ACTIVITY REPORT

2015

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Our project is to create the first Transdisciplinary Research Center on Longevity (‘Centre Transdisciplinaire de Recherche sur la Longévité’ - CTRL) in Lille. This center will receive €8 million of funding from the Region, the State and the Métropole Européenne de Lille based on calls for projects. The aim of this research center is both ambitious and modest: healthy ageing, i.e. living better longer. Thanks to the support of partners, donors and patrons, the aim of the project is to develop the prevention and early diagnosis of pathologies such as Alzheimer’s disease, cardiovascular diseases, diabetes and metabolic diseases, obesity, infectious diseases, cancer and chronic inflammatory respiratory and digestive ailments.

This project, developed in partnership with Lille University, INSERM, CNRS and Lille’s regional university hospital, will be focusing on the following two axes from 2016: “genetics and environment” researching the genetic, molecular, cellular and environmental factors of the pathologies associated with ageing, which can lead to the discovery of biological markers and new treatments; a second axis devoted to a better understanding of the biological ageing of the immune system and to the prevention of the chronic inflammation often associated with ageing.

This project will be run by Institut Pasteur de Lille during the next five years. It will rely on independent scientific expertise and on an international scientific advisory board made up of leading scientific personalities who are responsible for European research centers. The center will support young research teams through calls for research projects linked to clinical research teams that are selected according to innovation and cross-disciplinary criteria. It will also support post-doctorate programmes, emerging teams working on ageing and the platforms needed to promote it.

The project also deals with health and the environment. Projects were initiated so that these activities could enhance their long-term viability and occupy a fully-fledged longevity role, especially by reinforcing the connections of the health, education and prevention center with the university and the hospital.

2015 was also a year of renewal for the Foundation. In 2016, new statutes will be adopted and put in place. We will put together a new communication policy, a wide-reaching reorganisation of the administration in order to make it more efficient and more effective in serving the foundation’s activities. We are starting with the progressive renovation of the computing equipment. We have put together a code of conduct that is soon to be put in place. We created a quality department and implemented an eco-campus network. At the same time, wide-reaching studies were conducted to define a plan aiming to renovate the campus buildings of Institut Pasteur de Lille. All the research activities will be contained in three buildings, i.e. Guérin, Emile Roux and the biology Institute of Lille (“IBL”). The Calmette building will be refurbished. Lastly, we welcomed the Regional Health Observatory (“ORS”), with which we will be developing a large number of collaborative initiatives.

Our ambition is to become an internationally recognised European research center on longevity within a new Institut Pasteur de Lille that is proud of its past, able to adapt to a highly competitive and rapidly changing world, and works with all the research partners of our region.

Prof Patrick Berche
General Director
of Institut Pasteur de Lille

The key event of 2015 was the launch by Institut Pasteur de Lille of a new cooperative research project on the topic of longevity. This is a major issue for the future of our societies which will require the commitment of everyone, including the researchers, donors and patrons. The lengthening of life expectancy is expected to cause a significant increase in the population of those aged more than 65 years in not only all the western countries but also the third-world countries. This will lead not only to medical problems, but also ethical, economical, organisational or even architectural problems.
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Institut Pasteur de Lille, created in 1894 by the Lille city council, is a non-profit making private foundation, declared of public interest in 1898. Its object is biomedical research, education & health promotion.

Research excellence

With the biggest campus for biomedical research north of Paris, Institut Pasteur de Lille is located in the Lille city center. This foundation, which is unique in France, employs 326 people, hosts 6 research units, 32 fundamental research laboratories - including three laboratories of excellence and an integrated research site on cancer-, three applied research laboratories, 10 technology platforms, including two facilities of excellence, where, across all departments, a total of 717 researchers, engineers and technicians work on the century’s major diseases: cardiovascular diseases, neurodegenerative diseases, infectious diseases and parasitoses, inflammatory diseases, metabolic diseases and cancers.

Public Health mission

Ever since its creation, health prevention and education have been among the fundamental missions of Institut Pasteur de Lille. Created over thirty years ago, the Prevention and Health Education Center (CPES) is one of the largest health examination centers in France, it is also a public health skills platform to serve the community, public health players and health policies in the region. CPES also includes an international vaccination center approved by the World Health Organisation.

High level training

Over 140 students are studying for their master’s degree or Ph.D. within the research teams. Every year, over 1000 occupational trainees come to Institut Pasteur de Lille to train on the following subjects: nutrition, addictive behaviours management and laboratory best practices.
The history of Institut Pasteur de Lille is a very good example of this particular relationship that brings the people of this foundation together.

In the late 19th century, three quarters of the planet had been wiped out by infectious diseases and penicillin hadn’t been invented yet. In 1884, a serious outbreak of diphtheria hit Lille. A former dean of the Science University in Lille, Louis Pasteur has just opened the institute that bears his name in Paris where one of his associates, Emile Roux, has developed a serum against diphtheria. A delegation of the Lille City Council went to Paris to consult with Louis Pasteur on the quickest way to get the serum to the Lille population. Louis Pasteur proposed to create a laboratory to manufacture the serum in Lille. A laboratory, independent from Institut Pasteur in Paris, which will not only manufacturers the serum, but will also conduct scientific research. This is how Institut Pasteur de Lille came into being in 1894. Albert Calmette was the first director of this new institute. It was at Institut Pasteur de Lille that he developed the BCG vaccine against tuberculosis with Camille Guérin. Since the origin, while developing high flying scientific research, Institut Pasteur de Lille has always had a sense for serving the community, from Calmette’s antituberculosis free clinic, up to pilot activities in health prevention and education, its international vaccination service or its conferences for the general public.
Mixed governance

The Board of Directors of Institut Pasteur de Lille sees to the compliance with the foundation's fundamental values and statutes. The board defines the organisation's strategy, its business model, and controls the implementation by the managing director.

The Board of Directors is made up of:

Representatives from local authorities:
The founding members (Lille City Council, Nord and Pas-de-Calais Départements), joined later by Somme, Aisne and Ardennes Départements, and more recently by the Lille region Regional Council and Métropole Européenne de Lille.

Representatives from the scientific and health community who contribute to the consistency of the foundation’s actions with its mission, among others, the Director of Institut Pasteur in Paris, the Director of the Regional Health Agency (ARS), the Lille Chief Education Officer and the Chairman of the Lille 2 University, and the Director of the Lille University Hospital.

joined by personalities from various backgrounds, selected on their administrative and social, legal, financial, industrial or commercial skills for their capacity to understand the challenges of the foundation such as Préfet du Nord, the chairman of Chambre régionale des notaires (regional chamber of notaries) the chairman of Medef Nord Pas-de-Calais (Employers' union).

There are 21 directors in total

The Board of Directors is chaired ex officio by the Mayor of Lille. Martine Aubry has delegated this function to her fourth deputy: Dr Jacques Richir.

The director is a scientific personality. On 1 July 2014, Professor Patrick Berche was appointed Managing Director of Institut Pasteur de Lille, for a term of office of 6 years.
The Lille region's health issues have initiated the creation and guided the scientific orientations of Institut Pasteur de Lille. The research of Institut Pasteur de Lille, on issues often more acute in a region with an industrial legacy which accumulates bad health indicators, today benefits the whole of the French population and beyond.
A vision for the future: The Transdisciplinary Research Center on Longevity

With its prestigious scientific legacy and discoveries which have marked its history for the past hundred and twenty years, Institut Pasteur de Lille boasts an exceptional, world-renowned concentration of transdisciplinary skills. Relying on complementary themes and its partnership positioning, it has engaged today in the construction of a major project around longevity.
The project, which provides a continuum from fundamental approaches to the patient’s bedside, is oriented towards pathologies that concern us all. Mixed research teams (Institut Pasteur de Lille, Lille University, Inserm, CNRS) have joined forces around a common project, on longevity.

Research excellence combined with a health approach to provide the best answers

Institut Pasteur de Lille today hosts a fundamental research center divided into six units, with multidisciplinary, cross-cutting skills. It is organised around the following axes:

- Infectious, parasitic and inflammatory diseases
- Neurodegenerative diseases
- Cardiovascular diseases
- Metabolic diseases, diabetes, obesity
- Cancer
- Research for new prescription drugs

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 disease (DISTALZ)
- a LabEx dedicated to studying diabetes (EGID)
- a research center on infection and immunity (CIIl) involved in the ParaFrap LabEx
- an EquipEx dedicated to genomics (LIGAN-PM)
- an EquipEx dedicated to cellular imaging pharmacological screening (ImaginEx Biomed).

Institut Pasteur de Lille’s campus boasts an exceptional concentration of high level facilities and technology platforms whose mission is to serve all the researchers in the regional scientific community.

It also features a large molecule library – The chemical library – where thousands of tests are conducted every year, helping in the discovery of new prescription drugs.

And ever since its creation, health prevention and education have been among the fundamental missions of Institut Pasteur de Lille. Its professionals mingle on a daily basis with researchers, developing reactive synergies that can thus quickly benefit the community.

Grouping of the vital forces of Institut Pasteur de Lille around longevity

Longevity is today one of the main public health challenges all over the world. In 1900, there were ca. 100 centenarians in France. In 2014, there were 23,000. In 2060, the number will be close to 198,000. Soon, close to 25% of the population will be over 65.

Living to 100 years old in good health is a real challenge for our society, that is already faced by health, economic, and political leaders worldwide.

The last part of life is a major challenge for society. Attempting to prevent dependency and preserving the autonomy of the elderly are key if society is to adapt to ageing.

In this context, it has appeared indispensable to create regional scientific and medical dynamics capable of engaging the excellence teams and structures present in the region.

This is how in 2013-2014, a new project emerged on the campus, supported by the successful development of innovative tools and specific study models which help considering human beings from a global point of view as integrated biological systems where the mechanisms of diseases are often at work in an interrelated manner.

This common vision will strengthen the skills and tools that are already available to create a unique value chain in France : CTRL (Centre Transdisciplinaire de recherche sur la Longévité).

Creation of CTRL, the Transdisciplinary Research Center on Longevity

The Transdisciplinary Research Center on Longevity (so-called CTRL) gathers research teams in a consistent and organised manner representing a major potential for development, both in terms of job grouping and creation, in the fields of fundamental and translational research, of the discovery of therapeutic drugs, and prevention and social care, economic prospects which may be developed in cooperation with our partners.

The longevity project will develop two main axes. The first axis is entitled «Age, immunity and infection». The purpose is to be able to reduce age-related infectious mortality (30% of deaths have an infectious origin after the age of 65). Researchers will focus on understanding the mechanisms of immuno-senescence and will try and improve the efficiency of vaccines for older patients. The other objectives are : the prevention of age-related comorbidities, in particular chronic respiratory infections and inflammatory diseases frequent among older patients ; the study of the influence of age on the microbiome ; understanding the relation between chronic infections and cancers.

The second axis «Age, genes and environment» finds its origin from epidemiology studies which combine health condition, genes and environment. The strategy is to compare the whole genomes of people with pathologies to those of healthy individuals. Candidate genes are thus identified by their association to an increased risk of developing, for a given individual, a neurodegenerative disease, diabetes, a cardiovascular disease, a stroke, cancer, all these pathologies being widely represented in the Lille region.

The next step is to establish a causal link between the candidate genes thus identified and the disease thanks to experimental cellular and animal models. This strategy will help discover biomarkers and new prescription drugs thanks to the screening of molecules from our chemical library.
The ultimate objective is to improve preventive care management for these diseases. It will be possible to launch prevention clinical trials with adapted structures on a significant number of patients. These trials will benefit from an access to populations from the health prevention and education center, from the nutrition department, from the vaccination center of Institut Pasteur de Lille and the clinical services of public and private hospitals. All these activities will help develop a great number of regional cooperation programmes, in very diverse areas relating to old age and disability, including studies in human and social sciences, in Public Health, in Public Health, in health economics or in treatment education.

CTRL : the new backbone of Institut Pasteur de Lille

In addition to the prevention age-related diseases, the priority for Institut Pasteur de Lille researchers is first and foremost to help the population stay healthy as long as possible. The creation of CTRL represents the best way to pool the vital forces of Institut Pasteur de Lille, to promote the cooperation of geneticists, clinicians, epidemiologists, microbiologists, biochemists, immunologists... around this objective.
Institut Pasteur de Lille set up an international scientific council ("CSI") that gives opinions and supervises the foundation's major scientific guidelines.

It is composed of highly reputed international specialists:

- Prof Bernard Thorens, interactive genomics center of Lausanne
- Prof Folkert Kuipers Groningen Longevity Research Center
- Prof Miroslav Radman, Split, Croatia
- Prof Gordon Dougan Wellcome Trust Sanger Institute, Cambridge
- Prof Thomas Thum Hanover Medical School IFB
- Prof Philip Scheltens Alzheimer Center, Amsterdam

This Council, whose existence is now enshrined in the statutes of the foundation, met for the first time on 14 January 2016. The Council emphasises the excellence of the research teams working on the campus of the institute and approves the foundation's main guidelines, especially regarding the subject of longevity.

It emphasises the grounds for the creation of the longevity research center, which is a very promising project dealing with chronic illnesses that will considerably increase with the ageing of the population.

