES (CANTHER)

Inserm - University of Lille - CHU Lille - CNRS - Institut Pasteur de Lille - CLCC Lille - COL

- Efficacy and resistance to anti-tumour therapies | **Group Leader: David Tulasne**
- Senescence, fibrosis and cancer | **Group Leader: Corinne Abbadie**
- Mucins, cancer and drug resistance | **Group Leader: Isabelle Van Seuning**
- Cellular plasticity and cancer | **Group Leader: Xuefen Le Bourhis**
- Persistence factors of leukaemia cells | **Group Leader: Bruno Quesnel**



UMS3702

Director
Philippe Boutin

MIXED SERVICE UNIT OF THE INSTITUT DE BIOLOGIE DE LILLE

- IBL General Secretariat and Human Resources
- IBL Management Secretariat Teams and IBL teams
- IBL IT team

TECHNOLOGICAL PLATFORMS AS OF 1 JANUARY 2020

LILLE-BASED PLATFORMS IN BIOLOGY AND HEALTH

UMS2014 - US41

Director: **SOPHIE CRESPIN**



TISSUE AND CELL IMAGERY-CYTOMETRY

The Biolmaging Centre Lille-Nord de France (BICeL), offers a set of high resolution microscopes in biophotonic, electronic and atomic force imaging that is also associated with various cytometry techniques.

Group Leader: **FRANK LAFONT**

Inserm U1019, UMR 8204, Inserm, CNRS, Institut Pasteur de Lille, Lille University

Website: **www.bicel.org**



ARIADNE PLATFORM - HIGH THROUGHPUT (HTS) AND HIGH CONTENT (HCS) SCREENING

Platform that combines a chemical library and all the high-throughput screening tools (except for the techniques based on high-throughput confocal imaging which are available on the microscopic imaging platform).

Group Leader: **FLORENCE LEROUX**

U1177, Inserm, Institut Pasteur de Lille, University of Lille, Inserm U1019, UMR 8204

Website: **www.deprezlab.fr**



PROTEOMICS AND MODIFIED PEPTIDES PLATFORM (P3M)

Platform dedicated to proteomic analysis and the characterisation of proteins and peptides.

Group Leader: **JEAN-MICHEL SALIOU**

LabEx ParaFrap, Institut Pasteur de Lille, CNRS, Lille University



PLEHTA PLATFORM

Laboratory for research and experimentation

Group Leader:

FABRICE INFANTI

Institut Pasteur de Lille



BIOINFORMATICS, BIOANALYSIS AND BIOSTATISTICS OF LILLE (BILILLE)

Billie is a platform specialised in bioinformatics, bioanalysis and biostatistics that trains researchers in a methodology for analysing data and software.

Group Leaders: **HÉLÈNE TOUZET AND GUILLEMETTE MAROT**

University of Lille - CNRS - Inserm - Lille University Hospital - Institut Pasteur de Lille

Website:

<https://wikis.univ-lille.fr/bilille/>



TRANSCRIPTOMICS AND APPLIED GENOMICS

High-throughput genomics platform specialised in microbial genomics. Since 2012, TAG has been a member of the Genes Diffusion Genomic Platform for the implementation of a common structure called PEGASE, in order to offer cooperation and services pooling the skills of each of the entities.

Transcriptomics and Applied Genomics Group (TAG)

Group Leader: **DAVID HOT**

U1019, UMR8204, Inserm, CNRS, Institut Pasteur de Lille

OTHER PLATFORMS



NUCLEAR MAGNETIC RESONANCE

Nuclear magnetic resonance (NMR) spectroscopy helps probe the molecular structure by making the natural magnetization of nuclei interact with a magnetic field.

Nuclear Magnetic Resonance

Group Leader: **ISABELLE LANDRIEU**
U1167, CNRS, Institut Pasteur de Lille, Lille University



GENOMICS AND METABOLIC DISEASES

The Lille Ligan-PM platform for genome sequencing can establish the list of mutations likely to explain the clinical signs of each patient, predict the possible evolution of their disease, and predict the efficacy or side-effects of existing drugs.

Group Leader: **PHILIPPE FROGUEL**

EquipEx LIGAND-PM (Lille Integrated Genomics Advanced Network for Personalised Medicine)

Website: <http://ligan.good.cnrs.fr>



HIGH SECURITY LABORATORY (P3)

Level 3 microbiological safety laboratory

Group Leader: **MICHELE VIALETTE**

Institut Pasteur de Lille



LABORATORY FOR THE STUDY OF THE GENOME

Logistics and oversight of large collections of human biological samples with patients recruited mainly from epidemiological studies based on the cardiovascular, metabolic and neurodegenerative disease themes.

Genomic Analysis Laboratory

Group Leader: **PHILIPPE AMOUYEL AND NATHALIE FIEVET-VERRECAS**

U1167, Inserm, Institut Pasteur de Lille, Lille University



PEPTIDE CHEMISTRY

Peptide chemistry and protein chemical synthesis

Peptide Chemistry, Systems, Biology

Group Leader: **OLEG MELNYK**

UMR 8204 - U1019 CIL, Inserm, CNRS, Institut Pasteur de Lille, Lille University

Website: www.csb.cnrs.fr

THE BIOTECHS

DRAW THE ACADEMIC AND INDUSTRIAL SECTORS CLOSER TOGETHER TO ACCELERATE VALIDATION OF DISCOVERIES

At the heart of the campus, Institut Pasteur de Lille supports the development of projects, start-ups and biotechnology and health innovation companies. The aim is to bring new services and analysis or diagnosis products to the fore which stem directly from the fundamental research carried out in Lille. Institut Pasteur de Lille relies on the proximity of its research teams and their equipment (laboratories and technological platforms) to facilitate collaboration with the

entrepreneurs and start-ups of the sector, whether they be in the experimental or developmental phase. The Institute is also committed to fostering synergies and expertise in order to allow biotechs to move more easily into the maturation phase of their projects. These biotechs, located on the Pasteur Lille Campus, benefit from the available premises, equipment and skills.



Created on the Pasteur Lille campus in January 2001, GenoScreen offers kits and services in molecular biology to analyse all types of genomes (human, animal, plant, microbial) as well as bioinformatics solutions, for the "academic", hospital-based as well as the industrial research teams. This 100% French biotechnology company now has about thirty employees. It generates 30% of its turnover abroad. In recent years, specific research programmes, carried out in partnership with the research units from the Institut Pasteur de Lille, Inserm and INRA, have developed very competitive applications in areas such as predicting the antibiotic resistance of tuberculosis, the targeted metagenomic analysis of microbiota or the diagnosis and monitoring of biodiversity.

www.genoscreen.fr



Set up on the Lille Pasteur campus, the company X'ProChem markets proteins synthesized using a chemical method, an innovative technology stemming directly from the academic research of the laboratory of Oleg Melnyck. These 100% chemical proteins are custom-made to meet requirements that classic methods of recombinant biology are unable to synthesise, such as toxic, membrane proteins or proteins equipped with a probe so they may be traced in cellular imaging. The first papers published on protein chemical synthesis date back to the 30s, but we had to wait for the end of the first decade of this century before a cost-effective, easily replicable method was developed at Institut Pasteur de Lille.

www.xprochem.com/fr



Strengthened by its collaborations with the Pasteur Lille campus, 4 P-Pharma develops innovative molecules at an early stage of pre-clinical development and brings them to the preliminary phases of clinical trials. The company is positioned as an intermediary between entities that have developed high-potential early biomedical projects and the pharmaceutical companies.

Since September of 2016, 4 P-Pharma has also been financially supported by the mutual company "M comme Mutuelle" with an eye to conducting the first phase I clinical trial on one of its products possessing properties that constitute a deterrent to psycho-stimulant abuse.

R&D's activities focus on inflammatory diseases, oncology and the central nervous system. Around ten drug candidates are currently being developed in the molecule portfolio.

The ongoing projects of 4 P-Pharma have benefited from several collaborations with the teams of Institut Pasteur de Lille, especially with the Pharmacokinetics/ADME platform directed by Prof. Benoît Déprez, the Transcriptomics and Applied Genomics platform directed by Dr. David Hot, and the Genetic Toxicology Laboratory directed by Dr. Fabrice Nesslany.

www.4p-pharma.com



APTEEUS

engaging patients in discovery

Created in 2013 by Terence Beghyn, pharmacist and researcher, along with Prof. Benoit Deprez, Director of the Drug Discovery Center of Institut Pasteur de Lille, APTEEUS is an innovative company in the field of individualized medicine for patients with rare and orphan diseases. Thanks to their expertise acquired in the U1177 Research Unit (Inserm - Institut Pasteur de Lille - Lille University), their mission is to bring the miniaturized techniques of drug discovery to the bedside of patients suffering from orphan diseases.

The APTEEUS approach combines *in vitro* cell screening with drug repositioning. The team's savoir-faire, with the assistance of doctors and scientific experts in disease, have made it possible to develop a screening test for any new disease sufficiently characterized from a functional point of view. The test systematically uses cells taken from the patient to guarantee the link between the molecular cause of the disease that is specific to the patient with its symptomatic manifestations. Thus the idea is to measure the effect of each of the active ingredients of the medications from the global materia medica on the altered function at the root of the symptoms. It is the exhaustiveness of the collection of active ingredients, the relevance of the tests developed, and the environment of scientific excellence that constitute the strengths of APTEEUS today.

The company is currently evaluating the clinical benefit of two drug candidates in several rare and orphan pathologies. Drug repositioning is a means of quickly responding to the medical need of small populations of patients by mastering both the risks and costs of development.

The patient's involvement in the discovery process earned APTEEUS the prize in the category of Individualized Medicine of the Concours Mondial d'Innovation 2030. Today, several partnerships with teams from Institut Pasteur de Lille, various hospitals and pharmacy actors, are making it possible to broaden the scope of the technology.

<http://apteeus.fr>



Led by the doctors Nadira Delhem and Olivier Moralès and directed by Hamza Aboussemdai, this biotech officially commenced in July of 2016 on the premises of the Lille Institut de Biologie (CNRS) on the Institut Pasteur de Lille campus. Immune InsightT offers an unprecedented and effective method of validating the safety of new drug candidates prior to the

launch of clinical trials. A method directly stemming from Pasteurian research.

It offers unique services internationally making it possible to validate, in a preclinical phase, the safety of a drug candidate with regard to immune cells, and T regulatory lymphocytes in particular. Balance of the immune system Regulatory T lymphocytes (Tregs) are a particular population of white blood cells that maintain the proper balance of the immune system so that it can protect the organism from aggression. Some diseases deregulate the function of the Tregs. Thus, in cancers, Tregs are abnormally activated, which weakens the immune response directed against the tumour and facilitates its progression. Conversely, in the case of allergies, chronic inflammatory diseases or organ transplants, the Tregs underfunction and the immune response is excessive.

www.immune-insight.com



**PREVENT TODAY
IN ORDER TO AGE
WELL TOMORROW**

03

CENTRE FOR HEALTH AND LONGEVITY:

INNOVATION FOR AGEING WELL

The Centre for Health and Longevity brings together all of the institute's health and prevention activities: Health Examination Centre, International Vaccination Centre, Nutrition and Physical Activity Department and the Longevity Course in partnership with the Lille University Hospital.

The strategic objective of the centre is to reinforce an evaluated disease prevention plan to serve the population of Hauts-de-France, the regions and businesses.

With a team of 90 professionals working at the service of public healthcare, the centre completed the task of pooling the teams and equipment in 2019. As a result, the institute was able to respond to requests from institutions or companies thanks to the support of the Centre's Development Unit.

In 2019, 15,000 health check-ups were carried out for 4 Primary Health Insurance Funds (Lille/Douai, Roubaix/Tourcoing, Flandres and Artois), 26,000 vaccinations including 5,000 flu vaccines in businesses and more than 3,100 hours of training provided, with numerous appearances at seminars, trade fairs, events and conferences.

The Health Examinations Service is a research site and participates in projects such as the Constances Cohort (since 2012) and is an investigation centre for the CATOCOV¹ study, conducted by the Lille University Hospital (recruitment of control patients since 2019). The centre is developing its own approaches for facilitating evaluated prevention with its research unit.

The Longevity course of Institut Pasteur de Lille has continued to develop since 2017 thanks to the support of partners such as AG2R La Mondiale, CARSAT HdF, ARS HdF and the MACIF Foundation. From 2020, the Centre for Health and Longevity

is refining its disease prevention offer in order to respond to regional and business projects with an adapted Longevity Course. This is aimed at targeting the specific health/disease prevention issues of populations such as caregivers and vulnerable people, people in early retirement or retired people, young people (etc.)

Experiments with the Longevity Course will be conducted in areas identified in collaboration with local elected officials and local authorities. Funding for the process should be collaborative with organisations such as CARSAT, ARS, CPAM, etc.

The Institute, working in collaboration with Cabinet ADIX and AG2R La Mondiale, is developing its offer to support businesses facing health issues.

Given the success of this development, the long-term goal is to promote a network of longevity health centres in Hauts-de-France and nationally.

2019 KEY EVENTS

- ▶ The contract of objectives with CPAM was honoured both in terms of the number of assessments completed, as well as the assessments helping people in vulnerable situation and people who had access to these assessments for the first time
- ▶ The successful deployment of the "maintien de l'autonomie en EHPAD" (maintaining the autonomy of people in nursing homes) programme in the Hauts-de-France
- ▶ Welcoming 100 caregivers of the Longevity Course and 82 consultants in group coaching programmes
- ▶ Organising awareness building conferences for companies dealing with disease prevention issues related to longevity problems with the increase in the retirement age
- ▶ The extension of the collaboration with Auchan to continue providing customers and employees with food advice

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Centre Prévention Santé Longévité
Mieux vivre aujourd'hui pour bien vieillir demain

¹Analysis of Volatile Organic Compounds in Exhaled Air as a diagnostic tool for Thoracic Cancers

HEALTH CHECK-UPS AND EDUCATIONAL ACTIVITIES

The Centre for Health and Longevity has three parallel approaches regarding disease prevention pathways: the "Examen Prévention Santé" (EPS) health check as part of its delegation granted by the CPAM, the occupational health checks and the health check that is part of the Longevity Course. As part of the delegation of the CPAM, the centre participates in the Constances cohort.



44

PREVENTIVE HEALTH EXAMINATIONS (PHE) AND EDUCATIONAL ACTIVITIES

15,080
EPS

57 %
of people
in vulnerable
SITUATIONS

400
people for
HEALTH
EDUCATION

In 2019, within the context of agreements established between the "Caisses Primaires" (healthcare insurance funds) of Lille Douai, Artois, Flandres, Roubaix-Tourcoing and Côte d'Opale and Institut Pasteur de Lille, 15,080 insured people benefited from an EPS conducted at the health check-up centres of Lille and Tourcoing as well as at third-party locations (Nord and Pas-de-Calais). The "Examen Prévention Santé" health check-up is primarily intended for those who are on the very margins of the health system. The benefits for those concerned are the ability to assess their health, but also obtain information on their healthcare rights and be referred to the healthcare system if necessary. These so-called vulnerable populations (social vulnerability, isolation, lack of follow-up by the GP, people not registered with an organised healthcare system, screening or vaccination systems, etc.) represented in 2019 more than 57% of the consultants of the centres. The interviews and check-ups carried out by professionals at the centre (nurses, dentist,

dietitians, doctors) focus on motivation, health education and guidance after the EPS. EPS check-ups are tailored to the risk factors and personal and family history of the consultant. Consequently, for example, for a few months now, the CES have been offering adolescents aged 10 to 15 a "junior" EPS that meets the specific needs of young people and adopts a more personalised approach, focused on listening and dialogue. Within the institute, group activities may be offered during or after PE for young people aged 16 to 25 as part of the youth EPS on the topics of "pleasure and dependence", "sexual and emotional life", "food, physical activity and oral health", "let's talk about smoking" awareness stands, participation in the "smoking-free month" in November, therapeutic education sessions for type 2 diabetic patients, personal consultations on smoking addiction. In 2019, more than 400 consultants benefited from these educational offers from the CES.

HEALTH CHECK-UPS CONSTANCES

The National Health Insurance Fund, the National Institute of Health and Medical Research, the University of Versailles Saint Quentin, Paris V, the National Insurance Pension Fund and the General Directorate of Health joined forces to tackle a major cohort project for medical research and public health, conducted with the help of the Primary Health Insurance Funds ("CPAM") and health check-up centres ("CES"): the Constances cohort of health check-up centre consultants.

This is a general population-based epidemiological cohort addressing the following topics: professional and social health determinants, ageing and chronic diseases, women's health, genetic and biological factors, and interaction with the environment. It is designed as an "open epidemiological laboratory" accessible to the epidemiological research community, and as a public health tool allowing the highest authorities

to gain access to diversified sources of information on the health of the population, risk factors, the treatment and healthcare referral method and on the medical, professional and social paths of the people concerned. The CES of Institut Pasteur de Lille has been welcoming volunteers as part of the Constances cohort since 2012. These people, aged 18 to 69 at the time of inclusion, agree to get a health check every 5 years, send information through questionnaires and be followed in the national medical-administrative bases. More recently (since 2018), some of them participate in a collection of biological samples (Constances biobank). The year 2019 was the year of the last inclusions and the volunteers are now invited to the centre as part of repeat invitations, every 5 years.

COMPANY CHECK-UPS

The CPSL has developed personalised health checks, mainly offered to company employees. Most of these health examinations are carried out as part of a professional expatriation in connection with the international vaccination service. The turnover between 2018 and 2019

increased by more than €50,000. In 2020, it should be possible to strengthen the ties with companies and obtain new customers thanks to the actions carried out with the development unit.

LONGEVITY COURSE

In 2019, as part of the multi-annual Contract of Objective and Resources ("CPOM") signed with the ARS Hauts-de-France, 100 people, who declared that they were caring for a loved one suffering from a neurodegenerative or other disease, were welcomed. The collective coaching has been implemented and has formally recognised certain collective coaching courses. Two subjects have been developed, namely: Nutrition Physical Activity ("NAP") and Cognition, stress, memory, sleep ("COG"). 82 consultants were able to benefit from it and have given extremely

satisfactory feedback about their participation in these workshops. Through our partner, AG2R La Mondiale, companies have guided their employees on a voluntary basis so that they can benefit from a Longevity Course. New perspectives are opening up for the Longevity Course: experiments in regions or cities of Hauts-de-France and a modulation of the offer in order to make it match the expectations of each target population (caregivers, working people, people who have retired or are in early retirement, young people, people in vulnerable situations, etc.)

111
people hosted in
THE LONGEVITY COURSE

including **100 CAREGIVERS**

82
CONSULTANTS
benefited from collective coaching



RESEARCH WITHIN THE CENTRE FOR HEALTH AND LONGEVITY



The Centre for Health and Longevity pursues the following objectives: Identify and understand the influence of the factors that determine successful ageing; Contributing to the development of scientific prevention based on developing interventional research and evaluation of actions undertaken; Provide evidence-based interventions that improve health and well-being and reduce health inequalities. In order to successfully lead

and implement this work, the Centre for Health and Longevity aims to: Develop interactions between players in disease prevention, care and research; Facilitate the use of its work results to help in decision-making for health policy actors and group leaders. This department is at the centre of evaluated disease prevention.

NUTRITION AND PHYSICAL ACTIVITY DEPARTMENT

The activities of the Nutrition and Physical Activity Department revolve around clinical studies in nutrition (NUTRINVEST centre), specialist assessments, education, and training in Nutrition and Physical Activity.



THE "EXPERTISE, EDUCATION IN HEALTH AND TRAINING" DEPARTMENT (EESF)

The EESF department is a multidisciplinary team (nutrition engineers, dietitians, medico-sports educators and assistant project manager) that supports companies and public institutions on numerous scientific, health education and training projects. The department is recognised as a "public health support operator" by the Regional Health Agency in the fields of nutrition, physical activity, overall health and stress management.

The EESF department team operates mainly throughout the Hauts-de-France region but also for certain projects at the national level (Nutrissimo Junior, CETAF/CNAMTS training,

etc.)

The department brings its expertise to various groups and companies through bibliography reviews and summaries, the writing of scientific articles, regulations on labelling and nutritional communications, the assessment of nutritional composition and advice according to the dietary intake of populations, but also through support in the modelling of digital nutrition coaching platforms. In particular, the institute has been working with Auchan since 2017 on food advice.

2019 KEY EVENTS

EDUCATIONAL SUPPORT PROJECTS FOR PROFESSIONALS:

9 projects carried out with the support of the ARS, the regional authorities of the region, the UDAPEI and the MGEN: diet, physical activity, combating sedentary lifestyles, general health, project methodology (diagnosis, management, evaluation), skills development of healthcare players, creation and writing of educational tools, actions aimed at the general public, creation of action research protocols. The project supported by MGEN created an interactive "Flash Form" orientation course on a natural "Amaury Centre" site.

TRAINING FOR HEALTH, EDUCATION AND MEDICO-SOCIAL PROFESSIONALS:

14 training sessions on diet and physical activity adapted to specific populations (ageing, disability, obesity, early childhood, etc.) through the prevention and management of under-nutrition, excess weight, obesity, nutrition at work, balanced diet, physical activity, ageing, as well as smoking as a modifiable risk factor.

NUTRITION INTERVIEWS:

Obesity in detail.

GENERAL PUBLIC ADVISORY ACTIVITIES:

VitalSport with Decathlon, Emissions France Bleu Nord (physical activity, nutrition, stress management, successful ageing), Longevity conferences - Physical Activity & Nutrition, ETP type 2 diabetes programme (CPAM), EES overweight programme (CPAM), Business reviews (medical-sports consultations), Longevity Course (medical-sports consultations, coaching).

SHARING OF EXPERTISE:

Institut Pasteur de Lille's educational support system has been implemented as close as possible to professionals and young people from local missions, within the structures themselves in order to encourage everyone's participation and be at the very heart of living spaces, at a time when mobility issues are significant. This system was modelled in order to study its transferability to the topics of "nutrition, physical activity, combating sedentary lifestyles and general health". This work was carried out in collaboration with "Promotion Santé Hauts-de-France", the Regional Association of Elected Representatives for Training, Integration and Employment ("AREFIE"). These regional networking efforts have resulted in the extensive sharing and promotion of healthcare measures.



HEALTH TRAINING

The health examinations department is a validating internship field for medical students (externs and interns in general medicine and in public health in conjunction with Lille University

and the Lille University Hospital). The Centre for Health and Longevity also welcomes nursing students.

3,100
HOURS OF
TRAINING



CLINICAL STUDIES DEPARTMENT

The "clinical studies" department has for several years supported numerous agro-food companies (ingredients, nutriments, foods, diets, dietary supplements) in evaluating their products' health benefits. It also meets calls for projects to undertake "research-action" type studies aimed at public health. As a result, it has gained solid

expertise in the management of clinical studies in nutrition from proposals of pertinent study design on through submission of final reports.

THE CLINICAL STUDIES DEPARTMENT AND ITS INVESTIGATION CENTRE, NUTRINVEST, MANAGED FOUR CLINICAL NUTRITION STUDIES IN 2019 OR CLOSE TO 810 VISITS.

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1 THE IBS-GO STUDY looks at the effect of a probiotic yeast on improvements in gastrointestinal disorders associated with irritable bowel syndrome with predominant constipation.

2 THE TRUEGREEN STUDY is interested in the effect of an innovative infant formulae on the tolerance and growth of nursing babies from 0 to 6 months in comparison to breast feeding.

3 OBEMINALE-2 evaluates the effect of a dietary supplement in weight management in people with a metabolic syndrome.

4 THE NATICOL STUDY is working out the effect of a dietary supplement based on fish collagen peptides in the weight management of overweight or obese people.

The clinical studies department has implemented an active approach for the recruitment of voluntary participants in nutrition clinical trials:

■ In agreement with CPAM, people coming to Institut Pasteur de Lille for a health check (and having given their consent) may be re-contacted to participate in the studies offered by the clinical studies department.