The scientific Council has put forward a certain number of recommendations:

1/ Regarding the definition of the major objectives, it recommends a top-down approach: the team leaders of the 6 units, working in consultation with the unit managers, must define the innovative research questions that can only be resolved by sharing their expertise and the experimental approaches used.

2/ The CSI recommends a bottom-up approach for the call for research projects. As a matter of priority, it would like to retain projects coming from young investigators with new collaborations, particularly those that combine fundamental research and clinical research.

3/ The CSI recommends recruiting new research teams based on their scientific excellence and their potential to become integrated within the center.

4/ The CSI recommends conducting brainstorming discussions combined with the organisation of a symposium on longevity and ageing organised by Institut Pasteur de Lille.

5/ The CSI recommends increasing collaborations with the clinical teams and building international relations with the major centers involved in research on ageing (Groningen, Newcastle, etc.).
Institut Pasteur de Lille and sponsorship

In the near future, the lengthening of the lifespan will be one of the main challenges of our societies. It concerns not only the western countries, but also the entire world where life expectancy is increasing very rapidly. This is a major medical problem that also has socio-economic, political and human implications. It includes the treatment of all the major pathologies affecting civilisation itself.

In our country, we know that from the age of 65 years, one can expect to live for approximately another 20 years, made up of 10 years of good health and 10 years that will be characterised by the gradual loss of independence and the emergence of certain handicaps.

Institut Pasteur de Lille, with its Partners, has decided to gather all of its resources to work for a ‘Centre Transdisciplinaire de Recherche sur la Longévité’ (Transdisciplinary Research Center on Longevity).

The objective of this new research center, which is unique in France, is to identify the risk factors for the diseases associated with ageing, whether it is Alzheimer’s disease, cardiovascular diseases, cancer, diabetes, metabolic diseases or infectious diseases, which are still one of the primary causes of mortality after the age of 65 years.

The transdisciplinary approach – genetics, biochemical, cellular, clinical, epidemiological, public health, etc. – will be used to identify candidate genes that will open up opportunities for discovering new biomarkers that will be tested on those populations which are at risk, as well as new medicines by molecular screening. The early prevention of diseases before the emergence of the clinical symptoms can considerably improve the quality of life and delay the handicaps associated with age.

Currently, Institut Pasteur de Lille is launching a sponsorship campaign to support all the research topics contributing to the development of its project on longevity. Thanks to sponsorship, Institut Pasteur de Lille will be able to support such projects in order to make rapid progress in our research while enabling internationally renowned researchers to work in an optimal environment.

The main objective of the 2017-2022 sponsorship campaign is to raise €20 million in order to fund the research teams of today and tomorrow:

- supporting researchers in the fight against diabetes, metabolic and cardiovascular diseases, Alzheimer and degenerative diseases, cancer and infectious diseases;
- attracting new research teams on longevity to the site with knowledge complementing that of the current teams, including one or two teams specifically focused on the biology of ageing in particular.

The aim of the sponsorship is also to renovate and modernise the installations in order to prepare the foundation for the challenges of the future. Our bold property project is estimated at €40 million.

In particular, it will make it possible to:

- transform the Guérin building into research laboratories;
- prepare the laboratories for the technologies of the future;
- renovating the former dispensary.
of Albert Calmette;

- renovating the facade of the historic building and the Pasteur Lille museum.

Institut Pasteur de Lille is supported in its plans by an international scientific council made up of 7 highly reputed members who examine and validate the scientific projects, thereby guaranteeing the level of excellence and innovation of the institute’s projects.

By taking part in this unique and ambitious project today, you will be helping Institut Pasteur de Lille to take on the challenge of longevity so that the vast majority can live better for longer.

Becoming a sponsor of our foundation means getting involved in a wide-reaching project that has huge potential for the future and associating your name with major innovations for human health. Regardless of the form of your donation, the tax reduction for a corporation is equivalent to 60% of the total donation capped at 0.5% of the business’s annual pre-tax sales. For an individual sponsor, the tax exemption is 66% and 75% on the French solidarity tax on wealth (“ISF”).

CONTACT

In order to become a member of the friends of the Foundation and benefit from the compensations offered by Institut Pasteur de Lille, contact Cédric Bouquet - communications and sponsorship office
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II - Research

- Cardiovascular diseases and neuro-degenerative diseases
- Inflammatory, infectious and parasitic diseases
- Cardiovascular diseases and metabolic diseases: hypercholesterolemia, cardiovascular complications
- The metabolic and epigenetic diseases like diabetes and obesity
- Cancers
- Discovery of prescription drugs
- Genetic toxicology laboratory
- Microbiological safety unit
- International relations
- Technology platforms
- Promotion of research
- The biotech of Institut Pasteur de Lille
- Scientific papers
"Risk factors and molecular factors of diseases linked to ageing" unit
managed by Pr Philippe Amouyel
(PU-PH, Université de Lille)
UMR 1167 Inserm, Institut Pasteur de Lille, University Hospital of Lille, Lille University

This unit studies cardiovascular diseases and neuro-degenerative diseases with an emphasis on cardiac arrests, strokes and Alzheimer's disease. Within this unit, a team is dedicated to epidemiology and the public health of cardiovascular and cerebrovascular diseases. Dr Florence Pinet (Inserm research director) heads up the "molecular factors of heart deficiency and ventricular remodelling" and Dr Jean-Charles Lambert (Inserm research director) coordinates the team dedicated to the study of "molecular factors of Alzheimer's disease and cognitive disorders".

Cardiovascular diseases: Identifying the risks factors

Professor Philippe Amouyel's team has developed an epidemiological research programme in order to better understand the role of cardiovascular risk factors (Genetics, excess weight, obesity, type II diabetes, high blood pressure, cholesterol, tobacco dependence...). The programme particularly focuses on studying cardiovascular diseases at a population level.

The work is relying on the records of morbidity of ischemic heart diseases and cerebrovascular accidents in Lille. Medical researchers investigate in public hospitals, emergency services and private hospitals with a cardiology or neurology department. A biological resource center ensures the logistics and storage of biological samples and tissues.

The purpose of this studies is:
• to understand the evolution of the vascular pathology in terms of classification, management and prevention;
• and to analyse the role of genetic and environmental determinants of cardiovascular diseases.

Institut Pasteur de Lille has been taking part in international studies such as MONICA (MONItoring of trends and determinants of Cardiovascular diseases), PRIME (PRospective sur l’Infarctus du Myocarde - Prospects on myocardial infarction) or EUROASPIRE (EUROpean Action on Secondary and Primary Prevention by Intervention to Reduce Events).

What's more, the research team is tackling the Elisabet study "Enquête Littoral Souffle Air Biologie Environnement" – coastal breeze air biology environment study) in the Nord-Pas-de-Calais region that is examining the impact of pollution on pulmonary and cardiovascular functions, as well as the GECCOS (Gene-Environment in a Case-Control study on Obesity) study that is looking at the genetic and environmental factors associated with our dietary behaviour on weight gain.

Through all these activities, researchers have been following up on the development of vascular risk factors for the past 30 years, which means that the "risk factors and molecular factors of diseases associated with ageing" team is actually a unique observatory for these diseases in France!
Obesity: social status, dietary habits and genes are under the microscope of the researchers

The GECCOS (Gene and Environment Case Control Obesity Study) study is seeking to identify the role of the socio-economic status ("SSE") and certain dietary behaviour and attitudes in the risk of obesity. Since 2007, it has been conducted on obese people coming to the nutrition department of Prof Monique Romon at the regional university hospital of Lille (850 participants BMI ≥ 30 kg/m²) and 400 non-obese people (BMI <30 kg/m²), recruited from among the consultants of the prevention and health education centre of Institut Pasteur de Lille.

“We have put together a specific clinical questionnaire, that includes detailed questions on the personal and family history, physical activity, feelings of hunger and dietary behaviour and attitudes, explained the researcher, Aline Meirhaeghe. The socio-economic status ("SSE") score was calculated using the socio-professional category, the level of the education and income.

The results of the study revealed, among other things, that certain obesogenic behaviour partly explains the relationship that exists between the SSE and the risk of obesity. In particular, these included eating in a large plate, eating at night and having an uncontrolled diet”.

A better understanding of these factors and their relationship with the SSE should help to put together personalised strategies to help people with a low SSE improve their dietary choices, habits and dietary situation.

However, the study does not stop there. The participants have agreed to give some of their blood in order to conduct a wide-reaching study on the genetic factors of dietary behaviour.

Within the context of the EBOGENES network, co-ordinated by Aline Meirhaeghe, the DNA of the GECCOS cohort as well as that of other cohorts, who have worked with the same dietary questionnaires, will be studied during the course of 2016 at the national genotyping center of Evry as part of a genome-wide study (GWAS). “This will enable us to identify the genetic factors of dietary behaviour and then work out those that end up becoming genetic factors of body weight and a risk of obesity” added Aline Meirhaeghe.
Detecting and preventing heart failure

Following a myocardial infarction, the left ventricle may change shape and the patient then suffers from heart failure: the heart is no longer capable of pumping enough blood to meet the body’s oxygen demand. People who suffer from heart failure get out of breath and tire more easily. The survival rate five year after the diagnosis is approximately 50%. Heart failure concerns 10% of people over 70.

When the first signs of this heart failure appear at the ultrasound exam, one year after the myocardial infarction, the condition is already irreversible. So when Dr Florence Pinet proposed, in the early 2000s, to the Lille University Hospital cardiologists in the unit, to “recruit” patients in order to find earlier markers of this failure, there were all for it.

An Inserm research director, Florence Pinet is a specialist in proteomics, a science that is complementary to genomics, aiming at studying proteins, their functions and interactions inside the cell. Together with Pr Christophe Bauters of the University Hospital of Lille, she has designed a research protocol around a cohort of patients which led them to discover, in 2010, a first biological marker for left ventricular remodelling following a first myocardial infarction.

Since then, researchers have been refining antibody screening in order to develop a dosage that can be used in clinical routines and continue to search for new markers with the aim of offering a blood test for measuring the risk of developing a heart deficiency with a simple blood sample. This discovery, patented by INSERM and Institut Pasteur de Lille, is of interest to the diagnostics sector and should help to improve treatments for heart attack victims by selecting those that can benefit from circulatory assistance or a heart transplant at the appropriate time.

Alzheimer disease: the genetic lead

Alzheimer’s disease is a so-called neurodegenerative illness of the brain, i.e. it causes the gradual destruction of the neurones. Two main lesions progressively invade the brain and cause the death of the nerve cells:
- senile plaques or neuritic plaques
  This is a deposit, outside the neurones, of the beta-amyloid protein,
- neurofibrillary degeneration, that is an aggregate of another protein, the Tau protein, under the form of abnormal filaments inside the very neurones.

The lesions caused in the brain by Alzheimer disease remain silent for a long time, and then cause detectable signs as they spread and impact areas that are important to the brain function. So that when clinical signs appear, the disease has already been damaging the brain quite often for over ten years.

For research to progress, we need to find markers that will allow us to identify the disease as soon as possible, before the first signs, which will be clinically detectable only five or ten years later. Current research focus on three types of markers: cerebral markers that can be detected with imaging, blood markers and genetic markers.

This work was developed in a laboratory of excellence, DISTALZ (Development of innovative strategies for a cross-disciplinary approach to Alzheimer’s disease). Within this context, Jean-Charles Lambert’s team at Pasteur de Lille is interested in studying individual sensitivity to Alzheimer’s disease and using this to identify most of the genes involved in the emergence of this illness. “This research must allow us to understand why certain genes develop the disease more frequently than others in order to offer treatments blocking the triggering factors and/or strengthening the protecting factors.”
Genetic research boosted by automation

"When working on a chromosome, it is possible to observe changes in regions that often contain several dozen genes. In the case of Alzheimer’s disease, about 20 of these regions, called locus, have been identified and include more than 140 different genes in total. However, in order to make progress, we need to work individually on each gene to find out whether it is involved or not involved" explained Julien Chapuis, lecturer at Lille University.

Until recently, the process was lengthy (several years of work per gene), fastidious and costly. Thanks to the high content screening platform (HCS - see page 44) located on the campus of Institut Pasteur de Lille since 2014, the genetics of Alzheimer’s disease have made a huge step forward. Using this super microscope robot with an articulated arm, it’s possible to test thousands of conditions (gene extinction, therapeutic molecules, etc.) during the structural and functional screening of cells conducted at the same time with a single identical dosage.

Julien Chapuis was the first user of the platform: "It took more than 6 months to set up our cellular model in which we would like to see the fluorescence of the amyloid protein that we are studying. Afterwards, we succeeded in screening the entire human genome three times within three weeks. Consequently, the researchers were able to quickly identify the genes that play a role in the metabolism of the amyloid protein inside neurones. They are now studying one of these genes in particular."
Part of Pasteur’s “legacy”, bacterial and parasitic infections, as well as inflammatory diseases, are still today major causes of morbidity and mortality, killing every year over 17 million people throughout the world. And this is only the tip of the iceberg, as the morbidity and long-term impact of these infections on other conditions, such as chronic inflammatory diseases, cancers, cardiovascular and neurodegenerative diseases, are considerably higher.