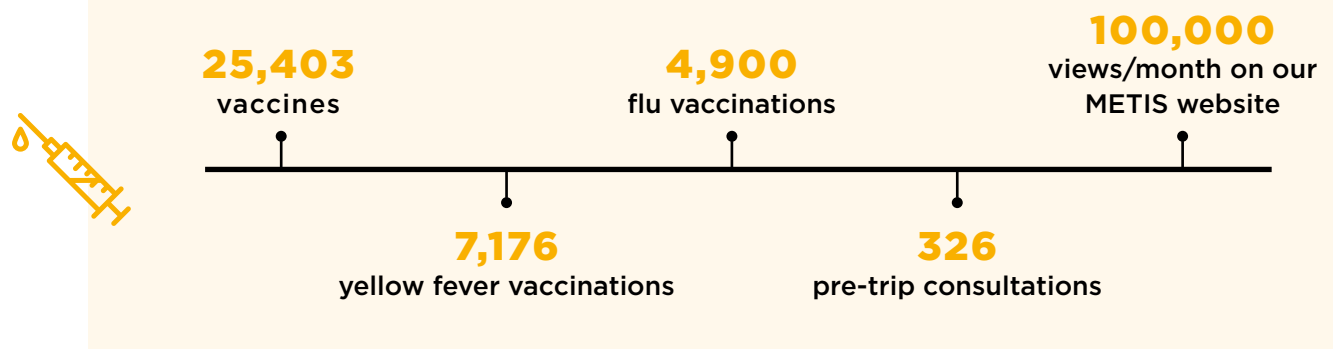
■ Thanks to the partnership between Institut Pasteur de Lille and Synlab Laboratories, volunteers (with their agreement) may be selected on the basis of their biological parameters.



27 AUGUST 2019
THE ISO 9001 CERTIFICATION - 2015
VERSION OF THE CLINICAL STUDIES
DEPARTMENT HAS BEEN RENEWED



THE INTERNATIONAL VACCINATION CENTRE



In 2019, 25,400 vaccines were carried out: Yellow fever (7,176), Hepatitis A and B, Typhoid fever, Meningitis, Japanese encephalitis, Tick-borne encephalitis, Rabies, Leptospirosis, etc.

The centre provides pre-travel consultations for expatriate managers and employees of large companies as well as simple tourists or people leaving for a round-the-world trip (326 consultations in 2019).

The centre is also an anti-rabies centre and completed 130 vaccine treatments in 2019 following stray animal bites contracted mainly in Asia and Africa.

On the METIS internet platform, available on the

Institut Pasteur de Lille website, travellers can find out directly about the diseases prevalent in the country or countries they wish to travel to and especially to obtain valuable advice for preparing their trips.

During the 2019 influenza vaccination campaign in businesses, the centre benefited from a cooperation protocol set up by the ARS, which extended the scope of action to recruit nurses to complement the vaccinating physicians; as a result, the centre was able to respond positively to a greater number of businesses and to vaccinate more people, i.e. 4,900 people.



THE DEVELOPMENT UNIT

Set up in March 2018, the Development unit runs the commercial development of the CPSL's health offers and takes part in deploying activities by collaborating with all the teams. It also organises the CPSL event days.

■ In 2019, the development unit notably structured an offer focused on "Corporate Health" with the aim of supporting businesses in their disease prevention and health promotion efforts. The desire to build, implement and evaluate real disease prevention programmes revolves around various measures such as conducting health checks and the Longevity Course for employees, setting up influenza vaccinations in companies, as well as deploying workshops, conferences and training courses.

■ The development unit is also managing a spin-off experiment for the Longevity Course in different areas of the Hauts-de-France region. Several partnerships have been established with the Pays de Mormal and the region of Roubaix in order to propose implementing the Longevity Course for the local population and ultimately incorporate it within the region's healthcare policy.

■ Regarding events,

- the 2019 Public Health Innovation Day brought together nearly 100 professionals to address the

topic of "Disease prevention at every age of life".

- 2 Workplace Healthcare Debates were also organised with our partner ADIX, aimed at building awareness in the workplace and getting the businesses of the region to take action in the area of disease prevention for their employees.

- In June, the Nutrition Interviews gathered together more than 220 participants over 2 days devoted to current topics in nutrition and obesity. On the other hand, the Nutrition Workshops had to be cancelled due to the transport strike in December. They were postponed in 2020.



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THE TEAMS

Administrative Director: **Cathy Brassart**

NUTRITION AND PHYSICAL ACTIVITY DEPARTMENT

Medical officer:

Jean-Michel Lecerf

NutrInvest Clinical Studies

Department

Group Leader:

Coralie Berthier

Expertise, Health

Education, and Training

Group Leader: **Eric Guiot**

MEDICAL EXAMINATION DEPARTMENT

CPAM

Medical officer: **Gwenaëlle**

Floch

Associate:

Florence Lejeune

Bespoke assessments

Medical officer:

Sophie Lahousse

Longevity Course

THE INTERNATIONAL VACCINATION CENTRE

Medical officer: **Emmanuel**
Dutoit

ADMINISTRATIVE UNIT

Administrative Manager:
Isabelle Dumon

THE DEVELOPMENT UNIT

Development manager:
Julie Padol

MICROBIOLOGICAL SAFETY UNIT

The Microbiological Safety Unit (MSU) examines the behaviour of pathogenic micro-organisms in the environment, and in particular, the response of bacteria and viruses to the means of control used to combat them. The Unit gathers together a set of skills and

organisations specialised in managing infectious risks in the following fields: water, air, surfaces, cosmetics, health products, hospital environments.

DR MICHÈLE VIALETTE

*Unit Manager,
Institut Pasteur de Lille*

The research objectives revolve around the study of the response of various microbial species (bacteria or viruses) to the conditions or their environment, whether natural or linked to human activities. The contribution of knowledge on the impact of a type of environment on the spread or destruction of micro-organisms has proven to be a major asset in the management of microbiological risks. The objective consists in evaluating and controlling the risks associated with the milieux, such as indoor air or hospital environments (combating hospital-acquired infections).

The team's expertise is nationally renowned for the study of bacteria and viruses that are

highly pathogenic to human beings. Dr Michèle Vialette is a microbiology expert for Anses (the national agency for food, environmental and occupational health & safety), serving on the committee of experts specialized in water.

The MSU also conducts specific studies for several industries in which there is some awareness of the management of contamination, such as the hospital sector or the cosmetics industry. Very involved with health actors, be they industrial, hospitals, or public authorities, the MSU contributes to the creation and evaluation of tools (products and processes) for the control of environmental contamination.



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KEY EVENTS

1 The ties with the hospital have been strengthened. The USM has collaborated with the Lille Catholic University Hospital Group ("GHICL") for the past 3 years within the context of a Research and Development project. This project aims to develop textiles with an antiviral action through contact aimed at combating hospital-acquired infections. This merger has also led to the creation, within the USM, of a bank of isolated antibiotic-resistant bacteria from the patients of the GHICL, with the aim of starting new projects focused on the prevention of infections by multidrug-resistant bacteria. The aim of a heightened scientific collaboration between these two institutions is becoming a reality as well as the Applied Research actions.

2 In 2019, the USM continued the partnership with Dyson France. Following an initial collaboration in 2017 on an air humidifier, studies on air purifiers developed by Dyson

enabled USM to demonstrate that these devices can eliminate 99% of the viruses likely to be present in the air (tests carried out on the Influenza H1N1 virus). Dyson France asserts these findings with the mention "Tested by Institut Pasteur de Lille". This partnership is destined to continue over the coming years.

3 The USM enhanced its training offer in 2019 by offering introductory and advanced training sessions in cell culture and virology. Handling viruses, including those that are pathogenic to humans, requires specific expertise that is not widely used. Thanks to their involvement in research projects and the cutting-edge expertise, the USM staff acquired a great deal of experience in these fields. As a result, the USM offers theoretical and, above all, practical training in order to teach the best practices for working in a level 2 laboratory for the handling of viruses.



**SUPPORT
THE FOUNDATION,
ADVANCE
TOGETHER!**

04

THANK YOU!

INSTITUT PASTEUR MEMBERS WORKING TOGETHER!

The research would come to nothing without the generosity of the public.

Whether it is individual donors, companies, volunteers, testators, etc. they all contribute to the success of the Foundation and to advances in research. From the first Euro to the bequest of assets, each donation counts and contributes to the successes of our researchers. **A huge thank you to everyone!**

In 2019, given the troubled economic and fiscal context, the foundation's faithful donors were able

to extend their support, new members signed up to the Institut Pasteur and many solidarity actions were initiated.

This great chain of generosity managed to raise **€8,100k** in research funding. It is a huge success in the fight against diseases that must be highlighted and extended so that researchers can continue their work.

8.1 million euros

**RAISED IN TOTAL IN
2019**

2.3 million euros

**FROM THE GENERAL
PUBLIC**

5.8 million euros

FROM GIFTS

DONATIONS, LEGACIES AND SOLIDARITY EVENTS

FUNDRAISING

In 2019, several fundraising campaigns were conducted to present the various projects and research teams supported by the foundation. The letters, email shots, websites, sources of information and fundraising are tailored to all donors.

Laboratory visits, conferences, meetings with researchers, events, etc. the foundation organises information events throughout the year so that donors can gain a better understanding of the research and benefits of their donation.

- 5 topical campaigns calling for donations
- 3 " Vivre Mieux Plus Longtemps" (living better for longer) magazines
- One digital newsletter each month
- 10 online topical files (sciences, research, health)
- 5 laboratory visits
- 10 "5 à 7" conferences

SOLIDARITY EVENTS

The commitment to researchers also involves organising events or raising funds from the people they know. Joyful and festive events... sporting challenges, birthdays, weddings, parties... but also more sorrowful events, such as the loss of a loved one and the organisation of death collections in their memory, are an opportunity to appeal for support for the foundation and thereby contribute to the advancement of research.

- 16 birthday fundraisers on Facebook
- 3 solidarity races
- 2 concerts
- 9 collection pages on the Alvarum
- 75 death collections in 2019

COMMITTED VOLUNTEERS

Nearly 20 volunteers got involved in supporting the researchers in 2019: organisation of events, help with fundraising, promotion of the foundation, etc. everyone gives the time and skills they can and thereby contributes to supporting the research.



SCHOOLS STANDING WITH RESEARCHERS

Thanks to the educational information provided by the institute, Year 6 classes can learn about science and the experiments carried out at the institute as part of Kid

Campus campaign. 20 selected classes were able to meet researchers, organise fundraisers and carry out laboratory experiments.

THANK YOU

As an agent of generosity, Institut Pasteur de Lille once again participated in the international GIVING TUESDAY, world day of generosity movement.

This solidarity movement, in response to Black Friday, aims to promote giving and generosity in all its forms. This gives the foundation the opportunity to thank all its donors while giving the partners the opportunity to show their support.



BEQUESTS, DONATIONS AND LIFE INSURANCE

Bequests, life insurance, donations are all ways of supporting research. The donations and bequests department provides information to people who are looking to bequeath assets and take to heart the duty of remembering and recognising this precious support.

It is possible to bequeath assets during one's lifetime as part of a donation in usufruct or bare ownership, given the benefits that these measures can have for the owners.

IN 2019, THE FOUNDATION RECEIVED €5.8 MILLION IN BEQUESTS AND LIFE INSURANCE SENT BY 41 PEOPLE AS WELL AS A DONATION IN BARE OWNERSHIP.

Bequests and life insurance

€4,402,472

Bare ownership donation

€1,400,000

Donations

€2,298,119

PRIVATE-SECTOR SPONSORSHIP

Developing relationships with the economic and industrial worlds through scientific collaboration, expertise, general interest missions, and sponsorship is essential for making research and prevention available for everyone's good health. With the international reach of its research and its local actions, Institut Pasteur de Lille contributes to the region's attractiveness and it wholeheartedly

plays its role as an economic and social actor. In 2019, business sponsorship brought funds of €0.75 million to the Foundation.

What's more, the partners also help to increase the exposure of the Foundation by promoting the institute among their networks, employees and clients.



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THE SPONSORS (2017-2022 CAMPAIGN)

ADIX	BASF	BEL FOUNDATION
AG2R LA MONDIALE	BRUNEAU	MACIF FOUNDATION
ANIOS	ENTREPRISES ET CITES	LACTALIS
API RESTAURATION	SANTELYS	M COMME MUTUELLE
AUCHAN RETAIL FRANCE	SYNLAB	VERSPIEREN

THE FRIENDS OF THE FOUNDATION

The friends of the foundation promote projects, participate in the life of the institute, and have an elected member and permanent guests on the Executive Board. Throughout the year, they support the foundation and the teams.

- André Tordeux (Genoscreen)
- Vincent Behague
- Thierry Letartre (ANIOS)
- Damien Debosque(API)
- Sebastien Duprez (E&C)
- Brigitte Villette (AG2R-LM)
- Patrice Lequint (KPMG)
- Laurent Coutant (LACTALIS)
- Jérôme Rehlinger (MCM)
- Thierry matthieu (SYNLAB)
- Johan Cailliez (VERSPIEREN)
- Patrick Vacossin (SCP Vacossin)
- Aurelien Cabezon (Weembi)

FRANCK THILLIEZ, A COMMITTED SPONSOR

Having supported the institute for several years, the writer Franck Thilliez is a committed ambassador who regularly visits researchers, promotes their work and organises annual digital fundraisers on the occasion of the release of one of his novels.



SPONSOR EVENTS

THE YEAR 2019 WAS PUNCTUATED
BY MANY EVENTS AND ACHIEVEMENTS.
EACH PARTNERSHIP LED BY INSTITUT PASTEUR DE LILLE
SEEKS TO BE UNIQUE.

PARTICIPATION IN THE 2019 ROUTE DU LOUVRE THANKS TO THE PARTNERSHIP WITH AG2R LA MONDIALE

For more than 10 years already, AG2R La Mondiale has partnered with Institut Pasteur de Lille to build public awareness of health issues and insist on the importance of prevention. This year, €15,000 was collected with the support of the company's employees who transformed their kilometres into euros.



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120TH ANNIVERSARY PARTY

In 2019, the Institute celebrated the 120th anniversary of its foundation with all of its business partners. The opportunity to give the professionals of the region a real-life laboratory experience and to introduce them to the current research projects.



SOLIDARITY FUNDRAISERS

KIABI

400 employees of KIABI and Institut Pasteur de Lille took part in the "Smart Mobility, let's do it!" challenge». What's the objective? Promoting regular physical activity and fund raising to finance research projects on Longevity. A total of €3,000 was collected!



WEEMBI

SOLID'AIR weekend is a unique collective action that revolves around a new challenge involving the world of wind tunnels: 24 hours of consecutive flight to profit scientific research. With each booked initiation flight, Weembi donated €15 to the foundation. The third SOLID'AIR event raised €1,500.



CIC

For World Alzheimer's Day, the CIC wanted to support the Foundation by broadcasting a message appealing for donations on their ATMs.



ENGIE

The ENGIE employees ran for a good cause! A solidarity race which raised €2,000 for research.



LILLE METROPOLE BASKET

For Giving Tuesday 2019 (day of generosity), the city's basketball club wanted to support Institut Pasteur de Lille by getting its players to participate. Videos of an appeal for donations were made by the players, and donation messages by text message were broadcast during the match against Blois.



DECATHLON

The institute's teams supported those of DECATHLON for two major events in 2019: the running show in Paris and Vital Sport in Lille. The opportunity to demonstrate the challenges faced by both organisations in supporting populations in order to improve life and live longer, and to appeal to the sports or non-sports customers of the major sports brand to donate to research.



A PAINTING FOR RESEARCH!

The Lille-based painter, Jean Pattou, donated a piece of work for the 120th anniversary of the Foundation. The painting was bought by the Rozé construction company and the proceeds were donated to research.



INSTITUT PASTEUR DE LILLE AND COMPANY NETWORKS

CLUB GAGNANTS (THE WINNERS CLUB)

Institut Pasteur de Lille is a member of "Club Gagnants" (winners' club). Their goal is to call attention to the economic dynamics and potential of Hauts-de-France. The Winners club regularly contributes to the outreach of the institute through its communications.



PASTEUR LILLE AWARD AT THE INDUSTRY TROPHIES

On the occasion of the Trophées de l'Industrie awards, Institut Pasteur de Lille, which is committed to developing its relations with the industrial world, awarded the Pasteur Lille prize to the Mediawit start-up for their system designed to prevent the risk of falling, thereby promoting the objective of living better, longer.



"CLUB DES ENTREPRISES CENTENAIRES" (100-YEAR-OLD BUSINESS CLUB)

This club, which is composed of regional companies over 100 years old, has produced a second work to put these companies in the spotlight: "Transformation made to last". As a 100-year-old foundation, Institut Pasteur de Lille is an example of how adapting to change enables ongoing improvements in innovation.



FLANDERS BUSINESS CLUB

The institute regularly participates in the FBC meetings bringing together business leaders from the Hauts-de-France region.



SERVICE CLUBS

Institut Pasteur de Lille is fortunate to be supported by many Rotary Clubs from the Haut-de-France region. They regularly organise events to promote research and are strongly involved alongside researchers.



INSTITUT PASTEUR DE LILLE MUSEUM

A NEW WAY TO DISCOVER HISTORY AND SCIENCE

Fully financed by the Anios Laboratories sponsorship and inaugurated in September 2017, the Institut Pasteur de Lille Museum reflects not only Institut Pasteur de Lille's history and its founders but also today's dynamic: many future projects on the topic of longevity as well as new collaborations with the business world, as demonstrated by the patronage of Laboratoires Anios.



Lodged in Albert Calmette's former apartment - it's within these walls that Dr. Calmette and the veterinarian Camille Guérin discovered *Bacillus Calmette-Guérin* (BCG), a vaccine against tuberculosis. The original stem cells are presented in the museum. Louis Pasteur and Lille are also linked with the history of alcoholic fermentation, which the scientist discovered at the Faculty of Sciences of Lille when he was the dean in 1854.

Since its creation, Institut Pasteur de Lille, a private state-recognised public-interest foundation, has sought to help local populations by putting science at the service of health.

At the time, certain private individuals, local communities and industrialists came together to create the institute which, in addition to creating serums, educated the population about the rules of hygiene.

While the lines of research and healthcare measures have evolved towards the diseases associated with ageing (cancers, cardiovascular diseases, infectious and parasitic diseases, Alzheimer's disease, diabetes, etc.), Institut Pasteur de Lille remains very attached to its roots and its history.

"AROUSING INTEREST IN SCIENCE,
RESEARCH AND HEALTH IS A MAJOR
CONCERN FOR INSTITUT PASTEUR DE
LILLE. »

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The museum is a mix between a cabinet of curiosities, a period laboratory and digital installations, revealing the mysteries of Institut Pasteur de Lille and its founders. This contemporary layout provides a tool that is undeniably suited to communicating science to all audiences. Arousing interest in science, research and health is a major concern for Institut Pasteur de Lille.

Visitors immerse themselves in a fantasy world where scientific research is poetically showcased in every corner of the museum. Installed on everyday furniture, they discover vials brought to life with video, a letter that writes itself by magic, a little mouse that crisscrosses the room, scales that wobble from left to right, etc. This contemporary exhibition has a very particular resonance in this location steeped in history.

4 REALMS:

Room A: Institut Pasteur de Lille

Room B: Louis Pasteur

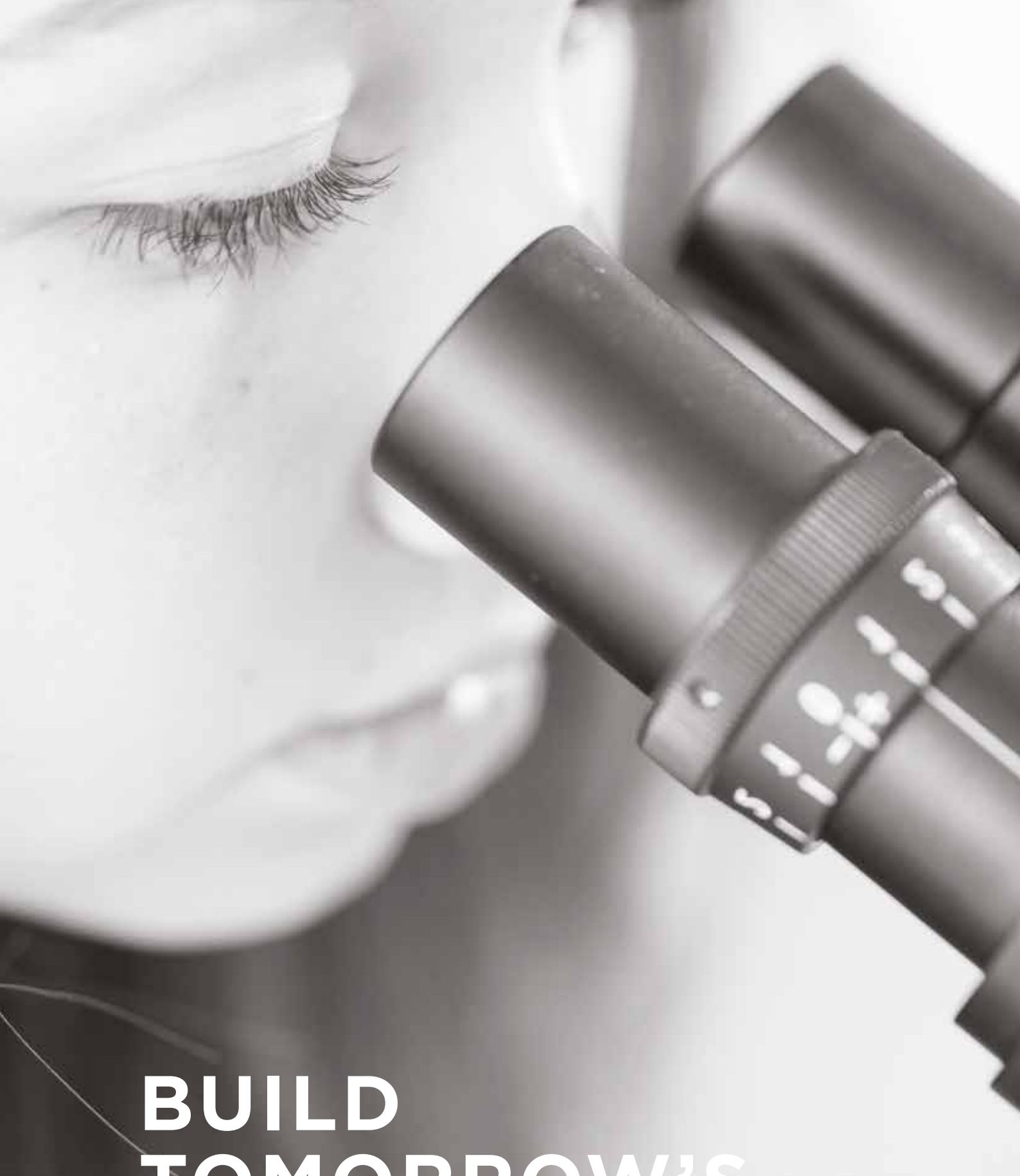
Room C: Albert Calmette and Camille Guérin

Room D: Institut Pasteur de Lille today

Open to the public: Saturday and Sunday:
10:00am to 12:00pm / 2:00pm to 5:00pm

Private events and guided tours.

Contact: +33 (0)3 20 87 72 42 - musee@pasteur-lille.fr



**BUILD
TOMORROW'S
FOUNDATION**

05

A FOUNDATION AT THE SERVICE OF THE POPULATION

Institut Pasteur de Lille (IPL) has been a private, non-profit organisation since 1898, whose purpose is to promote research, disease prevention and training in health. As a financially and legally independent member of the "Réseau International des Instituts Pasteur" (international network of Pasteur institutes), Institut Pasteur de Lille is authorised to receive donations, bequests and sponsorship for its research projects. The Institut Pasteur de Lille campus devotes itself every day to fundamental research and public health, aimed at giving everyone the means to live better, longer.

Institut Pasteur de Lille fights daily against cardiovascular and neurodegenerative diseases, infectious and inflammatory diseases, metabolic diseases, cancer and diabetes. This research is carried out in collaboration with the research bodies CNRS, INSERM, University of Lille and Lille University Hospital, international network of Pasteur institutes, etc.

Institut Pasteur de Lille also develops its relations with the business and industrial worlds through scientific collaborations, specialist services, general-interest activities and corporate sponsorship. This relationship, which is faithful to the origins of the institute, is necessary for the Foundation to fulfil its missions of research, specialist services and disease prevention in healthcare. Thanks to the permanent guest seats on the Executive Board, business and industrial players can find out about and be involved in the management of the Foundation.