A center coordinated by Dr Camille Locht, an Inserm research director, Unité Inserm U 1019, CNRS UMR 8204, Institut Pasteur de Lille, Lille University

Understanding infection and immunity, including the deregulation of the immune system, requires multidisciplinary, integrated approaches. These global approaches have been developed within the Lille infection and immunology center (CIIL), the biggest research unit set up at Institut Pasteur de Lille with 15 complementary teams.

Centre d’Infection et d’Immunité de Lille (CIIL) (Infection and Immunity Center of Lille) (CIIL)

A unit led by Dr Camille Locht (An Inserm research director)
Unité Inserm U 1019, CNRS UMR 8204, Institut Pasteur de Lille, Lille University

Understanding infection and immunity, including the deregulation of the immune system, requires multidisciplinary, integrated approaches. These global approaches have been developed within the Lille infection and immunology center (CIIL), the biggest research unit set up at Institut Pasteur de Lille with 15 complementary teams.

In concrete terms, the scientists are looking for a treatment against tuberculosis and particularly extensively drug-resistant TB, type C hepatitis, malaria, bilharziasis, plague, toxoplasmosis, whooping cough, inflammatory diseases, whether intestinal or pulmonary (Asthma, respiratory allergies, chronic bronchitis). The 15 teams are divided in three major fields: parasitology, molecular and cellular microbiology, immunity and inflammation.
As far as parasitology is concerned, research is concentrating on Toxoplasma gondii, agent of toxoplasmosis, Plasmodium, agent of malaria, schistosoma, agent of bilharziasis or certain intestinal parasites like Blastocystis and Cryptosporidium.

Toxoplasmosis is a harmless condition in the overwhelming majority of cases that presents major risks for foetuses and patients with a weaker immune defence system. The Toxoplasma gondii can remain dormant for years while forming cysts in the brain. When the cysts awaken, they provoke serious lesions: meningoencephalitis, loss of sight, partial paralysis, tremor, or coma. The specificity of toxoplasma is to be half animal half vegetable, but it isn’t the only parasite like this. This is also the case for other Apicomplexa parasites such as plasmodium, the agent responsible for malaria, or cryptosporidium, which causes cryptosporidiosis, a disease of the intestinal tract. The team coordinated by Sabrina Marion, lecturer at the University of Lille, and Mathieu Gissot, head of research at the CNRS, is researching the similarities between these parasites and the plant world. These discoveries may eventually be transposed to other Apicomplexa parasites.

No less than two teams are attempting to unravel the mysteries of malaria. Malaria or bilharzia (schistosoma) are parasitic diseases which are undeniably major causes of morbidity and mortality in tropical countries with more than 3 billion people exposed to the risk of infection. Children and pregnant women are particularly affected. The team led by Jamal Khalife, head of research at the CNRS, is interested in the molecular and cellular mechanisms involved in the growth and differentiation of the parasites in question in order to offer new ways of controlling these infections. “Within this context, we are studying the signalling pathways involved in controlling the development and reduction of schistosomas. In particular, we examine the role played by histone deacetylases, which are partly responsible for controlling gene expression in space and time on the one hand and by receptor tyrosine kinases on the other hand. Of these receptors, the VKRs (Venus Kinase Receptor) play an essential role in the oogenesis and fertility of the female worms. Given that the VKRs are not present in humans, they are a new target for combating this parasitic disease” pointed out Dr Khalife. Regarding the plasmodium, which is the parasite that causes malaria, the team is studying the regulation of the phosphorylation phenomena involved in the life/survival of the parasite. “As a result, we characterised four new regulators of the protein phosphatase 1 and showed that breaking the link between two of these regulators and the phosphatase was fatal for the parasite. At the same time, as part of the "A-ParaDDisE" project funded by the European Union and coordinated within the team, we are aiming to develop new medicines against four neglected parasitic diseases, including malaria and schistosoma.”

The team around Sylviane Pied, a Research Director at CNRS, has focussed on the immune response to a primary infection by Plasmodium falciparum, the parasite responsible for malaria. These studies combine fundamental research and clinical research in cohorts of African or Indian patients. Field research has been conducted thanks to a collaboration network, including in Gabon and India. This integrated approach should allow researchers to better understand the host-pathogen relationship and identify new vaccine and/or therapeutic targets.

In Sylviane Pied’s team, Gilles Riveau, a Research Director at CNRS, has been working on the malaria-bilharzia co-infection in order to understand the specific immune reaction of people confronted simultaneously to both parasitosis. On the African field, Gilles Riveau has been directing a structure called Espoir pour la santé (Hope for health) (see p 24) which combines research in immuno-epidemiology of bilharziasis and malaria and clinical trials.

Finally, the biology and diversity of emerging eukaryotic pathogens team led by Eric Viscogliosi, a Research Director at CNRS has studied many parasites lesser-known by the general public. Past work include recommendations for professional of the fishing industry on fish parasites (ANR Fish-Parasites, 2010-2013, research programme followed by the original programme: ABC Fish in 2014). The team has also worked and will continue to focus its efforts in the years to come on the study of intestinal parasites such as the blastocystis protozoan, responsible for skin breakdown and digestive disorders including the irritable bowel syndrome or even the cryptosporidium involved in the development of cancers of the digestive tract in animals and, potentially, in humans.
Langoustines against bilharzia

The parasite that causes bilharzia, a small worm called schistosoma, is present in freshwater. It penetrates the skin and then contaminates the blood system causing a chronic inflammatory reaction in tissues that can lead, depending on the type of schistosoma involved, to fibrosis of the liver and the spleen or serious lesions of the urogenital system, which can degenerate into cancer.

The larvae of the schistosoma multiply in freshwater snails before being released into the water. When people bathe, walk or draw water from the lakes, backwaters or rivers, which are often the only local source of water, the larvae get through the skin and contaminate the blood vessels.

Certain freshwater langoustines are natural predators of these snails that carry the bilharzia parasite. Indeed, this was demonstrated in laboratory tests by the Californian universities that started this project. This hypothesis was given further support through observations in the field in Senegal of an increase in bilharzia since the construction of selective dams. These dams, which prevent salt water from flowing far upstream in the river valleys, entirely modified the environment and eliminated the langoustines.

An initial phase of experiments, the results of which have just been published in the reports of the American academy of science (PNAS) demonstrates the benefit of langoustines and an approach aimed at reintroducing them in the rivers. The researchers compared the situation of two Senegalese villages. In the first, the EPLS teams released a large number of langoustines at a point on a river that is used every day by the local population.

After 18 months, the researchers observed an 80% drop in the number of snails infected by the parasites as well as a 50% decrease in people contaminated by these worms compared with the control village. «When it is not possible to eliminate bilharzia using medicines only given the excessively high rate of re-infection, langoustines could provide a complementary strategy for controlling the illness,” they explain.

«These crustaceans can offer a synergy between the efforts made at local level in the poorer countries to combat this parasitic disease and the development of a new economic activity based on aquaculture», adds Dr Susanne Sokolow of the University of Stanford, a co-writer of this study.

Following the promising results of the initial experiments, “we have proceeded to set up the so-called ‘proof of concept’ phase in order to verify the initial observations with a much larger sample of villages using methods that have been improved as a result of the lessons learnt in our initial experiment. In the very near future, we will also start to experiment with the aquaculture of river langoustines on a much wider scale, with the aim of actually reintroducing this shellfish in the Senegal River” pointed out, Dr Riveau.

The first study was partly financed by the Bill and Melinda Gates foundation, the American National Institute of Health (NIH) and the National foundation of science of the United States. All those involved in the new project form part of the UpStream Alliance network which is always supported by the Bill and Melinda Gates foundation and by Grand Challenges Canada for the aquaculture aspects.
For over 25 years, Camille Locht and his team have been analysing the mechanisms of the development of whooping cough and tuberculosis, from molecular research up to therapeutic or prophylactic applications. "We have been trying to understand the mechanisms induced by these germs that make people sick in order to improve the efficacy of vaccines, and find new antibiotics and new diagnoses" explained Dr Locht.

For tuberculosis, the Lille researchers are working on the development of a booster vaccine which could help extend the efficacy of the initial BCG. This vaccine molecule may also turn out to be an excellent tool for developing a diagnostic test for screening healthy carriers. Regarding possible treatments, researchers have found, in cooperation with Benoît Deprez's "medicines and molecules for acting on living systems" laboratory, how to make the tuberculosis bacillus more sensitive to antibiotic treatments.

As for whooping cough, the team has worked on the development of a nasal spray vaccine which should make it possible to vaccinate young children at birth. The young team led by Priscille Brodin, an Inserm Research Director, has studied the intra-cellular chemical genomics of mycobacteria, thanks to a unique high-throughput imaging system.

They have just made an important discovery concerning Buruli ulcer (See opposite) but have mainly focused on Mycobacterium tuberculosis, the agent of tuberculosis. They have identified new inhibitors to the bacillus of tuberculosis inside the host cells, which could be used as a base for new drugs and have studied the biological markers of the reactivation of latent tuberculosis.

The genomics technology platform coordinated by David Hot, a researcher at the Institut Pasteur of Lille, has also developed a research programme on the study of the virulence regulation of the mycobacteria.
Bordetella pertussis (The agent responsible for whooping cough).

The team led by Jean Dubuisson, a Research Director at CNRS, have studied the biology of the virus of type C hepatitis. It is attempting to understand how the virus interacts with liver cells in order to propagate itself. “We have shown that the sugars present in the viral envelope contribute to reducing the recognition of the virus by the immune system. We have also participated in the characterization of the cellular protein involved in the penetration of the virus. Finally, we have identified and characterised the inhibitors of this virus” explained Dr Dubuisson. This team is also attempting to understand the interactions of another virus, the hepatitis E virus, with liver cells. It is also endeavouring to characterise the MERS-CoV, a new and very deadly coronavirus on the Arabian peninsula.

The team led by Florent Sebbane, Inserm Research director, have reproduced the mechanism of the infection in laboratory in order to better understand the molecular mechanisms underlying the spread of the plague. More particularly, they have tried to identify the genes that help the bacteria be more efficiently transmitted by the flea as well as those responsible for the disease in mammals.

A structure coordinated by Frank Lafont, a Research Director at CNRS, the “Laboratory for cellular microbiology in the cell-pathogen interface” has studied, using a panel of imaging techniques that is unique in Europe, the future of the cells and their reaction to infection in order to identify the common mechanisms to respond to an attack and the mechanisms specific to each pathogen. “Our work is complementary to genetic research. We try and understand how pathogenic bacteria, bacterial toxins or parasites enter the cell in order to identify cellular targets to create new therapeutic tools” explained Dr Lafont.

Tuberculosis: the updated origins of multi-drug resistant strains

In order to gain a better understanding and find better ways of combating the forms of tuberculosis that are resistant to multiple antibiotics, a team of researchers supported by the infection and immunity center of Lille (“CII”) studied the changing history of the mycobacteria involved, using the genetic data of almost 5000 strains from the Beijing lineage, associated with the propagation of multi-drug resistant cases in Eurasia. The results, published on 19 January 2015 in the Nature Genetics review, reveal a correlation between the development of resistances and recent human history and identify new potential targets for the treatment and diagnosis of illnesses.

“With Thierry Wirth of the Natural History Museum and Stefan Niemann of the Research Center in Borstel, we took an interest in the Beijing lineage because it represents a family of mycobacteria strains which are at the origin of a large number of multi-drug resistant tuberculosis strains. Tuberculosis strains are said to be multi-drug resistant when they cannot be treated by the two main antibiotics, which are immediately recommended, necessitating more intrusive and less efficient treatments,” explained Philip Supply, CNRS research director at the CII.

“This family of strains emerged about 7000 years ago in a region located between north-east China, Korea and Japan and spread to the rest of the world in a succession of waves linked to the movements of the human population. In recent times, the bacterial population initially experienced an upswing during the Industrial Revolution and the First World War. The only subsequent observed decrease is consistent with the generalised use of antibiotics in the 1960s. This decline was interrupted at the end of the 1980s as a result of the AIDS epidemic and the epidemic expansion of strains resistant to multiple antibiotics associated with the collapse of the public health system in the former Soviet Union.”

This latest “upsurge” demonstrates the catastrophic consequences of the lack of monitoring and an effective treatment in cases of tuberculosis. Philip Supply makes the point that, “according to a British study, if strains that are resistant to antibiotics continue to grow at the same rate, the death rate from infectious diseases will surpass the death rate from cancer in the western world by 2050.”

This highlights the importance of these works because the researchers have identified a series of mutations and genes that may be associated with epidemic propagation and the resistance to antibiotics. These genes are a potential target for treatment and the development of quicker diagnostic tests for multiple resistances to antibiotics based on genome sequencing.

*Consortium coordinated by the Center of infection and immunity of Lille (CII: CNRS/Institut Pasteur de Lille/INSERM/Lille University), at the Institute of systems analysis, revolution, biodiversity (CNRS/National Museum of Natural History/UPMC/EPHE), and the Borstel Research Center (Germany), with the collaboration of the Center for Disease Control in the United States. The analyses were conducted using an internationally standardised molecular method by the CII team working in collaboration with Genoscreen.
Five teams have been working more specifically on immunity and inflammation, issues both in the pulmonary and intestinal fields.