Further, to fully play its role as an Hauts-de-France scientific and economic actor, Institut Pasteur de Lille participates in different company networks such as Club Gagnants, FBC, and Club des Entreprises Centenaires. Institut Pasteur de Lille also collaborates with many structures and associations to fulfil its role as a social and societal agent at the service of the population.



VALUES OF THE INSTITUT PASTEUR

Since its creation, Institut Pasteur de Lille has endeavoured to put science at the service of health by relying on the commitment of teams and shared values.

THE 5 CORE VALUES OF INSTITUT PASTEUR DE LILLE:

- 1** Putting science at the service of health
- 2** Contributing to scientific excellence
- 3** Acting responsibly and in solidarity
- 4** Putting discipline and ethics at the heart of projects
- 5** Passing on knowledge

1 Putting science at the service of health

"Improving human health guides the actions of the teams." This quote from Louis Pasteur also illustrates the spirit of the institute that guides all the Pasteur institutes around the world (RIIP).

2 Contributing to scientific excellence

Since its creation, Institut Pasteur de Lille has contributed to major innovations in health through high-level scientific research. The teams strive to maintain this level of excellence through an interdisciplinary approach, collaborations and national and international research programmes.

3 Acting responsibly and in solidarity

Everyone works in the general interest to improve

society through their daily actions: The CSR (Corporate Social Responsibility) commitment within the Campus, support to the Foundation, access to health for all including to people in vulnerable situations, etc. on the one hand and observation of the population in relation to mechanistic assumptions on the other hand. Regarding this third point, the experience of Institut Pasteur de Lille is unique in France, and has no equivalent in the academic or hospital infrastructures.

4 Putting discipline and ethics at the heart of projects

Ethics and discipline are at the heart of all the actions and decisions of the Foundation: code of conduct, research ethics charter, governance audit, public procurement, multidisci-

plinary disease prevention consultation meetings, account and donation controls, transparency in the use of funds, etc.

5 Passing on knowledge

Everyone contributes through their commitment and actions to sharing their knowledge: teaching, scientific publications, information and public health actions aimed at the general public (Kid Campus, apprentice researchers, conferences, files, workshops, etc.)



OUR CSR COMMITMENTS

Institut Pasteur de Lille has implemented a Corporate Social Responsibility (CSR) approach since 2016. Its approach is structured around 4 main objectives (Governance, Social, Societal and Environmental) for which the actions accomplished during the 2018 - 2019 period and the objectives for the 2020 - 2022 period are presented.

Due to the foundation's vocation and missions of general interest, the CSR has been in the DNA of the institute since its creation and guides its strategic project. However, the foundation's CSR

commitment was assessed and structured as part of the foundation's strategic project. Three specific issues have been identified:

- **Unite the campus teams around societal and environmental themes that go beyond its scientific research and healthcare activities**
- **Increase employee well-being at work**
- **Control the environmental impact of the campus**

As a result of the business initiatives undertaken by Institut Pasteur de Lille, it won the **silver trophy of the responsible economy prizes of the Hauts-de-France "Réseau Alliances" (Alliances network)** in 2019, thanks to the following, including but not limited to:

- **Transparent communication of the institute's activities to the members of the executive board in order to build unity around the Foundation's project**

- **Identification and prevention system for conflicts of interest** Attention paid to employee training
- **Taking into account the environmental**
- **Conducting health checks for populations in vulnerable situations in particular**
- **Increased security regarding personal data**
- **Opening of the Campus to the public** for scientific visits and public scientific conferences



“

CSR IS PART OF THE DNA OF INSTITUT PASTEUR DE LILLE, THROUGH ITS RESEARCH ACTIVITIES AND ACTIONS OF GENERAL INTEREST. OUR APPROACH TODAY AIMS TO GIVE EXPRESSION TO THIS DNA IN THE FOUNDATION'S CORE ATTITUDES AND INSPIRE OUR EMPLOYEES.

Didier Bonneau, Deputy Managing Director

2018-2019 CSR REPORT

GOVERNANCE

ORGANISING AND INCREASING THE EXPOSURE OF THE CSR APPROACH OF INSTITUT PASTEUR DE LILLE

INITIAL CSR AUDIT

Conducted by a working group with a corporate patronage, this work defined the major issues and assessed the current level of the IPL approach.

These tools need to be developed in order to implement the institute's CSR approach in a more structured and visible way.

HAUTS-DE-FRANCE CSR TROPHY

This competition organised by the Alliances Network made it possible to compare the level of the IPL's CSR approach on a voluntary basis to other companies involved and to be assessed by a panel of professionals.

Silver prize in the Organisation category

SOCIETAL

BE AT THE SERVICE OF ITS COMMUNITIES: LOCAL POPULATIONS AND SCIENTISTS

LIVING BETTER FOR LONGER

- ▶ Creation of the Longevity Course in order to detect the weaknesses of the consultants as early as possible and offer them an action plan to overturn these weaknesses.
- ▶ Completion of 220 longevity check-ups.

HEALTH, DISEASE PREVENTION AND VACCINATION

Detecting weaknesses in people in vulnerable situations as a matter of priority.

55% of people treated by the health examination centre are in a vulnerable situation.

ETHICAL PRACTICES

Institut Pasteur de Lille promises to provide independent and ethical research thanks to:

- ▶ A scientific code of conduct;
- ▶ A business code of conduct;
- ▶ A policy on the use of the institute's corporate name and visuals by third parties for promotional purposes.

MANAGEMENT OF PERSONAL DATA

- ▶ Compliance with the general data protection regulations.
- ▶ Appointment of a data protection officer.
- ▶ Increasing the awareness of the management about personal data protection.
- ▶ Identification of the processing of personal data.

COMMUNICATE - RAISE AWARENESS

- ▶ Kid Campus - raising awareness among young people in order to encourage vocations to the scientific professions.
- ▶ Opening of the campus to all those interested through conferences, laboratory visits, events, etc.
- ▶ Renovation of the IPL museum dealing with the history of Institut Pasteur de Lille and the work of Pasteur and Calmette.

SOCIAL

BE A CREATOR OF HUMAN VALUES

DEVELOP EMPLOYABILITY

Lifelong training for staff is a key aspect for the Pasteur campus. To achieve this, a training plan is deployed.

2019: training budget of 2% of the payroll

EQUAL OPPORTUNITIES

From recruitment to professional development, be watchful of the fair treatment of people.

Professional equality index: 98/100 (2019)

More than 6% of the staff with disabilities

SECURE WORKING CONDITIONS FOR EMPLOYEES AND RESIDENTS

The disease prevention approach in place respects the principles of the ISO45001 standard, in partnership with Inserm, CNRS and the University of Lille.

The Psycho-Social Risks approach was implemented by a participatory study and an action plan in 2019.

Work accident:

Frequency rate: 8 in 2019, 4 in 2018

Severity rate: 0.11 in 2019, 0.15 in 2018

PROFESSIONAL INTERVIEWS

They are used to feed back requirements in terms of development or mobility supported by the company.

ENVIRONMENTAL

BE A COMMITTED AND RESPONSIBLE PLAYER

REDUCE THE IMPACT OF WASTE

Measures to reduce the production of waste at source have been put in place.

The use of eco-cups in the company restaurant has resulted in the elimination of 250 disposable cups/day

Directing the different types of waste towards specific channels.

14,000 cigarette butts, i.e. 7kg, collected and processed in 6 months

REDUCING THE CONSUMPTION OF ENERGY

By renovating buildings and acting on consumer equipment.

REDUCING GREENHOUSE GAS EMISSIONS

This aspect is mainly linked to staff travel when commuting.

For this, a Mobility Plan has been deployed since 2018.

► Raising awareness among staff through challenges: "Mobilité Hauts-de-France", "Tous en selle",

► Bicycle kilometre allowance.

2018 and 2019 "best participation rate" winner in the Hauts-de-France Mobility Challenge. In 2019, 188 participants.

EXECUTIVE BOARD

COLLEGE OF FOUNDERS

Jacques Richir, Deputy mayor of Lille. Chairman of the Executive Board (*)

Marc Bodirot, Deputy mayor of Lille

Dominique Picault, Deputy mayor of Lille

Jérémie Crepel, Deputy mayor of Lille

Isabelle Mahieu, Advisor City Council of Lille

COLLEGE OF INSTITUTIONAL PARTNERS

François Kinget, City Councillor, representative of Métropole Européenne de Lille (MEL) Secretary (*)

Nicolas Lebas, Vice-Chairman of Higher Education, research and universities, representative of

the Hauts de France region. Vice-Chairman (*)

Nicolas Siegler, Departmental Advisor, representative of the County Council of the Nord

Stewart Cole, General Manager of Institut Pasteur

Samir Ould Ali, North-West Regional representative, representing the CEO of the National Institute of Health and Medical Research (Inserm)

Christophe Muller, Hauts-de-France Regional representative, representing the President of the National Centre for Scientific Research (CNRS)

Jean-Christophe Camart, Chairman of the Lille University

COLLEGE OF QUALIFIED PERSONALITIES

Prof François-René Pruvot, Chairman of the Medical Commission Establishment of Lille University Hospital

Patrick Vacossin, Chamber of Notaries of the Nord. Treasurer (*)

COLLEGE OF FRIENDS OF THE FOUNDATION

Thierry Letartre, Managing director of ANIOS. Member of the office (*)

PERMANENT GUEST MEMBERS

Antoine Pernod, Auchan

Brigitte Villette, AG2R LA MONDIALE

Thierry Mathieu, Eurabio/ Synlab

(*) member of the office

THE ORGANISATION CHART AS OF 1 JANUARY 2020

GENERAL

MANAGING DIRECTOR
Prof Xavier Nassif

SCIENTIFIC

SCIENTIFIC DIRECTOR
Pr Benoît Déprez

INTERNATIONAL RELATIONS MANAGER
Dr Nathalie Mielcarek

CENTRE FOR
RESEARCH ON
LONGEVITY

Center for Infection and
Immunity of Lille (CIIL)
Dr Jean Dubuisson

Risk factors and molecular
determinants of
aging-related diseases
Pr Philippe Amouyel

Nuclear receptors,
metabolic and
cardiovascular diseases
Pr Bart Staels

Metabolic functional
(epi)-genomics and
molecular mechanisms
involved in type 2 diabetes
and related diseases
Pr Philippe Froguel

Translational Research
in Diabetes (TRD)
Prof François Pattou

Drugs and molecules
for living systems
Pr Benoît Déprez

CANcer Heterogeneity,
plasticity and resistance
to THERapies
Dr Isabelle Van Seuningen

Laboratory of genetic
laboratory
Dr Fabrice Nesslany

Mixed service unit
Dr Philippe Boutin

PLATFORMS

Biolmaging Centre Lille -
North of France (BICel)
Dr Frank Lafont

ARIADNE - HTS-HCS
Screening
Dr Florence Leroux

Proteomics and modified
peptides
Dr Jean-Michel Saliou

PLEHTA platform
Fabrice Infanti

Bioinformatics, bioanalysis
and biostatistics of Lille
(Bilille)
Helene Touzet /
Guillemette Marot

Transcriptomics and
Applied Genomics (TAG)
Dr David Hot

Nuclear magnetic
resonance
Dr. Isabelle LANDRIEU

EquipEx genomics
LIGAN-PM
Pr Philippe Froguel

High Security Laboratory
Dr Michèle Vialette

Genome Study Laboratory
("LAG")
Nathalie Fiévet

Peptide chemistry platform
Dr Oleg Melnyk

CENTRE FOR
HEALTH AND
LONGEVITY

Prof Xavier Nassif

CPAM health check
Dr Gwenaëlle Floc'h

Flexible check-up
Dr Sophie Lahousse

Vaccination
Dr Emmanuel Dutoit

Nutrition and Physical
Activity
Dr Jean-Michel Lecerf

Longevity Course
Dr Pascaline Cassagnaud

Epidemiological research
Dr Maël Barthoulot

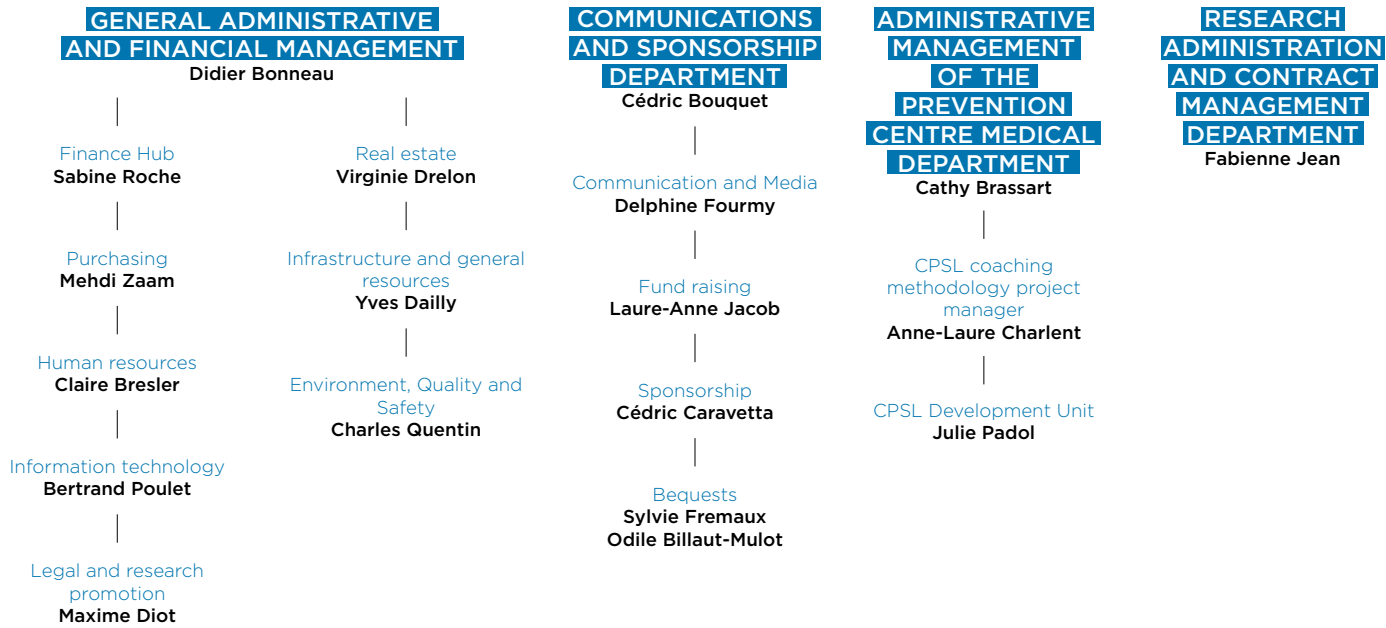
Microbiological Safety Unit
Dr Michèle Vialette

MANAGEMENT

DEPUTY MANAGING DIRECTOR
Didier Bonneau

ADMINISTRATIVE

ASSISTANT MANAGER
Sylvie Amoravain



807 EMPLOYEES
ON THE CAMPUS



352
Employees
Institut Pasteur de Lille



109
Men



243
Women



455
Employees
and trainees
other institutions *

* INSERM, CNRS,
Lille University,
Lille University Hospital,
startups...



27
Nationalities

€17.1 million
dedicated to research in 2019

The financing for Institut Pasteur de Lille’s missions comes from a variety of private and public sources.

In 2019, Institut Pasteur de Lille spent **€28.8 million** on its principal missions of research (**€17.1m**), disease prevention and public information (**€9.8m**).



THE **€17.1M**
OF RESEARCH CAN BE BROKEN DOWN AS FOLLOWS:

€5.2m

for infectious and inflammatory diseases

€3.6m

for the running of the technology platforms

€0.9m

for cancer research

€0.9m

for the discovery of medicines

€2.1m

for research in cardiovascular and metabolic diseases

€3.3m

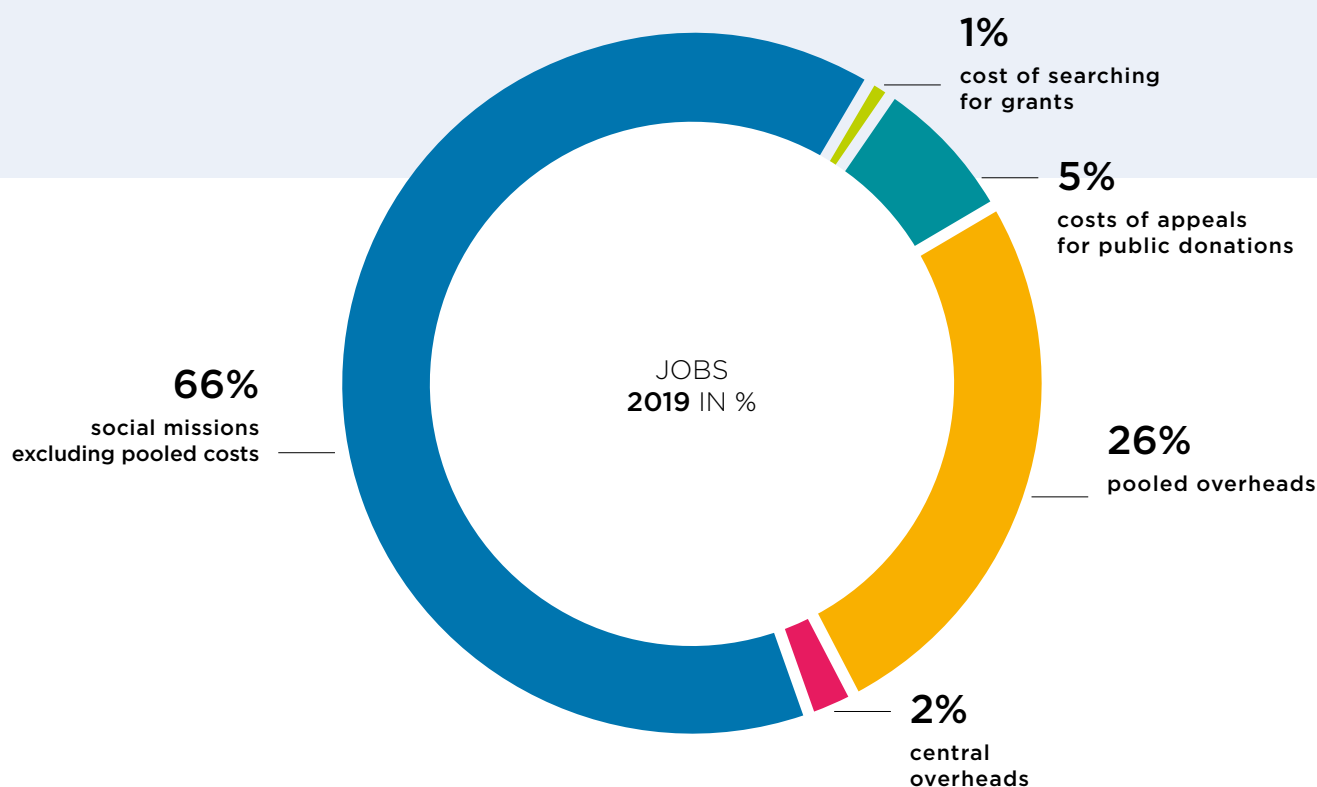
for cardiovascular and inflammatory diseases