The team of pulmonologists led by Anne Tsicopoulos, an Inserm Research Director, has been trying to better understand the mechanisms at play in asthma at the level of the inflammatory cells of the lymphocyte tissues and cells (the leucocyte involved in immunity). The researchers have been analysing how the cells and their mediators orchestrate the inflammatory reaction and tissue remodelling, in order to find new therapeutic targets.

The team led by François Trottein, a Research Director at CNRS, has been focussing on two pathogenic agents of considerable clinical importance: the flu virus (virus influenza A) and Streptococcus pneumoniae (pneumococcus) Its prime objective is to identify the early immune mechanisms triggered during an infection by the flu and pneumococcus viruses. In addition, it has been trying to define the cellular and molecular factors of the host creating a predisposition for secondary bacterial infections following a flu infection, to the chronic obstructive pulmonary disease (COPD) and during obesity. Finally, the laboratory has developed new therapeutic strategies in order to strengthen the defence mechanism against respiratory infections.

The team led by Mathias Chamaillard, an Inserm Research Fellow, has been working on the role of NOD2, the main gene for the predisposition to Crohn’s disease, in chronic intestinal lesions caused by infectious, inflammatory, and carcinogenous agents. The benefits of this research could also prove essential to identify new therapeutic targets to prevent the development of tumours, mitigate inflammation and strengthen intestinal defences. As for the team led by Bruno Pot, an Institut Pasteur de Lille research director, they have been studying the positive effect of probiotics (Microorganisms with beneficial effects on health) on the prevention and treatment of intestinal inflammatory diseases. The team is more particularly interested in the mechanistic aspects of the interaction between the probiotics selected and their hosts. Its specific task is to understand the role of the wall components and their interaction with NOD2 in the anti-inflammatory capacities of lactic acid bacteria. They have also been analysing the potential role of probiotics in the prevention or treatment of opportunistic infections such as Clostridium difficile or salmonella and the potential role in the fortification of the immune system.

Since 2012, the team led by Lionel Poulin, an CNRS Research fellow, have studied the dendritic cells that "decode" the pathogens’ information for the immune system. Better understanding these mechanisms would help improve the efficacy of vaccines or better target them.
Gut flora backing up immunotherapy in oncology

The crucial role played by gut flora in the success of immunotherapy has recently been revealed in a study published by the Science review. Some intestinal bacteria capable of improving the therapeutic response of this medicine and reducing a side-effect that is regularly encountered with this treatment, namely "inflammatory bowel disease", were identified.

Underpinning this research work is the fact that the effectiveness of immunotherapy in oncology may in the future be governed by the composition of the gut flora of patients, in particular. The researchers are hoping to be able to put together a predictive test in response to these treatments by analysing the gut flora on the one hand and gain the ability to offer those patients that require it, the opportunity to reconstitute a flora that will restore the anti-tumour effect of the immunotherapy on the other hand.

This research work was conducted jointly by the French researchers of Gustave Roussy, INSERM, Institut Pasteur of Lille and Paris, the AP-HP and Paris-South University, working in collaboration with the team from INRA.

The role of two gut flora bacteria in improving the side-effects and increasing the efficiency of immunotherapy using anti-CTLA4 antibodies (ipilimumab) has recently been demonstrated by the team of Prof Laurence Zitvogel, supported by the teams of Dr Mathias Chamaillard of Institut Pasteur de Lille, Dr Ivo Gomperts Boneca of Institut Pasteur in Paris and Dr Patricia Lepage of INRA.

The researchers demonstrated that when the gut flora lacks the two bacteria identified, either in germ-free mice or after broad-spectrum antibiotic treatment and a treatment with ipilimumab, the medicine was no longer effective in combating the tumour. The colonisation of the gut flora by one or other of these bacteria is necessary and sufficient in order to restore the effect of the monoclonal antibody and improve the symptomatology of the inflammatory bowel disease in these mice.

The relevance of this information has also been successfully researched in humans.

The teams of Pr Caroline Robert, head of the dermatology department at Gustave Roussy and Prof Franck Carbonnel, head of the gastroenterology at the Bicêtre hospital, AP-HP, have begun a clinical trial to demonstrate the relevance of this information among patients suffering from melanoma. Consequently, the analysis of the gut flora of patients suffering from a metastatic melanoma following treatment with ipilimumab has demonstrated the significance of this immunogenic bacteria in the treatment sensitivity and reducing tumours. These results suggest the interest in considering immunogenic bacteria as auxiliary treatments in oncology.

The researchers are hoping to be able to offer patients with relatively unfavourable gut flora a compensatory bacterial composition, either using prebiotics or using immunogenic bacteria coming from gut flora or by a faecal transplant. But currently, in France, there is a lack of clarity in the rules regarding the transformation of gut flora in medicines that could become auxiliary therapies in oncology, with the help of legislators and the regulatory agencies.

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Marie Vétizou1,2,3, Jonathan M. Pitt1,2,3, Romain Dalilâtre1,2,3, Patricia Lepage5, Nadine Waisdorn11,3, Caroline Flamant1,2,4, Sylvie Rusakiewicz1,2,4, Bertrand Roux1,2,3, Maria P. Robert1,2,4, Connie PM. Duong1,2,4, Vichnou Poirier-Colame1,2, Antoine Roux1,2,19, Sonia Bechare1,2,4, Silvia Formenti16, Encause Gitanel6, Sascha Corling7, Gerard Ebert7, Andreas Schützer8, Florent Ginhoux8, Sidhar Mani12, Takahiro Yamazaki1,2, Nicolas Jacquelot1,2,3, David P. Enot1,10, Marion Bérand23, Jérôme Nigou14,15, Paule Opolon1, Alexander Eggert1,1,16, Paul-Louis Woerther17, Elisabeth Chachaty17, Nathalie Chaput1,26, Caroline Robert1,16,24, Cristina Matteu1,16, Guido Kroener9,10,11,18,19, Didier Raoult20, Ivo Gomperts Boneca21,22†, Franck Carbonnel13,25†, Mathias Chamaillard13†, and Laurence Zitvogel1,2,3.
The nuclear receptors are proteins that act on gene expression. When the expression or the function of these receptors is altered, the genes are modified and diseases such as the metabolic syndrome, obesity or high blood pressure can develop. Bart Staels’ team has been trying to propose a therapeutic approach to modify or counter these alterations, by working particularly on the nuclear receptors of the peroxisomes proliferator-activated receptors (PPARα) family involved in the metabolic control and inflammation, of FXR, the receptor of bile acids which also plays its role in the way our body metabolise glucose; and finally Rev-erb and ROR that have a role in the way our biological clock works. Finally, the team has been working on intestinal hormones which trigger the secretion of insulin in response to the ingestion of a meal.

The immune system plays an important role in the triggering and the chronicity of cardiovascular diseases. If the link between inflammation and atherosclerosis (accumulation of bad cholesterol in the blood vessels) has been known for a long time, it has been established much more recently for type 2 diabetes, obesity or the metabolic syndrome. This is why David Dombrowicz, an INSERM research director, has studied the evolution of immune cells, lymphocytes, macrophages and dendritic cells in cardiovascular diseases in order to find out whether all or some of these cells could be therapeutic targets.

Sophie Susen, haematologist, and Eric Van Belle, cardiologist, are seeking to understand the mechanisms involved in the calcification of heart valves in order to offer innovative therapeutic methods for preventing or slowing this process down. These calcified valves gradually become an obstacle to the flow of blood. The team is also involved in understanding and identifying the complications associated with valvular heart diseases and put forward therapeutic solutions. It demonstrated that anomalies in the multimerisation of the Willebrand factor, which is the key haemostasis protein, could be a biomarker of these flow anomalies. It is pursuing this work by studying the impact of these anomalies of the Willebrand factor on the prognosis and therapeutic treatment of patients.

Philipppe Lefebvre, an INSERM research director, has studied the modifications, resulting from the metabolic diseases of the action mechanisms of the nuclear receptors and the way these proteins regulate metabolism. This type of approach helps better understand the mechanisms at play inside the cells, find new therapeutic targets in this area and better predict and/or limit the side-effects of the small molecules with a medicinal effect that may interact with these targets.
A medicine against nonalcoholic steatohepatitis (NASH) made in Lille

Despite the fact that non-alcoholic steatohepatitis, commonly known as NASH, is making the headlines on the other side of the Atlantic, this "fatty liver disease" is not yet very well known in France. However, it is on the rise in France as it is in all Western countries where it has become the primary cause of hepatic deficiency. Consequently, the development in Lille of the first treatment against this disease – treatment coming directly from the research conducted at Genfit in collaboration with the team of Institut Pasteur de Lille may well be revolutionary.

NASH is a chronic hepatic disease characterised by excess fat in the liver that is not linked to alcohol consumption, but which can nevertheless lead to cirrhosis. In the United States alone, no less than 600,000 people suffer from cirrhosis associated with NASH. The American medicine authority, the FDA, estimates that between 12 to 15% of the population of the United States could be affected by this pathology. It has consequently opened the way to fast-track the commercialisation of the future treatment developed by Genfit, a company based in Lille.

The origin of the discovery of this medicine goes back to the beginning of the 1990s and the fundamental research conducted by Institut Pasteur de Lille under the scientific direction of Bart Staels. This research was aimed at gaining a better understanding of the workings of nuclear receptors inside cells that enable the organism to adapt to the consumption of fat. During a period of excessive eating, among an increasingly large group of individuals, these receptors become disordered leading to dyslipemia, diabetes and NASH.

Scientists are therefore seeking therapeutic targets that can be used to reset the organism. This work has made it possible for Genfit to identify a small molecule called elafibranor, which could restore the balance. "We have already produced more than a dozen scientific publications about this molecule, explained Prof Bart Staels, who is also chairman of the scientific council for Genfit. In the laboratory, our molecule has proven its effectiveness in combating diabetes and NASH. We have chosen to develop clinical studies on NASH given that there is currently no medicine available against this disease. When we started, NASH was a little-known and rarely documented disease. It has now become a massive pathology that may overtake viral hepatitis, the treatment of which is becoming increasingly effective."

Elafibranor, the initial results of which are encouraging, is currently in phase 3 of its clinical development.

Type II diabetes: a new mechanism for regulating the sugar content has been brought to light

The percentage of sugar in the body is not only regulated by the insulin. Another hormone, glucagon, stimulates the production of sugar by the liver when it detects insufficient quantities of sugar in the cells.

Some researchers from Lille, the teams of Professors François Pattou (Lille University, INSERM, Lille regional university hospital) and Bart Staels (Lille University, INSERM, Lille regional university hospital, Institut Pasteur de Lille) have closely studied this hormone that is secreted by the alpha cells of the islets of Langherans of the pancreas. They discovered that a glucose cotransporter (SGLT2), of which we are already aware for the reabsorption of glucose in the kidney, is also present in the alpha cells where it controls the secretion of glucagon. By revealing this mechanism, the researchers can explain why a new class of anti-diabetics, namely the "Gliflozins", marketed in the United States and the United Kingdom for type II insulin-resistant diabetes, is not as effective as was originally hoped. Although it lowers the sugar content, it also leads to the secretion of glucagon that is an additional source of glucose. Prior to its commercialisation in France planned for the coming months, the researchers are suggesting that other molecules for reducing the secretion of glucagon should be administered at the same time.

The results obtained in Lille at the Labex EGID (European Genomic Institute for Diabetes) were published in the Nature Medicine journal on 20 April 2015.
Glucose and diabetes: a new identified measure

Diabetes currently affects more than 300 million people and is directly responsible for 4 million deaths per year. It is characterised by an unusually high concentration of glucose in the blood. Although the role of the pancreas in not secreting enough insulin has been known for a long time, other mechanisms are also involved, particularly in the intestines. Prof Bart Staels’ team from Lille has recently discovered the activity of a nuclear receptor in this tissue. A discovery that helps to better understand the role of certain medicines in controlling glycaemia and which may also help to understand the mechanisms at work in obesity surgery.

The nuclear receptors, which are active proteins in the cells’ nuclei have the ability to modify gene expression. Several research teams, including those of Bart Staels, have already demonstrated that the FXR nuclear receptor plays an important role in controlling the energy balance by fixing the bile acids: it modifies the intestinal absorption of glucose and the metabolism of the liver and the adipose tissue. “This time, we wanted to understand the role played by FXR in the endocrine activity of the intestine, i.e. in its hormone secretion functions” explained Prof Sophie Lestavel (Lille University). We found FXR in the L-cells which represent 1% of the intestine’s cells and which produce the glucagon-like peptide-1 (GLP-1) incretin that is essential for secreting insulin after a meal. We showed that the activation of FXR in the cells has a negative effect on not only the synthesis, but also the secretion of GLP-1.”

GLP-1 is already a therapeutic target for diabetes: non-degradable analogues of GLP-1 and inhibitors of its degradation were recently developed. The discovery of researchers from Lille finally confirmed the importance of the signalling of FXR in the intestine. “If these new medicines were coupled with FXR antagonists, the results will probably be even better” commented Sophie Lestavel.