€1.1m

for genetic and metabolic diseases

JOBS

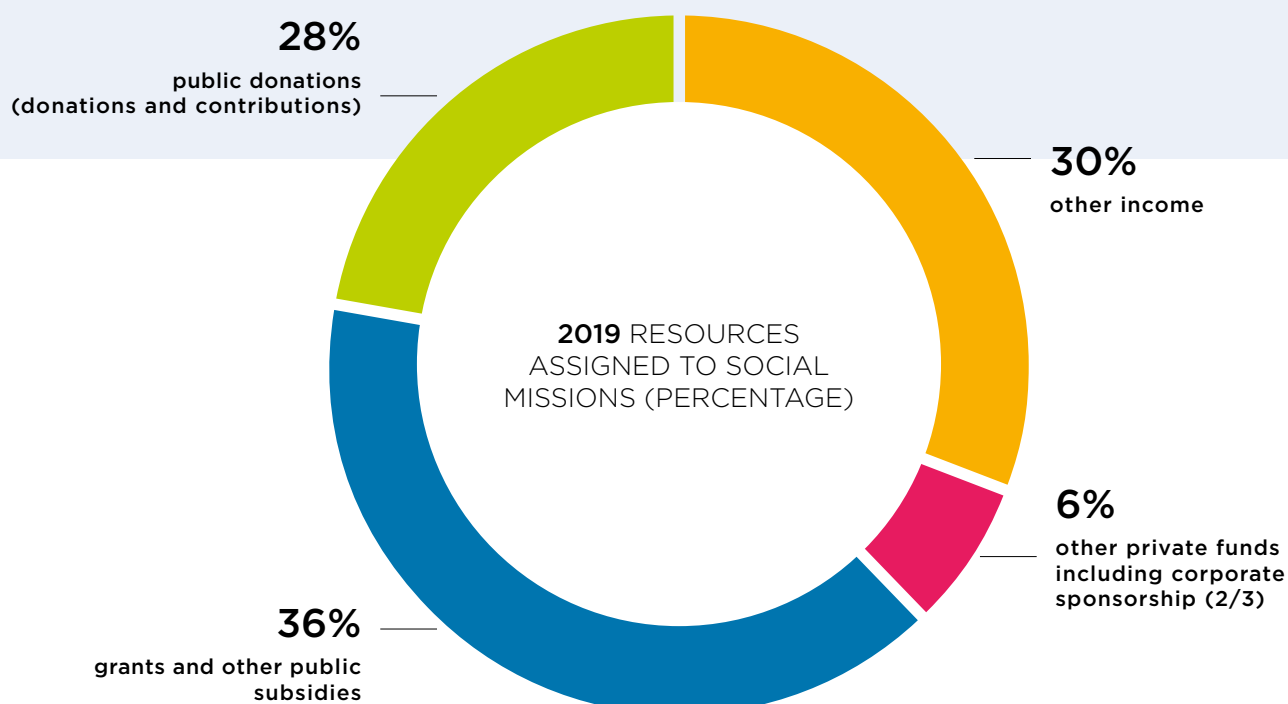
€31.6m



69

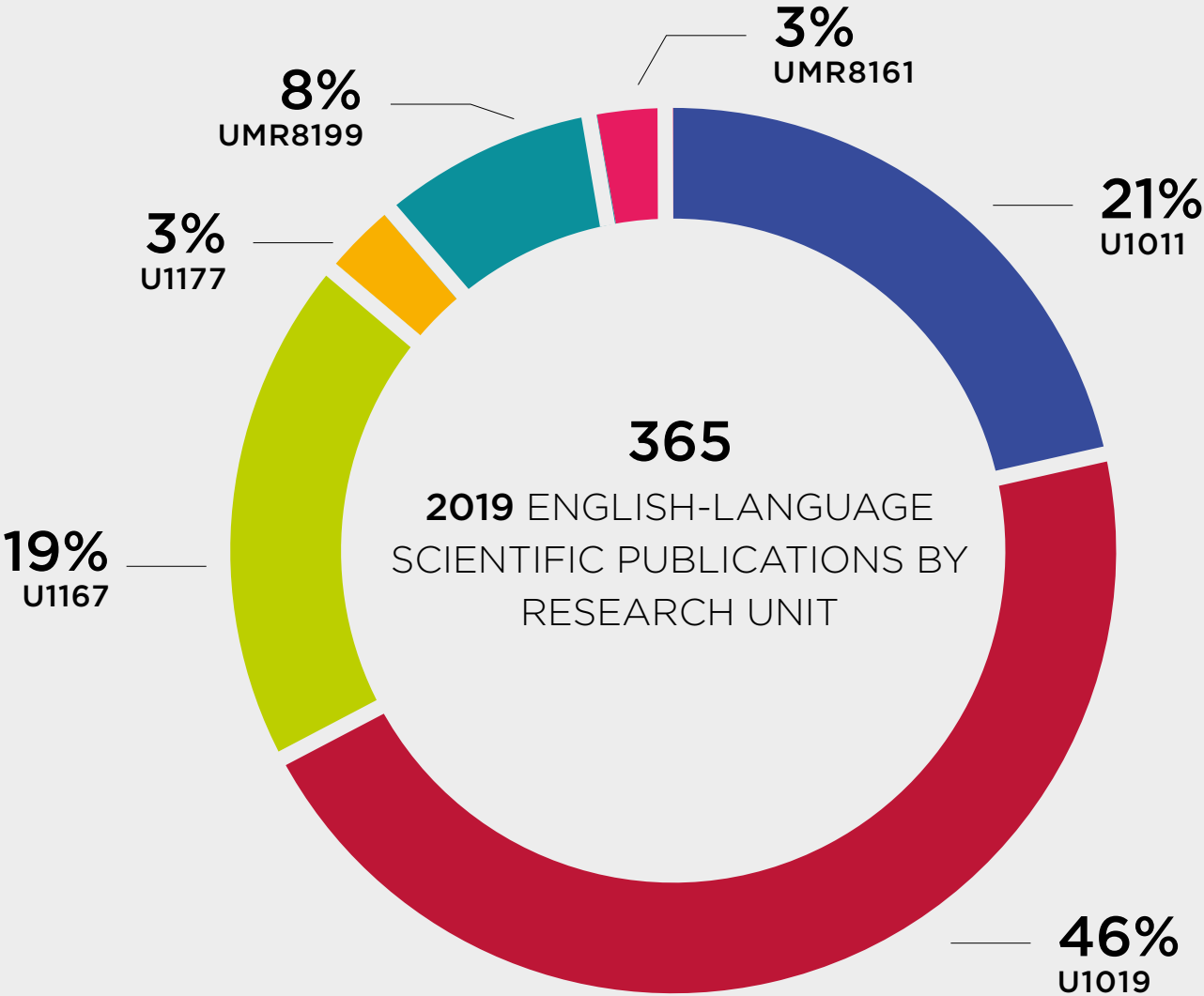
RESOURCES

€29.4m



2019 SCIENTIFIC PUBLICATIONS

70



Is Institut Pasteur de Lille the leading player (1st or 2nd or last author)?	YES	NO	All publications
2015	189	157	346
2016	162	174	336
2017	181	162	343
2018	181	161	342
2019	133	232	365

SCIENTIFIC PAPERS WITH A HIGH IMPACT FACTOR

U1011

Grzych G, Maboudou P, Brousseau T, Factitious severe acidosis in a patient, preanalytical considerations and prevention., *Clin. Chem. Lab. Med.*, 2019

Grzych G, Lopez B, Pekar JD, Increased Triglycerides in a Child., *Clin. Chem.*, 2019 , 1180-1181

Pekar JD, Grzych G, Durand G, Haas J, Lionet A, Brousseau T & al, Calcium state estimation by total calcium: the evidence to end the never-ending story., *Clin. Chem. Lab. Med.*, 2019

Coisne A, Pontana F, Tchéché D, Richardson M, Longère B, Vahdat O & al, Transcatheter Mitral Valve Replacement: Factors Associated with Screening Success and Failure., *EuroIntervention*, 2019

Vermersch M, Longère B, Coisne A, Schmidt M, Forman C, Monnet A & al, Compressed sensing real-time cine imaging for assessment of ventricular function, volumes and mass in clinical practice., *Eur Radiol*, 2019

Grzych G, Pekar JD, Maboudou P, Better Glucose Stability in Serum than in Plasma Samples after 12 h Stay at Room Temperature., *Diabetes Technol. Ther.*, 2019

Mogilenko DA, Haas JT, L'homme L, Fleury S, Quemener S, Levavasseur M & al, Metabolic and Innate Immune Cues Merge into a Specific Inflammatory Response via the UPR., *Cell*, 2019

Haas JT, Staels B, Understanding lipid metabolism through hepatic steat-omics., *Nat Rev Endocrinol*, 2019

Grzych G, Pekar JD, Maboudou P, Lippi G, Leucocytosis-induced plasma hyperkalaemia in samples conveyed by a pneumatic transport system: tips and tricks., *Br. J. Haematol.*, 2019

Grzych G, Pekar JD, Durand G, Deckmyn B, Maboudou P, Lippi G, Albumin-Adjusted Calcium and Ionized Calcium for Assessing Calcium Status in Hospitalized Patients., *Clin. Chem.*, 2019

Pekar JD, Carpentier T, Maboudou P, Grzych G, Blood from heparin tubes is an acceptable alternative to assess hematocrit determination., *Clin. Chem. Lab. Med.*, 2019

Chávez-Talavera O, Haas J, Grzych G, Tailleux A, Staels B, B, ile acid alterations in nonalcoholic fatty liver disease, obesity, insulin resistance and type 2 diabetes: what do the human studies tell?, *Curr. Opin. Lipidol.*, 2019

Van Belle E, Vincent F, Rauch A, Casari C, Jeanpierre E, Loobuyck V & al, von Willebrand Factor and Management of Heart Valve Disease: JACC Review Topic of the Week., *J. Am. Coll. Cardiol.*, 2019 , 1078-1088

Dupont A, Soukaseum C, Cheptou M, Adam F, Nipoti T, Lourenco-Rodrigues MD & al, Relevance of platelet desialylation and thrombocytopenia in type 2B von Willebrand disease: preclinical and clinical evidence., *Haematologica*, 2019

Rauch A, Susen S, Zieger B, Acquired von Willebrand Syndrome in Patients With Ventricular Assist Device, *Front. Med.*, 2019

Paumelle R, Haas J, Hennuyer N, Bauge E, Deleye Y, Mesotten D & al, Hepatic PPAR γ is critical in the metabolic adaptation to sepsis., *J. Hepatol.*, 2019

Butruille L, Marouze L, Pourpe C, Oger F, Lecoutre S, Catheline D & al, Maternal high-fat diet during suckling programs visceral adiposity and epigenetic regulation of adipose tissue stearoyl-CoA desaturase-1 in offspring., *Int J Obes (Lond)*, 2019

Butruille L, Marouze L, Pourpe C, Oger F, Lecoutre S, Catheline D & al, Maternal high-fat diet during suckling programs visceral adiposity and epigenetic regulation of adipose tissue stearoyl-CoA desaturase-1 in offspring, *Int. J. Obes.*, 2019 , 2381-2393

U1019

Grosbois JM, Heluain-Robiquet J, Machuron F, Terce G, Chenivresse C, Wallaert B & al, Influence Of Socioeconomic Deprivation On Short-And Long-Term Outcomes Of Home-Based Pulmonary Rehabilitation In Patients With Chronic Obstructive Pulmonary Disease, *Int. J. Chronic Obstr. Pulm. Dis.*, 2019, 2441-2449

Veyron-Churlet R, Loch C, Virulence., *Pathogens*, 2019

El Achkar S, Demanche C, Osman M, Rafei R, Ismail MB, Gaudin C & al, oonotic tuberculosis in humans assessed by next-generation sequencing: an 18-month nationwide study in Lebanon., *Eur. Respir. J.*, 2019

El Achkar S, Demanche C, Osman M, Rafei R, Ismail MB, Gaudin C & al, oonotic tuberculosis in humans assessed by next-generation sequencing: an 18-month nationwide study in Lebanon., *Eur. Respir. J.*, 2019

Baille G, Perez T, Devos D, Machuron F, Dujardin K, Chenivresse C & al, Dyspnea Is a Specific Symptom in Parkinson's Disease., *J Parkinsons Dis*, 2019

Kamela C S Ng, Supply P, Cobelens Frank GJ, Gaudin C, Gonzalez-Martin J, Bouke C de Jong, & al, How Well Do Routine Molecular Diagnostics Detect Rifampin Heteroresistance in Mycobacterium Tuberculosis?, *J. Clin. Microbiol.*, 2019

Hollin T, De Witte C, Fréville A, Guerrero IC, Chhuon C, Saliou JM & al, Essential role of GEXPI5, a specific protein Phosphatase type 1 partner, in Plasmodium berghei in asexual erythrocytic proliferation and transmission., *PLoS Pathog.*, 2019, e1007973

Lavie M, Linna L, Moustafa RI, Belouzard S, Fukasawa M, Dubuisson J, Role of the cytosolic domain of occludin in trafficking and HCV infection., *Traffic*, 2019

Perez T, Deslee G, Burgel PR, Caillaud D, Le Rouzic O, Zysman M & al, Predictors in routine practice of 6-min walking distance and oxygen desaturation in patients with COPD: impact of comorbidities, *Int. J. Chronic Obstr. Pulm. Dis.*, 2019 , 1399-1410

Gaudet A, Parmentier E, De Freitas Caires N, Portier L, Dubucquoi S, Poissy J & al, Decrease of the plasmatic endocan cleavage ratio is associated with the hyperinflammatory phenotype of acute respiratory distress syndrome., *Crit Care*, 2019 , 252

Pastor A, Machelart A, Li X, Willand N, Baulard A, Brodin P & al, A novel codrug made of the combination of ethionamide and its potentiating booster: synthesis, self-assembly into nanoparticles and antimycobacterial evaluation., *Org. Biomol. Chem.*, 2019

Agouridas V, El Mahdi O, Diemer V, Cargoët M, Monbaliu JM, Melnyk O, Native Chemical Ligation and Extended Methods: Mechanisms, Catalysis, Scope, and Limitations., *Chem. Rev.*, 2019

Matarazzo L, Casilag F, Porte R, Wallet F, Cayet D, Faveeuw C & al, Therapeutic Synergy Between Antibiotics and Pulmonary Toll-Like Receptor 5 Stimulation in Antibiotic-Sensitive or -Resistant Pneumonia, *Front. Immunol.*, 2019

Tonk M, Pierrot C, Cabezas-Cruz A, Rahnamaeian M, Khalife J, Vilcinskis A, The *Drosophila melanogaster* antimicrobial peptides Mtk-1 and Mtk-2 are active against the malarial parasite *Plasmodium falciparum*., **Parasitol. Res.**, 2019

de la Fuente J, Pacheco I, Villar M, Cabezas-Cruz A, The alpha-Gal syndrome: new insights into the tick-host conflict and cooperation., **Parasit Vectors**, 2019 , 154

Cabezas-Cruz A, Zweggarth E, Aguiar DM, Ehrlichia minasensis, an old demon with a new name., **Ticks Tick Borne Dis**, 2019

Paget C, Trottein F, Mechanisms of Bacterial Superinfection Post-influenza: A Role for Unconventional T Cells, **Front. Immunol.**, 2019

Gaudet A, Parmentier E, Dubucquoi S, Poissy J, Duburcq T, Portier L & al, The complex kinetics of blood endocan during the time course of sepsis and acute respiratory distress syndrome., **Crit Care**, 2019 , 86

Sahuc ME, Sahli R, Rivière C, Pène V, Lavie M, Vandeputte A & al, Is a New Inhibitor of Hepatitis C Virus RNA Replication., **J. Virol.**, 2019

Machelart A, Salzano G, Li X, Demars A, Debie AS, Menendez-Miranda M & al, Intrinsic Antibacterial Activity of Nanoparticles Made of β -Cyclodextrins Potentiates Their Effect as Drug Nanocarriers Against Tuberculosis., **ACS Nano**, 2019

Paget C, Deng S, Souillard D, Priestman DA, Specia S, von Gerichten J & al, TLR9-mediated dendritic cell activation uncovers mammalian ganglioside species with specific ceramide backbones that activate invariant natural killer T cells., **PLoS Biol.**, 2019 , e3000169

Pauwels AM, Härtlova A, Peltier J, Driege Y, Baudelet G, Brodin P & al, Spatiotemporal changes of the phagosomal proteome in dendritic cells in response to LPS stimulation., **Mol. Cell Proteomics**, 2019

El Achkar S, Demanche C, Osman M, Rafei R, Ismail MB, Yaacoub H & al, Drug-Resistant Tuberculosis, Lebanon, 2016 - 2017., **Emerging Infect. Dis.**, 2019 , 564-568

Gaudet A, Parmentier E, De Freitas Caires N, Portier L, Dubucquoi S, Poissy J & al, Impact of acute renal failure on plasmatic levels of cleaved endocan., **Crit Care**, 2019 , 55

Forde PM, Scherpereel A, Tsao AS, Use of Immune Checkpoint Inhibitors in Mesothelioma., **Curr Treat Options Oncol**, 2019 , 18