Another lesson learned from this discovery: This new FXR/GLP-1 pathway helps to gain a better understanding of the mechanisms responsible for the beneficial effects on the glycaemic control of the sequestering agents of bile acids, which are the medicines used in France to combat hypercholesterolemia but whose indication in the United States also includes diabetes.

44% of type II diabetes cases can be attributed to excess weight and obesity. Obesity and type II diabetes are metabolic diseases that are attaining pandemic levels. According to the figures of the WHO, 20% of the world population is overweight and 7% are obese. Currently, the only means that has proved to be effective in controlling the glycaemia of diabetic obese patients has been gastrointestinal surgery, in the knowledge that we are as yet unable to explain all of the reasons for this. We already knew that surgery increased the secretion of GLP-1 and modified the composition of the intestinal microbiota and the quantity of bile acid produced at the same time. We are now able to make the hypothesis that the bile acid/intestinal FXR/GLP-1 pathway could be involved. This discovery provides a slight indication of potential future improvements in the arsenal of available therapeutic tools for combating type II diabetes.

Article published in the Nature Communications Journal on 2 July 2015 (Trabelsi et al.)
THE METABOLIC AND EPIGENETIC DISEASES LIKE DIABETES AND OBESITY

Integrative genomics and modelling of metabolic diseases
A unit led by Pr Philippe Froguel (Lille University)
CNRS UMR 8199 - Institut Pasteur de Lille - Lille University

The heritability of diabetes is currently 90% and that of obesity is 70%. About 5% of patients carry a unique genetic anomaly that is sufficient to make them sick. The ability to identify them often makes it possible to set up a more effective, less restrictive and less expensive personalised treatment. For the other diabetic and/or obese people, there are many genes involved: since 2007, about 100 genes have been identified, at Institut Pasteur de Lille predominantly, but they only explain 20% of the genetic risk of these diseases. So the research conducted by the Lille team is moving towards rarely encountered mutations that nevertheless have more significant effects on their carriers and on the epigenetic modifications associated with the internal or external environment.

Thanks to the Equipex LIGAN very high-throughput human genomics platform—Personalised Medicine and its expertise in genetics, which is unique in France, the team of Prof Philippe Froguel, the first to identify the genes responsible for type II diabetes and obesity, has the keys to understanding, preventing and providing better treatment, or even healing certain cases of these diseases. “I began working on obesity because 80% of obese people are diabetic and I believed that the genetics of obesity would help to advance the genetics of diabetes. However, in the end, genetics has taught us that, despite the fact that these 2 diseases are highly connected, they have different origins. In short, obesity comes primarily from the brain and the intestines and has to do with the regulation of the diet, whereas diabetes comes primarily from the pancreas and the secretion of insulin. Resistance to the effects of insulin is very often present in obese as well as diabetic people (although this is not always true) and although it modifies the risk of diabetes, its effects are primarily observed in the complications of obesity and diabetes, whether they are hepatic or cardiovascular. The increase in the risk of several types of cancer in obese and diabetic people is probably linked to insulin resistance”. That’s why the team of Prof Froguel is directing part of its research to epigenetics. Epigenetics study changes in the way genes work that are not caused by changes in the DNA sequence. These modifications begin to emerge during the foetal period and subsequently as a reaction to the environment. Epigenetics, when compared to evolution that advances slowly, is the short-term adaptation of the genetic material to its environment. This is fundamental as it enables us to read the genetic code differently. It explains, for example, the differences that exist with identical twins. In order to undertake these studies, researchers, who are following in the footsteps of Pasteur, begin their work on humans. Then, once they have found new genetic or epigenetic factors, they create laboratory models in human cell lineage or stem cells, similar to the research already successfully undertaken on certain cancers. Philippe Froguel’s team have cultured stem cells from pancreatic cells and fat tissue from diabetes patients to test drugs. When all these genetic and epigenetic anomalies are clearly identified, the scientists hope to progress towards individual care, or true personalised medicine.
In search of rare mutations

“The search for mutations has helped to open up many new avenues of research on genes with some unexpected results regarding their field of action, but it was not the hoped-for Holy Grail that explains the development of the disease,” explained Amélie Bonnefond, responsible for research at INSERM. So we asked ourselves the question of whether some rare mutations that have occurred relatively recently in the history of human life, which have had an effect on common types of diabetes, could be important.”

“We wanted to check this idea with a gene, i.e. the melatonin receptor, and we found some very rare and harmful genes associated with type II diabetes. This means that the frequency of rare mutations of this gene in diabetics is much more frequent than in the population as a whole. Now, with next-generation sequencing, since summer 2015 at Institut Pasteur de Lille, we have been testing 1200 genes on 10,000 individuals whose DNA we possess and that we will evaluate with a view to the study of diabetes and obesity. This work will take us 18 months. The most interesting mutations in the cellular models, especially stem cells, must then be reviewed.”

Could this lead to new treatments? Amélie Bonnefond suspects that it might. “A similar study provided the basis for developing a new therapeutic model directed against the PCSK9 enzymes that may end up depositing statins in the treatment of cholesterol.”

The molecular bases and modelling of diabetes and obesity

Since 1st January 2015, the unit has been divided up into two teams. Although most of the researchers are dedicating their research to genomics, Dr Jean-Sébastien Annicotte, responsible for research at INSERM, is studying the molecular bases of these diseases. "If I take the example of diabetes, in order to find new treatments, we need ways of acting on the molecules at the core of the sick cells. Diabetes is partly characterised by a dysfunction of the insulin-producer cells, i.e. the pancreatic $\beta$-cells, as well as the tissues targeted by the insulin, like the liver, the muscle and the adipose tissue."

“We therefore trigger diabetes in the laboratory models and then look at the DNA cells, the expression of the genes, the epigenetics, that is the changes occurring in the gene activity in order to discover specific inhibitors or activators in each organ. As part of the labex EGID, we are also working closely with the team of Prof François Pattou at the regional university hospital of Lille in the analysis human tissue in order to understand what is not working properly in humans.”
From a biological point of view, cancer results from the onset of a dysfunction in certain cells in the body. These start to multiply haphazardly and grow out of control, first locally, and then in the surrounding tissue, and eventually at a distance where they form what is referred to as metastasis.

“There are nearly as many different cancers as there are patients. Each tumour is associated to a different molecular mechanism. There is no longer breast cancer but a dozen diseases which are taken care of based on their own characteristics and those of the patient. For 15 years now, targeted therapy has been a reality, a reality that we try to improve every day” noted Dr Yvan de Launoit.

With this in mind, his teams focus more specifically on the blood network specific to cancer cells to find a way to starve them while continuing to feed healthy cells. Researchers have also studied the role of receptors, including the Met receptor, which regulate at the surface of the cells, their survival, growth and migration. The malfunction of the Met receptor is responsible for the most deadly cancers (lung, colon, aerodigestive tracts). The objective is to deactivate these receptors in a targeted way in order to adapt the therapies according to the molecular modifications observed in the patients.

Researchers also observe how the cells of the immune system those that are in charge of defending our body against aggression, are capable of identifying and then destroying newly appeared cancer cells, more particularly in liver cancers. They try and understand why normal cells change to cancer cells with time (in skin cancers) and including how to detect and fight metastases in prostate cancers. They try to decipher the mechanisms of tumour dormancy which allow cancer cells to leave the primary tumour to lodge themselves in new organs and remain dormant there, sometimes for many years before waking up.
2015 MATWIN prize "for the best project in response to an unsatisfied medical need"

Backed by the federation of centers involved in the struggle against cancer, Unicancer, MATWIN (Maturation & Accelerating Translation With Industry) is a French programme, which is unique in Europe, for detecting and supporting research projects in oncology. It makes it possible for academic programmes to meet industrial and financial partners with the aim of developing the pre-clinical research phases.

The Galimab project, put forward by Dr Delhem, aims to synthesise a new candidate medicine that can neutralise regulatory T (Treg) cells that increase exponentially in the event of cancer and that reduce the effectiveness of our immune system. This therapeutic tool was included in a patent submitted in June 2014 and an international extension submitted in June 2015 by the society for the transfer of technology (SATT Nord).

"The Treg cells increase significantly in cancers and are associated with a bad prognosis. Unlike Treg cells, T lymphocytes are the good soldiers of our immune system. Yet, until now, no treatment that specifically targets Treg cells without affecting the T lymphocytes had been found. We discovered that a protein known as Galectin-9 was specifically expressed by the Treg cells and not by the activated T lymphocytes and we developed an antibody to neutralise it. In the laboratory, we were able to prove that this candidate medicine reduced the growth of the tumour and made the immune system more active."

However, in order to complete all the preliminary phases in the development of a medicine, the resources required are exorbitant and beyond the reach of an academic laboratory. This is why the laboratory must now seek out industrial partners. Thanks to the MATWIN certification, several pharmaceutical laboratories have already shown an interest.

Rather than replacing existing treatments, Galimab, if it should prove to be effective, may boost their efficiency or even reinstate promising medicines whose development has been dropped because they boosted the Treg cells.

2015 Santelys Prize

As part of its 2015 call for projects, the Santelys association retained a study on the identification of early biomarkers of tumour response in high-dose hypfractionated radiotherapy, proposed by the team of Dr Delhem in collaboration with the team of Dr Xavier Mirabel at the Center Oscar Lambret within the context of the SIRIC OncoLille. This involves verifying the impact of more powerful and more targeted radiotherapy on both the immune system and on eradicating the tumour.
Both a scientific contact point and a partnership with the researchers of the Egid Labex and of the infection and immunity center in Lille (CIIL), the researchers of the unit design compounds that modulate the molecular targets selected with the biologists in the team. These compounds, which must be powerful, selective and bioavailable, are assessed in increasing complex models, from in vitro miniaturised tests to trials in animals suffering from the pathology studied.

To discover the first "hits" on these molecular targets, the laboratory has at its disposal the biggest academic chemical library* in Europe (80,000 different products, i.e. over 1 million single use samples) In cooperation with the biologists, the unit’s researchers rebuild and miniaturise the molecular mechanism at the origin of the disease studied in order to test, quickly and at a low cost, tens of thousands of compounds, and find among them, those that will correct the molecular defect. In 2014, the Equipex ImaginexBiomed equipped the laboratory with an automated screening platform that is unique in France, managed with CIIL.

Thanks to progressive adjustments in the chemical structure, researchers will design more powerful and selective compounds. But these two required properties are not sufficient. The compound must also reach its target in the organism as when it is metabolized or eliminated before reaching the relevant cell, it will have no therapeutic effect. Benoît Deprez and his team have therefore modelled the natural barriers that protect our organs from foreign chemicals, in order to check, before trials in animals, that the compound, which could become a drug candidate, will be able to cross them.

Thanks to this unique combination of know-how in pharmacodynamics and in pharmacokinetics make it possible to study simultaneously what the compound does to the living system and what the living system does to the compound. It is the harmony between these two phenomena that makes the future drug.

“The harmony between these two phenomena that makes the future drug.”

Currently, 4 treatments are being designed or developed. Around metabolic diseases and tuberculosis. One of them has been the subject of a cooperation between Bioversys and the GSK pharmaceutical company.

For example, with Alain Baulard who has worked with Camille Locht on the treatment of extensively drug-resistant tuberculosis, we have developed antibiotic boosters (See p 26). “With Bart Staels (see p 30), we have been working on intestine or pancreas cells to find products that improve the management of sugars to treat diabetes” explained Dr Deprez.

In parallel with the discovery of new drugs, the compounds we are preparing enable us to act “surgically” on the molecular components of the cell and study specifically the biological roles of a receptor or an enzyme of interest. This approach, called “chemical biology”, is complementary to genetic approaches used by our team members. With Bart Staels and Philippe Froguel, this is how we have been studying an enzyme whose role is still poorly understood, called Insulin Degrading Enzyme.”

*collection of molecules, synthetic products
Research - Discovery of prescription drugs

The teams for Lille are lifting the veil on the role of the Insulin Degrading Enzyme

The Insulin Degrading Enzyme (IDE) is a kind of protein that is unique in the entire realm of living beings. The function of this enzyme that was discovered in 1949 is not yet very well understood in the plant world but we know that, in the animal kingdom, it degrades insulin, hence its name. It is expressed in most of the cells of the human body and plays a role in Alzheimer’s disease where it seems to have an effect on eliminating the amyloid peptide and on diabetes because it contributes to the degradation of the insulin.

Some research teams, most of which are located on the campus of Institut Pasteur de Lille, wanted to check if the inhibition of this enzyme could have a protective effect against diabetes.

«Paradoxically, the exact opposite occurred and this, in an of itself, is already a very important element of information” commented Prof Benoit Deprez. Furthermore, this relatively unique collaboration between chemists, biologists and physicists has made it possible to develop an original method that the enzyme uses to make its own inhibitor by itself. We are continuing to study the enzyme’s other more ancient functions, which are also found in plants and which are not necessarily linked to the production of insulin.»

Catalytic site inhibition of insulin-degrading enzyme by a small molecule induces glucose intolerance in mice, Nature communication, 23 septembre 2015.

Prof Rebecca Deprez-Poulain appointed at the IUF

The "Institut Universitaire de France" (IUF) is a department of the ministry responsible for higher education, whose task is to promote the development of high-level university research. The educators appointed to the IUF benefit from 5 years of scientific funding amounting to €15,000 per year and the cost of two-thirds of their education service.

Professor at the University of Lille 2 (Faculty of Pharmacy) and researcher at the INSERM-Institut Pasteur de Lille-Lille University ”Medicines and molecules for acting on living systems” mixed unit, Rebecca Deprez-Poulain was appointed junior member of the IUF. This appointment took effect in October 2015. Her research project was devoted to designing and developing selective inhibitors of metalloproteinases involved in cancer and auto-immune diseases, using sophisticated in-situ click chemistry techniques and the screening of fragments.

Metalloproteinases are a class of proteins involved in significant biological phenomena, such as cellular proliferation, signalling, multiplication and migration, hormonal signalling, angiogenesis or even the growth of pathogenic agents.

The IUF encourages the search for excellence, interdisciplinarity and tries to promote the place of women in research. Rebecca, who has been honoured by this appointment, has all three of these qualities. The appointment is both a sign of recognition and a booster for her research.

On the Pasteur Lille campus, Prof Rebecca Deprez-Poulain has been working with the teams of Prof Bart Staels on metalloproteinases in diabetes for the last few years.

For the research connected to her IUF project, Rebecca has joined up with the teams of Dr Stratikos (Demokritos Center, Athens), Prof Ed James (Southampton University) and Prof Van Endert (Necker Hospital, Center for research in molecular medicine).
A laboratory directed by Dr Fabrice Nesslany, an Institut Pasteur de Lille research director

The genetic toxicity laboratory directed by Dr Fabrice Nesslany, research director at Institut Pasteur de Lille, has been studying the mutagenic, i.e. potentially carcinogenic, activity of substances present in our environment.

He has conducted, among others, regulatory stories to assess the genotoxic potential (Primary lesion of DNA) and the induction of mutations (Stable and Irreversible changes to the genetic heritage transmissible from cell division to cell division) for many types of substances.

This reference laboratory is one of the biggest centers for genotoxicity in France. With a very wide field of competence (Human health, animal health, cosmetics, chemicals, plants/vegetable, nanotechnologies, environment...), the experts from the genetic toxicology laboratory have been cooperating with the pharmaceutical, cosmetics, food, chemicals... Industries.

The laboratory also participates in research programmes at a national and European level aimed at evaluating the genotoxic potential of atmospheric particles, manufactured nanoparticles, heavy metals, mycotoxins and even composts coming from biodegradable packaging, etc.

Dr Nesslany recently set up a new technological platform specialised in analysing endocrine disruptors, which are molecules that can always be found in the environment in common consumer products (cosmetics, plastics, packaging, maintenance products, electronics, toys, etc.) and which belong to different chemical families (including some phthalates, bisphenols, PCBs, polybrominated compounds, perfluor-compounds, certain pesticides, parabens, etc.).

Consequently, the laboratory developed four in-vitro study models for the following activities in 2015:

- so-called specific receptors (on the oestrogenic and/or androgenic objective),
- for the modulation of steroidogenesis.

These models will be used to study the activity of the potential endocrine disruption of substances, which are currently being developed in the chemistry, food industry and cosmetics sectors, at the earliest possible stage.

The nanoparticles of PLGA, a candidate drug carrier?

Having worked out the intracellular penetration pathways (clathrin-mediated endocytosis), the researchers demonstrated that the nanoparticles of poly(lactic-co-glycolic) acid (PLGA), which could potentially be used to convey active substances in anticancer treatment or as an aid to vaccination (by boosting the immune response of the organism) had no genotoxic effects: no induction of primary DNA lesions and no chromosome aberrations. The results were observed on three different types of cellular lineages with one flaw: an aneugenic effect was however observed on pulmonary cells.

The axis of research revolves around the study of the response of different microbial species (Bacteria or viruses) to the conditions or their environment whether natural or connected to human activities. The contribution of the knowledge on the impact of a type of environment on the spread or the destruction of the microorganisms has proved a major asset in the control of microbiological risks. The project involves evaluating and controlling the risks associated with 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 (French national health and safety agency) in the committee of experts specialised in water.

USM also conducts specific studies for several industries where the awareness is raised on the management of contamination, such as the hospital sector or the cosmetics industry.

**Perspective**

**Fabrics that form a barrier to infection**

Nosocomial infections concern one hospital patient out of 20. There is even been a slight increase since 5.1% of hospital patients were infected in 2012 against 4.97 in 2006 according to the survey of the French Institut de veille sanitaire. This is why it was relevant to develop fabrics, bedlinen and uniform for healthcare professionals that block infections in hospitals.

The USM studies the antimicrobial properties of these technical fabrics by means of Research and Innovation programmes. After the antibacterial fabrics, the laboratory began researching molecules which could give textiles virucidal properties against the enteric viruses responsible for gastroenteritis. The fabric could be used to manufacture hospital linen and protection masks. This work led to a presentation that was made at the 31st "Clinical Virology Symposium" – an international congress on virology in Florida – in 2015. Following initial promising results, this work is currently being pursued as part of a cross-border project involving some SMEs of the Nord region and Belgium as well as a group of hospitals. The objective this time is to reach an end product that is in keeping with user requirements.
Institut Pasteur de Lille is an active member of the International Network of Pasteur Institutes ("RIIP"), which is a group of 33 institutes present on 5 continents sharing the same values upheld by Pasteur. Furthermore, Institut Pasteur de Lille signed a framework cooperation agreement with the Lebanese University (the only public Lebanese university institution) and is welcoming several Lebanese students as part of a joint thesis supervision in keeping with its training mission. Institut Pasteur de Lille also has strong links with the "Espoir Pour la Santé" biomedical research center in Senegal that focuses particularly on the infectious diseases affecting the sub-Saharan countries (see p. 26).

The open-minded attitude of Institut Pasteur de Lille can also be seen in the composition of its staff: 37% of the research directors are, mainly Belgian, foreigners while 19% of the post-doctoral positions and 33% of the doctoral positions come from abroad. Regardless of positions, among the scientists working on campus, 60% come from Europe, 20% from Asia, 14% from Africa & 6% from America.

Institut Pasteur de Lille has always developed a determined policy of international level partnerships. The teams cooperate with universities, laboratories, companies or not-for-profit organisations from over 53 and different countries. Over half of our partnerships are located outside European borders: in Africa, in Asia, in America and also in Australia.

Nathalie Mielcarek, international relations manager
MAP OF THE WORLD OF THE SCIENTIFIC LINKS OF THE INSTITUT PASTEUR DE LILLE
27 and 28 May
The international network of Pasteur institutes met in Lille

33 centers for research into health throughout the world are grouped together within the international network of Pasteur institutes. On 27 and 28 May 2015, Institut Pasteur de Lille organised the regional meeting of this network gathering together all the European institutes.

Resistance to antibiotics, re-emerging diseases, infections and cancer, environment and health, microbiota… a very wide reaching programme for scientists: researchers coming from Athens (Greece), Brussels (Belgium), the Bucharest (Romania), Rome (Italy), Saint-Petersburg (Russia), Sofia (Bulgaria) and Paris worked together for 2 days, thereby building ties with their colleagues from Lille, with the promise of further collaborations. Dr Ruxandra Draghia-Akli, health director at the general office of research at the European commission also made the trip from Brussels to present the priorities of the commission in the area of health.

“it is a fantastic network that we can use to work very closely with our colleagues who are working in countries where many of the pathologies that we are studying are endemic” commented Nathalie Mielcarek, head of international relations at Institut Pasteur de Lille (on the right of the photo).

Some institutes have been created at the initiative of governments. Others, like us, are private foundations recognised of public interest. During the last three years, we have ramped up our presence in this network where we are involved through many collaborative scientific projects and also through the implementation of a course in medical bacteriology in Madagascar.”

Perspective

3 to 6 February
Inauguration of the LIA SIGID, the Indian-style institute

Raising of the Indian flag, captivating baroque chants in the room of the executive board and, especially, a high-flying scientific conference lasting three days, during which Institut Pasteur de Lille danced to the music of India for the inauguration of the SIGID (Systems Immunology and Genetics of Infectious Diseases) associated international laboratory. This laboratory, co-ordinated by Dr Sylviane Pied and supported by the CNRS for the French part, gathers together those actively involved in immunology and the genetics of infectious and parasitic diseases in both countries.

This “partition-free laboratory” has emerged from the exemplary collaboration started over 30 years ago between the CNRS teams, those of INSERM, Institut Pasteur de Lille, Lille University, the Pierre and Marie Curie University in France and some teams from the Department of Biotechnology (DBT) with the Tata Institute for Fundamental Research (TIFR), as well as the SCB medical College and the ISPAT General Hospital in India.

Officially created on 14 November 2012 at Bhubaneswar in India, the LIA SIGID is a multi-disciplinary and integrated research network that combines clinical and fundamental studies in the areas of immunology and genetics with high-throughput exploration technologies, bioinformatics and mathematics. Its teams include the following: clinicians, immunologists, geneticians, molecular biologists, mathematicians in India as well is in France.
The LIA SIGID is primarily devoted to the study of the immunology and genetics of parasitic infections, especially malaria, filariasis and leishmaniasis, the three most widespread parasitic diseases spread by insect bites in India. These diseases, which can be fatal, are a genuine scourge because they affect millions of individuals per year. The fight against these infections is one of the millennium Development Goals (MDG) passed by 193 member states of the UN and more than 20 international organisations.

"These diseases have a complex genetic and immunological control, influenced by multiple exogenous parameters, e.g. socio-economic and cultural factors, the ecology, meteorology, urbanisation and farming practices" explained Sylviane Pied, CNRS research director at the CIL and coordinator of the French part of the LIA.

One of the main objectives of the LIA SIGID is to better understand the interactions between these multiple parameters using a holistic approach based on the “disease triangle” model (hence the triangular logo of the SIGID) developed in the 1960s by phytopathologists. This model is currently being used in the agricultural sector. It is used to predict and contain infections in the plant world. Until now, this approach has been used in predicting human infectious diseases.

"Our measures do not compare unfavourably with those of our Indian colleagues, quite the reverse pointed out Sylvian Pied. However, we can help them with our experience in working with networks and training because, currently, India lacks researchers with adequate training in immunology."

That’s why the partners of the LIA EGID very soon realised the need to organise an international Master’s programme between the Indian and French higher education institutions, called: “Systems Immunology and Genetics of Infectious Diseases”, adopting same name as that of the consortium. This Master’s programme will give the students a detailed knowledge of the most modern approaches used in Biology systems, processes, genomics and integrative immunology, bioinformatics and mathematics applied to the study of infectious diseases. This course will welcome French students and Indian students and, for the first time in the education sector, will be run partly in France and partly in India.

For Sylviane Pied, this is the first building block in the construction of a new adventure that it hopes to pursue over the long term, with, ultimately, the creation of a genuine Franco-Indian research center into infectious diseases “relying on a social perspective of science and research, following in the footsteps of the legacy of Louis Pasteur and Albert Calmette!”
**Imaging microscopy & cytometry**

Inserm U 761, Inserm U 1019, CNRS UMR 8204, Institut Pasteur de Lille, Lille University  
Manager: Frank Lafont  
BiolImaging Center Lille-Nord de France (BICeL), represents the most important part of EquipEx ImaginEx BioMed.  
Website: www.bicel.org

**Transcriptomics and Applied Genomics**

Transcriptomics and Applied Genomics Group [tAG]  
Inserm U 1019, CNRS UMR 8204, Institut Pasteur de Lille, Université de Lille  
Manager: David Hot  
High-throughput genomics platform specialised in microbial genomics. Since 2012, TAG has joined the genomics platform of Genes diffusion for the implementation of a common structure called Pegase-biosciences, in order to propose cooperation and services pooling the skills of each entity.

**Peptide Chemistry**

Peptide Chemistry, Systems, Biology  
CNRS UMR 8161, Institut Pasteur de Lille, Université de Lille  
Manager: Oleg Melnyk  
Peptide chemistry and protein chemical synthesis.  
Website: www.csb.ibl.fr

**High-Throughput Screening (HTS) and High Content Screening (HCS)**

Inserm U 761, Institut Pasteur de Lille, Université de Lille  
Manager: Benoît Deprez  
Platform combining a chemical library with all the High-throughput screening tools (with the exception of techniques based on high-throughput confocal imaging which are available on the microscopic imaging platform).  
Website: www.deprezlab.fr

**Pharmacokinetics**

ADME-PK screening lab  
Inserm U 761, Institut Pasteur de Lille, Université de Lille  
Manager: Benoît Deprez  
Platform allowing for the quality and quantity characterisation of the future of experimental active principles in animals.  
Website: www.deprezlab.fr

**Nuclear magnetic resonance**

Nuclear Magnetic Resonance  
CNRS UMR 8576, Institut Pasteur de Lille, Université de Lille  
Manager: Guy Lippens  
Nuclear magnetic resonance (NMR) spectroscopy helps probe the molecular structure by making the natural magnetisation of nuclei interact with a magnetic field.
High Security Laboratory and Animal House
Institut Pasteur de Lille
Manager: Jean-Pierre De Cavel
Animal house for research and experimentation NSB3 high biological security laboratory bellowing for the secure handling of infectious biological agents (prions, viruses, bacteria…) or others (toxines, radiation…).