Estrada-Peña A, Cabezas-Cruz A, Phyloproteomic and functional analyses do not support a split in the genus *Borrelia* (phylum Spirochaetes)., **BMC Evol. Biol.**, 2019, 54

Cabezas-Cruz A, Espinosa P, Alberdi P, de la Fuente J, Tick-Pathogen Interactions: The Metabolic Perspective., **Trends Parasitol.**, 2019

Obregón D, Cabezas-Cruz A, Armas Y, Silva JB, Fonseca AH, André MR & al, High co-infection rates of *Babesia bovis*, *Babesia bigemina*, and *Anaplasma marginale* in water buffalo in Western Cuba., **Parasitol. Res.**, 2019

Solans L, Locht C, The Role of Mucosal Immunity in Pertussis, **Front. Immunol.**, 2019

Ciczora Y, Janel S, Soyer M, Popoff M, Werkmeister E, Lafont F, Blocking bacterial entry at the adhesion step reveals dynamic recruitment of membrane and cytosolic probes., **Biol. Cell**, 2019

Scherpereel A, Mazieres J, Greillier L, Lantuejoul S, Dô P, Bylicki O & al, Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial., **Lancet Oncol.**, 2019

Paluch M, Lejeune S, Hecquet E, Prévotat A, Deschildre A, Fréalle E, / L98H isolates in the home of a cystic fibrosis patient harbouring chronic colonisation with azole-resistant *H285Y A. fumigatus*., **J. Cyst. Fibros.**, 2019

Le Rouzic O, Roche N, Housset B, Response., **Chest**, 2019 , 241-242

Cabezas-Cruz A, Allain E, Ahmad AS, Saeed MA, Rashid I, Ashraf K & al, Low genetic diversity of *Ehrlichia canis* associated with high co-infection rates in *Rhipicephalus sanguineus* (s.l.)., **Parasit Vectors**, 2019 , 12

Cabezas-Cruz A, Gallois M, Fontugne M, Allain E, Denoual M, Moutailler S & al, Epidemiology and genetic diversity of *Anaplasma ovis* in goats in Corsica, France., **Parasit Vectors**, 2019 , 3

Scherpereel A, Mazieres J, Greillier L, Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial (vol 20, pg 239, 2019), **Lancet Oncol.**, 2019 , E132-E132

U1167

Bellenguez C, Grenier-Boley B, Lambert JC, Genetics of Alzheimer's disease: where we are, and where we are going., **Curr. Opin. Neurobiol.**, 2019 , 40-48

Spear R, Boytard L, Blervaque R, Chwastyniak M, Hot D, Vanhoutte J & al, Let-7f: A New Potential Circulating Biomarker Identified by miRNA Profiling of Cells Isolated from Human Abdominal Aortic Aneurysm., **Int J Mol Sci**, 2019

Trouiller-Gerfaux P, Podglajen E, Hulo S, Richeval C, Allorge D, Garat A & al, The association between blood cadmium and glycated haemoglobin among never-, former, and current smokers: A cross-sectional study in France., **Environ. Res.**, 2019 , 108673

Pinet F, Bauters C, Bar C, Thum T, Letter by Pinet et al Regarding Article, "Comparative Analysis of Circulating Noncoding RNAs Versus Protein Biomarkers in the Detection of Myocardial Injury", **Circ.Res.**, 2019, E20-E21

Kunkle BW, Grenier-Boley B, Sims R, Bis JC, Damotte V, Naj AC & al, Author Correction: Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates A β , tau, immunity and lipid processing., **Nat. Genet.**, 2019

Turkieh A, Porouchani S, Beseme O, Chwastyniak M, Amouyel P, Lamblin N & al, Increased clusterin levels after myocardial infarction is due to a defect in protein degradation systems activity., **Cell Death Dis**, 2019, 608

Turkieh A, Charrier H, Dubois-Deruy E, Porouchani S, Bouvet M, Pinet F, Noncoding RNAs in Cardiac Autophagy following Myocardial Infarction., **Oxidative Med. Cell. Longev.**, 2019

Sartori M, Mendes T, Desai S, Lasorsa A, Herledan A, Malmanche N & al, phosphorylation., **Acta Neuropathol.**, 2019

Dourlen P, Kilinc D, Malmanche N, Chapuis J, Lambert JC, The new genetic landscape of Alzheimer's disease: from amyloid cascade to genetically driven synaptic failure hypothesis?, **Acta Neuropathol.**, 2019

Kunkle BW, Grenier-Boley B, Sims R, Bis JC, Damotte V, Naj AC & al, Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates A β , tau, immunity and lipid processing., **Nat. Genet.**, 2019, 414-430

Colin B, Deprez B, Couturier C, High-Throughput DNA Plasmid Transfection Using Acoustic Droplet Ejection Technology. *SLAS Discovery* 2019, 24, 492-500.

Colin B, Rocq N, Deprez B, Couturier C, High-Throughput DNA Plasmid Multiplexing and Transfection Using Acoustic Nanodispensing Technology. *J. is. Exp.* 2019, 150, e59570.

Lagarde N, Goldwasser E, Pencheva T, Jereva D, Pajeva I, Rey J & al, A Free Web-Based Protocol to Assist Structure-Based Virtual Screening Experiments. *International journal of molecular sciences* 2019, 20, 4648.

Leroux F, Bosc D, Beghyn T, Hermant P, Warenghem S, Landry V & al, Identification of ebselen as a potent inhibitor of insulin degrading enzyme by a drug repurposing screening. *Eur J Med Chem*, 2019, 179, 557-566.

Machelart A, Salzano G, Li X, Demars A, Debie A.S, Menendez-Miranda M & al, Intrinsic Antibacterial Activity of Nanoparticles Made of D-Cyclodextrins Potentiates Their Effect as Drug Nanocarriers against Tuberculosis. *ACS Nano* 2019, 13, 3992-4007.

Pastor A, Machelart A, Li X, Willand N, Baulard A, Brodin P & al, A Novel Codrug Made of the Combination of Ethionamide and Its Potentiating Booster: Synthesis, Self-Assembly into Nanoparticles and Antimycobacterial Evaluation. *Org. Biomol. Chem.* 2019, 17, 5129-5137.

Prevot H, Moune M, Tanina A, Kemmer C, Herledan A, Frita R, & al, A Fragment-Based Approach Towards the Discovery of N-Substituted Tropinones as Inhibitors of Mycobacterium Tuberculosis Transcriptional Regulator EthR2. *Eur. J. Med. Chem.* 2019, 167, 426-438.

Sartori M, Mendes T, Desai S, Lasorsa A, Herledan A, Malmanche N, & al, Bin1 Recovers Tauopathy-Induced Long-Term Memory Deficits in Mice and Interacts with Tau through Thr348 Phosphorylation. *Acta Neuropathol. (Berl).* 2019, 138, 631-652.

Tanina A, Wohlkönig A, Soror S.H, Flipo M, Villemagne B, Prevot H & al, A Comprehensive Analysis of the Protein-Ligand Interactions in Crystal Structures of Mycobacterium Tuberculosis EthR. *Biochimica et Biophysica Acta (BBA). Proteins and Proteomics* 2019, 1867, 248-258.

Valderrama K, Pradel E, Firsov A. M, Drobecq H, Bauderlique-le Roy H, Villemagne B & al, Pyrrolomycins Are Potent Natural Protonophores. *Antimicrob. Agents Chemother.* 2019, 63, e01450-19.

Willand N, Flipo M, Villemagne B, Baulard A, Deprez B. Chapter Five - Recent Advances in the Design of Inhibitors of Mycobacterial Transcriptional Regulators to Boost Thioamides Anti-Tubercular Activity and Circumvent Acquired-Resistance. *In Annual Reports in Medicinal Chemistry, Chibale, K., Ed. Academic Press: 2019; Vol. 52, pp 131-152.*

ULR4483

Amrani I, Haddam N, Garat A, Allorge D, Zerimech F, Schraen S & al, Exposure to metal fumes and circulating miRNAs in Algerian welders. *Int Arch Occup Environ Health*, 2019

Pagin A, Bergougnoux A, Girodon E, Reboul MP, Willoquaux C, Kesteloot M & al, Novel ADGRG2 truncating variants in patients with X-linked Congenital Absence of Vas Deferens. *Andrology*, 2019

Platel A, Privat K, S Talahari, Delobel A, Dourdin G, Gateau E & al, Study in Vitro and in Vivo Genotoxic Effects of Air Pollution Fine and Quasi-Ultrafine Particles on Lung Models. *Sci. Total Environ.*, 2019, 134666

Sauvain JJ, Edmé JL, Wild P, Suarez G, de Paula Alvez Bezerra OM, Talvani A & al, Does exposure to inflammatory particles modify the pattern of anion in exhaled breath condensate? *J Breath Res*, 2019

Maanaoui M, Lenain R, Hamroun A, Van der Hauwaert C, Lopez B, Gibier JB & al, Caveolin-1 rs4730751 single-nucleotide polymorphism may not influence kidney transplant allograft survival. *Sci Rep*, 2019, 15541

Hamroun A, Lenain R, Bigna JJ, Speyer E, Bui L, Chamley P & al, Prevention of Cisplatin-Induced Acute Kidney Injury: A Systematic Review and Meta-Analysis. *Drugs*, 2019

Sotty J, Garçon G, Denayer FO, Alleman LY, Saleh Y, Perdrix E & al, Toxicological Effects of Ambient Fine and Ultrafine Particles in healthy and diseased 3D organo-typic mucociliary-phenotype models. *Environ. Res.*, 2019, 108538

Van der Hauwaert C, Glowacki F, Pottier N, Cauffiez C, Non-Coding RNAs as New Therapeutic Targets in the Context of Renal Fibrosis. *Int J Mol Sci*, 2019

Saleh Y, Antherieu S, Dusautoir R, Y Alleman L, Sotty J, De Sousa C & al, Exposure to Atmospheric Ultrafine Particles Induces Severe Lung Inflammatory Response and Tissue Remodeling in Mice. *Int J Environ Res Public Health*, 2019

Savary G, Dewaeles E, Diazi S, Buscot M, Nottet N, Fassy J & al, The Long Non-Coding RNA DNM3OS is a Reservoir of FibromiRs with Major Functions in Lung Fibroblast Response to TGF- β and Pulmonary Fibrosis. *Am. J. Respir. Crit. Care Med.*, 2019

Richeval C, Dumestre-Toulet V, Wiart JF, Vanhoye X, Humbert L, Nachon-Phanithavong M & al, New psychoactive substances in oral fluid of drivers around a music festival in south-west France in 2017. *Forensic Sci. Int.*, 2019, 265-269

Abbas I, Badran G, Verdin A, Ledoux F, Roumie M, Lo Guidice JM & al, using human bronchial epithelial BEAS-2B cells: Cytotoxicity, oxidative stress, pro-inflammatory response, genotoxicity, and cell cycle deregulation. *Environ. Res.*, 2019, 510-522

Lanier C, Deram A, Cuny MA, Cuny D, Occelli F, Spatial analysis of environmental inequalities caused by multiple air pollutants: A cumulative impact screening method, applied to the north of France. *Ecol. Indic.*, 2019, 91-100

UMR8199

Vaxillaire M, Froguel P, Bonnefond A, How Recent Advances in Genomics Improve Precision Diagnosis and Personalized Care of Maturity-Onset Diabetes of the Young. *Curr. Diab. Rep.*, 2019, 79

Khamis A, Canouil M, Siddiq A, Crouch H, Falchi M, Bulow MV & al, Laser capture microdissection of human pancreatic islets reveals novel eQTLs associated with type 2 diabetes. *Mol Metab*, 2019

UMR8161

Brustia R, Boleslawski E, Danion J, Savier E, Barrou B, Scatton O, The Impact of Deceased Donor Liver Extraction Time on Early Allograft Function in Adult Liver Transplant Recipients. *"Vite fait, bien fait."* *Transplantation*, 2019, e218-e219

Prodeau M, Drumez E, Duhamel A, Vibert E, Farges O, Lassailly G & al, An Ordinal Model to Predict the Risk of Symptomatic Liver Failure in Patients with Cirrhosis undergoing Hepatectomy. *J. Hepatol.*, 2019

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