Genomic Analysis Laboratory
Genomic Analysis Laboratory
Inserm U 744, Institut Pasteur de Lille, Université de Lille
Managers: Philippe Amouyel and Nathalie Fievet-Verrecas
Logistics and follow-up of large collections of human biological samples with patients recruited mainly from epidemiological studies based on the cardiovascular, metabolic and neurodegenerative disease themes.

Genomics and Metabolic Diseases
EquipEx LiGAND-PM (Lille Integrated Genomics Advanced Network for Personnalized Medicine)
CNRS UMR 8199, Institut Pasteur de Lille, Université de Lille
Manager: Philippe Froguel
The Lille Ligan-PM platform for the sequencing of the genome can establish the list of mutations which could explain the list of signs for each patient, predict the possible evolution of his/her disease, and predict the efficacy or side-effects of existing drugs. Website: www-good.ibl.fr

Proteomics and Analysis of Modified Peptides
Plateforme Protéomique et peptides modifiés (P3M)
LabEx Parafrap, Institut Pasteur de Lille, CNRS, Université de Lille
Manager: Jean-Michel Saliou
Platform dedicated to the analysis of parasites’ proteins.

Promotion of research
The department for the commercialisation of research, directed by Pr Yves Lemoine, follows up on approximately 50 patents filed jointly by Institut Pasteur de Lille and its partners who are, according to teams, Inserm (represented by Inserm-transfert), CNRS and the Lille universities (Represented by Société d’accélération du transfert de technologies SATT Nord), or even, depending on the type of works, other French or foreign universities.
On the Institut Pasteur de Lille campus, bio-technology companies, market, throughout the world, analysis or diagnosis products, directly stemming from fundamental research conducted in Lille.

**Genoscreen**

Genoscreen proposes analytical services in genomics on all types of genomes (Human, animal, vegetable, microbial) and bio-computing analyses and training, both for academic research teams and for hospital or industrial research. This 100% French biotechnology company was created on the Pasteur-Lille campus in January 2001 and employs today approximately 30 employees. 80% of its turnover is made outside the greater Lille area, of which 30% is exported. Over these last years, own research programmes, conducted in partnership with research units from Institut Pasteur de Lille, Inserm and INRA have helped develop very competitive applications in areas such as the genetics of Alzheimer disease, microbial molecular typing or the control of biodiversity.

[http://genoscreen.fr](http://genoscreen.fr)
Lunginnov

Lunginnov produces Endocan, a biomarker of the state of blood vessels which can be used to treat sepsis and cancers. Endocan or endothelial cell specific molecule (ESM-1) was discovered in 1996 by Philippe Lassalle and his colleagues from the pulmonary immunity team at CIIL (CNRS, INSERM, Institut Pasteur de Lille). Its biochemical structure was characterised in 2001. Endocan biomarkers assess the dysfunction of the endothelial cells that make up blood vessels. A relevant element in the event of sepsis (the number of symptoms which lead to organ failure) or cancer.

https://www.lunginnov.com

X’Prochem

X’ProChem markets proteins synthesised from a chemical reaction. An innovative technology directly stemming from academic research in Oleg Melnyck’s laboratory. These 100% chemical properties are custom-made to meet requirements that classic recombinant methods cannot synthesise, such as toxic, membrane proteins or proteins equipped with a probe so it can 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 2000s before a cost-effective, easily repeatable method is developed at Institut Pasteur de Lille.

http://xprochem.com

APTEEUS

APTEEUS has developed an innovative solution for the individual care management of patients with rare diseases. APTEEUS’s technology make it possible to test thousands of molecules from the existing pharmacopeia and directly on primary cells from the patient. APTEEUS’ administrative headquarters are located at the school of pharmacy with a laboratory on the Institut Pasteur de Lille campus.

http://apteeus.fr

4P Pharma

4P Pharma is developing pre-clinical trials that are suited to the scientific needs of each product. These programmes are based on the following 4 pillars: the proof of the mechanism, the proof of the principle, the proof of the concept and the proof of the relevance. 4P Pharma offers a flexible range of pre-clinical trials as well as consultancy services for supporting R&D projects. The activities are essentially focused on cancers and infectious diseases.

http://www.4p-pharma.com
Here the list of scientific international publications with impact factor is greater than 10. All publications are available on our website.
The Bile Acid Chenodeoxycholic Acid Increases Immune response and suppresses tumour initiation through a microbiome-influenced intestinal inhibition of Atg7 prevents tumour growth.

Liver microRNA-21 is overexpressed in non-alcoholic steatohepatitis and contributes to the disease in experimental models by inhibiting PPARα expression.

Liver microRNA-21 is overexpressed in non-alcoholic steatohepatitis and contributes to the disease in experimental models by inhibiting PPARα expression.

The impact of diet on asthma and allergic diseases

The impact of diet on asthma and allergic diseases

Activity Report 2015

51
# Scientific Production of Institut Pasteur de Lille

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## Distribution 2015 by Group of Research

- **CIL (U1019)**: 25
e- **Santé publique (U1167)**: 20
- **Maladies cardiovasculaires et diabète (U1011)**: 14
- **Cancer (UMR 8181)**: 23
- **Maladies métaboliques (UMR 8199)**: 162
- **Plateformes technologiques**
- **Découverte de médicaments**
- **Santé publique et environnement (toxicologie, sécurité microbiologique, CPES, nutrition)**
III - Health

- The Prevention and health education center
- Medical biology laboratory
- The nutrition department
Anticipating

The CPES is involved in intelligence gathering and the monitoring of the state of health of the regional population. Indeed, the people (over 30,000) welcomed each year form a recognised observatory for conducting epidemiological studies such as the Esteban study, the monitoring of cohorts, especially the Constances cohort.

Esteban

Esteban (health survey on the environment, bio-monitoring, physical activity and nutrition), began in April 2014. This study concerns the environment, nutrition, physical activity and frequently encountered chronic diseases. Supported by the French Ministry for social affairs and health, and the French Ministry for environment, sustainable development and energy, this study is conducted by InVS, the French Institute for Public health surveillance. Esteban has concerned in mainland France a sample of 4000 adults aged 18 to 74 and 1000 children aged 6 to 17. The specificity of the study resides in the number of health themes it covers: environment, biomonitoring, eating habits, physical activity, frequent chronic diseases and their risk factors. As it combines a health examination, a nutritional aspect and assay of environmental biomarkers, it will help obtain a comprehensive review of the health and environmental exposure of the population living in France at a given time. 73 health examination centers are taking part in the study.

Constances

Constances (Consultants of health testing centers), launched in March 2013, is the largest epidemiological cohort ever constituted in France, which will combine a representative sample of 200,000 adults aged between 18 and 69 years old by the end of 2016. This project is under the scientific and technical responsibility of the Cohortes team of the center for research into epidemiology and the health of populations - INSERM U1018 - Versailles University St-Quentin, in collaboration with the technical support and training center of the health insurance health testing centers (“CETAF”). Constances’ objective is both to provide descriptive information on the health status of the French population and its evolution and to make up a database that is relevant for epidemiological research. 16 health examination centers are taking part in the study. The teams of the CPES examined 2486 “Constances volunteers” in 2015.

Head of Department, Dr Dominique Bonte

The prevention and health education center ("CPES") is one of the key players in the institute’s global public health policy. Its objectives link up with the priorities of the major players responsible for public health in the Hauts de France region. This involves:

- **anticipating** situations using intelligence, monitoring of the state of health of the population;
- **understanding** with a better knowledge of the health factors and attitudes and the creation of intervention strategies, experimentation and evaluation;
- **acting** through prevention, education, the promotion of health, responding to threats and sanitary crises.

* certified norm iso 9001-2008
First Nord Pas-de-Calais results of the Constances study

Here are the first Lille results of a study conducted on 3995 Constances volunteers recruited between 2012 and 2014 at the prevention and health education center. The average fill age is 47 years with 56% women and 44% men. 13% of those surveyed come from the 18-29 age group.

PERCEIVED STATE OF HEALTH
This question comes from the "Web life and Health". The exact title is "How would you evaluate your general state of health?"

BMI
The body mass index was calculated using health checkup data. It is defined as the weight (in kg) divided by the height squared (in m²).

The following thresholds were retained:
- «Thin» = BMI less than or equal to 18.4;
- «Normal» = BMI from 18.5 to 24.9;
- «Overweight» for a BMI from 25 to 29.9 and «Obesity» for a BMI of 30 or more.

GIVING UP TREATMENT
"During the last 12 months, have you or your partner given up some health treatment for financial reasons?"

This question comes from the "Way of Life and health" questionnaire, with a yes/no answer.

Source: abstract from UMS011 Inserm UVSQ epidemiologic studies
Cervical cancer screening and anti-papillomavirus vaccination: like mother, like daughter?

The coverage rate for vaccination against human papillomavirus (HPV) infections is low (<30%). The participation rate in cervical cancer screening remains sub-optimal (<70%). The objective of the study is to explore the link between the screening of mothers and their decision to give the anti-HPV vaccination to their daughters.

Working together with the Epidemiology, Health Economy and Prevention Department (regional university hospital and Lille University), the Prevention and Health Education Center asked its consultants, aged 28 to 65 years with at least one daughter between the age of 11 and 29 years, to answer a questionnaire on their attitudes regarding anti-HPV preventive practices and the reasons that motivate them.

Out of 299 women questioned, 241 (80.6%) claim that they have undergone a cervical cancer screening test in the last 3 years. There is a correlation between those that undergo screening tests and those living in vulnerable situations (EPICES score > 30), those affiliated to the French universal health care coverage, those with a high number of daughters (≥3) and the smoking status of the person. Of the 422 girls eligible for the vaccine, only 157 were actually vaccinated (37.2%). The vaccination status of girls does not vary according to the mother’s screening profile. The most common reason given by mothers for the non-vaccination of their daughters is the lack of information, particularly among women who do not screen themselves.

The study does not observe any link between the preventive attitude of mothers regarding pathologies associated with HPV (screening of cervical cancer) and that which they apply to their daughters (anti-HPV vaccination), unlike what has been observed among certain population samples in California and Belgium.

Study achieved by Mohamed-Béchir Ben Hadj Yahia, Marielle Wathelet (CHRU et Université et de Lille) et Fabienne Irel et Dominique Bonche (Institut Pasteur de Lille)
Using medical check-ups and health workshops

In 2015, 12,985 targeted health check-ups were carried out in the health check-up centers of Lille and Tourcoing as well as outside the region in Lens, Arras or Boulogne. Their implementation was completed as part of the agreements with the CPAMs of Lille-Douai, Artois, Flanders, Roubaix Tourcoing and the Opal Coast. The health insurance system assigns these medical check-ups more specifically to the more vulnerable people (people who are socially vulnerable, living alone, people who benefit little or not at all from the preventive measures offered by GPs, people who do not benefit from organised monitoring systems, screening and vaccination, etc.) These so-called vulnerable people represented more than 50% of the consultants of the centers in 2015. During half a day, they undergo a series of medical tests (Blood tests, hearing test, ECG, diet survey…) carried out by CPES professionals: doctors, nurses. The risk factors and healthy behaviour are also addressed with dieticians and medical-sports educators. The following guidelines are proposed as a consequence:

---> either towards workshops:
- therapeutic education course for people with type II diabetes
- workshops on the themes of food, physical activity and oral-dental issues

---> or towards the structures of external partners.

The check-up is then sent to the GP. “In addition to the guidelines, we conduct motivational meetings to encourage the person to commit to an attainable objective. Rather than apportioning blame, it is more a question of arouing the desire to take a step forward in adopting behaviour that is more beneficial for one’s health” explained Dr Dominique Bonte.

As a partner that is recognised by the regional stakeholders

The general Council of the Nord region passed a three-yearly agreement with the CPES in 2014 to provide paraclinical and biological support in monitoring some of the beneficiaries who were taken into the health prevention departments. These initiatives, called “health meetings” were used to reach out, in 2015, to 195 people who had become isolated from the health care system.

The CPES is recognised as a major operator by the regional health authority. In particular, it takes action on a daily basis in preventing cardiovascular problems through improved diet and physical activity. These initiatives are aimed more particularly at vulnerable people. In 2015, 1206 people were able to benefit from medical-sports checkups, dietary workshops or courses or to re-adapt exercise regimes.

The CPES also supports businesses in defining and setting up their health prevention projects: evaluation, expertise and/or bespoke health workshops…

Finally, the center trains healthcare professionals and those involved in social issues. More than 240 people attended courses or were given support for the project in 2015 on a variety of topics including the approach to health among vulnerable populations and the approach to addictive behaviour (smoking, cannabis, etc.).

Through the medical advice given to travellers and vaccination

The international vaccination center of Institut Pasteur de Lille, located within CPES, is approved by the World Health Organisation (WHO), and delivers over 40,000 vaccines a year.

It is the largest international vaccination center north of Paris.

The service is open to the public for compulsory or recommended vaccines for travellers and also for tropical medicine consultation (before and after a trip).

Institut Pasteur de Lille is also a leading antirabies center for the Nord-Pas-de-Calais region.

Then, the Institut Pasteur of Lille organises on-site vaccination campaigns against flu, upon request from companies and/or local authorities in the Lille and Paris regions every year between October & December.
Metis, world tour of sanitary recommendations to travellers

METIS is an online tool that lists the practical recommendations in terms of preventive measures, treatments and (or) vaccines to be taken, according to the destination and conditions of the trip. This website, which was created in July 2015, is currently the only tool providing information that complies exactly with the recommendations of the HCSP (French public health authority).

The doctors and IT engineers of the institute have entered 100,000 GPS coordinates that can be used to define more than 200 different high-risk zones.

Seven diseases, considered to be major diseases, have been studied in detail: malaria, yellow fever, meningitis, Japanese encephalitis, tickborne encephalitis, chikungunya, and, since 2016, the Zika virus. The experts of Institut Pasteur de Lille are permanently monitoring the news in terms of health and update this entirely free website on a daily basis.

Dynamic maps

In order to find out all the recommendations associated with the country visited or continent transited, the traveller/web user simply specifies his destination (country, town, address, the name of a hotel or tourist site) and selects a disease from the seven recorded diseases, which are of a major interest. Using the Google Maps search engine, the recommendations are displayed in a few seconds. For those planning to make an itinerant trip there is a cursor that gives the option to navigate freely across the map with a system that memorises the different elements of data gathered.

In the end, for each place visited on the map, the web user can print out a summary that lists all the potential health issues, in addition to the eight main diseases for which there is an in-depth analysis.

Direct link: http://www.pasteur-lille.fr/vaccinations-voyages

Medical Biology laboratory

Directed by Dr François Regnault
Institut Pasteur de Lille

The laboratory has been carrying out all types of Medical biology examinations health check-ups proposed by CPES (Health prevention and education center) as well as the biological monitoring of clinical studies delivered by various research and clinical studies centers (Scientific and logistics advice, selection and management of the analytical platform, development and validation of analysing methods, preparation of sampling kits, storage of samples...).
The nutrition department conducts clinical research projects in nutrition and study-initiatives in public health, trains professionals and conducts specialist assignments and advisory assignments in all the dietary domains provided to businesses and institutions.

Created in 1982 upon the initiative of Dr Jean-Michel Lecerf, an endocrinologist and nutritionist doctor, the center was from the onset oriented towards health education and the training of health & social professionals. For about twenty years, it has also been offering training and expertise to companies in the agro-food and catering industries. In 2012, they opened Nutrinvest, a clinical research center in nutrition.

Thanks to a multi-disciplinary team (doctor, doctors of education, engineers in nutrition and dieticians), the nutrition department is capable of assisting and advising all those involved in the food chain: from food sector industrialists to authorities and health professionals, as well as collective catering professionals.

This pluralism makes it possible to have a cross-sector perspective and analysis of nutrition and guarantees its independence.

They are also at the origin of the creation of the alternative menu to the consumption of meat for collective catering, the development with the Lactalis group of the Primevère margarine, the first French margarine free of trans fatty acids and enhanced in omega 3, and the designing of Nutrissimo Junior®, an educational board game.

The Nutrition department works actively with recognised national authorities such as Anses, HAS, AFNOR, ANIA. It is an important player in the Nutrition-Health-Longevity competitiveness cluster of the Hauts de France.

The team of the public health and training unit contributes to the regional implementation of public policies linked to diet. Working in collaboration with many recognised authorities of the public sector (ARS, regional council, DRAAF) or the private sector (insurance, mutual insurance companies, foundations), it implements projects and creates teaching tools in the area of food education for every category of the population.

The Public Health division has also been offering training sessions on the following themes: food education and dietary balance, diet for children and seniors, health and diet, food labelling, sustainable nutrition for collective catering, etc. Events on very targeted themes (Autism, Alzheimer…) and conferences (Entretiens de nutrition, nutrition workshops…) are also organised every year. Institut Pasteur of Lille’s Entretiens de nutrition will celebrate their 18th anniversary in 2016.
Expert assessments and clinical studies

The clinical studies and expertise unit conducts comprehensive “turnkey” clinical studies in nutrition by evaluating food or food supplements on healthy volunteers in its Nutrinvest Nutrition clinical research center. It also offers support to the businesses of the food industry, mass distribution sector and the catering sector in creating and developing products. Its offer relies on:

- advice and assistance in nutritional and dietetics regulations;
- Study of the impact of processes on nutritional quality;
- writing of scientific papers for publication, desktop research reports and applications for health claim;
- the completion of nutritional audits of existing products and the assistance given in formulating products or creating nutritional labelling.

Perspective

The Nutrition Department conducted a study that showed that an improvement in the food offered (texture and composition) at the evening meals in EPHAD retirement homes increased the dietary intake and physical strength of elderly people.

The Nutrition Department conducted an initiative that, thanks to the measurement of physical activity using an accelerometer, showed that an amusing games kit could increase physical activity in children between the age of 9 and 10 years old.

Institut Pasteur de Lille’s nutrition workshops will address the following topic in 2015:

- Inactivity – the plague of the 21st-century

Institut Pasteur de Lille’s nutrition meetings will address the following topic in 2015:

- microbiota
- pre- and probiotics
IV - DISSEMINATION OF KNOWLEDGE

- Scientific mediation and health information
- The teaching
Dissemination of knowledge

The dissemination of knowledge, including to enable individuals to better care for their health, has been an integral part of the missions of Institut Pasteur de Lille. This dissemination is illustrated through a series of general public conferences, participating in a number of national or international events, opening a museum which tells the story of Pasteur, Calmette and Guérin in Lille, scientific workshops for the younger public.

**5-7 conferences draw crowds**

For the past ten years, one Tuesday a month from 5 to 7, researchers from the Institut and their partners organise a general public health conference, the *5 to 7 conference*, giving each time an update in a specific field about research, prevention and treatments. These free conferences have been getting so popular that the Institut has had to organise preregistration for the past three years. These conferences can be consulted online at: [www.pasteur-lille.fr](http://www.pasteur-lille.fr)

**A museum at the core of the history of scientific discoveries**

Set in the old tuberculosis prophylaxis center created by Albert Calmette, the *Institut Pasteur de Lille’s Museum* relates the lives and works of Louis Pasteur, Albert Calmette & Camille Guérin, the discoverers of the BCG vaccine. With 3,000 visitors a year, the museum is very popular with schoolchildren coming as part of group visits and guided tours.

**Not-to-be-missed events**

Opening of the laboratories for *science day* in October and *Europe day* in May, activities and exhibitions at the *Museum for the European Heritage Days* in September... Institut Pasteur of Lille never misses an opportunity to make Science accessible to all.
Kid Campus: A day in the life of a researcher

Every year, in January and February, Institut Pasteur de Lille takes a gulp from the Fountain of Youth by devoting an afternoon to ten-year-old schoolchildren and inviting them to put themselves in the shoes of researchers. The “Kid Campus” workshops were designed to be both educational and fun, with a pragmatic approach of research, to give children a new outlook on science… and why not stimulate new career interests.

The Kid Campus workshops are in 4 parts:

1. A visit of the Institut Pasteur de Lille Museum…
   Helps children understand the history, the values of the Institut and discover the basics of microbiology.

2. A « hygiene and germs » demonstration…
   Reviews the basic rules of hygiene and let children observe through a microscope moulds, bacteria, or yeast, all these microorganisms they unknowingly mingle with every day.

3. Manipulation in a science classroom
   After donning the researchers’ uniform, coat and gloves, the youngsters complete a task at a bench.

4. Free discussion between the researcher and the class
   This is the opportunity for children to know everything about the job of researcher.

Every year, a dozen teams devote six weeks to welcoming over 400 pupils around the following themes: Malaria, vaccination, prescription drugs, fat, viruses, mucosa, DNA (Of the onion and the banana), cells, bacterial pathogens, nutrition and diabetes.

When our researchers inspire the summer bestseller: «Pandemia» by Franck Thilliez

«More than just an inspiration, the researchers of Institut Pasteur de Lille have actually given impetus to this story. I always seek to interview specialists for my novels, however, in this case it was more than a simple documentary interview. There was genuine enthusiasm on both sides,» explained Franck Thilliez.

The adventure began in 2013, when the novelist agreed to have his picture taken for the book called “La passion d’épauler” (the love of supporting others). «Marie-José Hermant, who came to interview me, asked me to visit the institute. At the time, I was finishing writing Angor and I had already begun thinking about my next novel. For a long time, I had thought about writing a story revolving around germs. I had never had the opportunity to study the subject and so this was a fantastic opportunity to dive into the birthplace of microbiology.»

Bioterrorism, plague, flu, etc. Like a policeman hunting murderer, the novelist became fascinated about the work of these scientists who research viruses. Six months of documentation, six months of discussions with his “new friends” of the institute. Franck Thilliez even read the works of a certain Patrick Berche before discovering that he was the new director of Institut Pasteur de Lille.

Pandemia, Fleuve noir, 648 p. 21,90 €.
Institut Pasteur de Lille offers professional training in three main areas in which its expertise is unanimously recognised: scientific techniques and biological safety, nutrition and addictive behaviour.

**Scientific and biological safety courses** cover a wide spectrum of skills that are necessary to technical and scientific personnel: virology, parasitology, proteomics, bioinformatics, genomics, imaging, cellular biology, mutagenesis, genotoxicity, statistics, animal manipulation, regulations, biological safety et OHS.

The **nutrition Department** offers training sessions adapted to various professionals likely to deal with the issue of eating habits with certain audiences: health professionals (doctors, nurses, dieticians), medical and welfare personnel, catering or food industry personnel, without forgetting certain key events: "Entretiens de nutrition" more specifically dedicated to doctors and dieticians and "Ateliers de nutrition" for professionals in the social sector.

Finally, the **doctors specialising in addictions from the Center for prevention and health education** have been organising training sessions adapted to professionals working with tobacco and/or cannabis users.

Institut Pasteur de Lille has joined forces with the IUT A of Lille in an organisational management sandwich course that leads to a **diploma with a specialisation in food safety and quality ("SQAI")**. Institut Pasteur de Lille and the IUTA brought together their skills and specific qualities to form a level II course with the aim of getting people back into work. The Quality, Hygiene, Safety, Health, Environment sandwich course has been training the professionals of the food sector and in treatment practices since 2000.

The education department implemented an **e-learning platform** in 2013 for courses combined with self-training modules.

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**Head of training: Dr Marie-José Truong**

Institut Pasteur de Lille

Since its foundation, initiation and continuous training have been an integral part of the missions of Institut Pasteur de Lille. Every year, over 1000 people attend professional education sessions and over 130 young scientists are welcomed by the laboratories of Institut Pasteur de Lille to develop their research projects.
V - Key figures

- Headcount
- Employment/Resources
- and more...
- The teams of the Transdisciplinary Research Center on Longevity, in 2015
Key figures about Institut Pasteur de Lille...

Headcount

811 EMPLOYEES ON THE CAMPUS INCLUDING:

- 326 INSTITUT PASTEUR DE LILLE EMPLOYEES
  - INCLUDING 233 WOMEN
  - INCLUDING 93 MEN

AND 420 EMPLOYEES FROM OTHER RESEARCH (INSERM, CNRS, UNIVERSITIES...)

AND 65 TRAINEES STAYING MORE THAN 2 MONTHS

23 NATIONALITIES ON CAMPUS
Employment/Resources

Institut Pasteur de Lille finances the completion of its missions, which require elements from various private as well as public sources.

In 2015, Institut Pasteur de Lille devoted €24.7m to its main missions, i.e. research (€14.1m), prevention and information to the public (€8.0m).

The €14.1m devoted to research can be broken down as follows:

- €0.9m for research into cancer
- €0.8m for the discovery of medicines
- €1.4m for research into cardiovascular and metabolic diseases
- €3.1m for cardiovascular and neurodegenerative diseases
- €0.5m for genetic and metabolic diseases
- €4.4m for inflammatory, infectious and parasitic diseases
- €3.1m for the running of technological platforms
- €0.3m for parasitic antigens

The social missions of Institut Pasteur de Lille have been made possible thanks to:

- €2.9m from public donations
- €3.7m of private funds
- €6.0m of subsidies
- €8.3m of income from services directly linked to the social missions (excluding rental income)
- €4.5m collected from the reserves of the foundation
And more...

- **50,000 m² of Laboratories**
- **10 Technology Platforms**
- **342 Scientific Papers in 2015**
- **Over 40,000 Vaccinations Delivered**
- **12,985 Health Checkups**
- **7,700 Hours of Training Given on the Campus** (Public Health, Nutrition, Scientific Training, etc.)
The teams of Transdisciplinary Research Center on Longevity of the Institut Pasteur de Lille, in 2015

6 MIXED RESEARCH UNITS

- U1167 Inserm - Institut Pasteur de Lille - Université de Lille - Pr Philippe Amouyel
- U1019 Inserm - UMR 8204 CNRS - Institut Pasteur de Lille - Université de Lille - Dr Camille Locht
- U1011 Inserm - Institut Pasteur de Lille - Université de Lille - Pr Baert Staels
- UMR 8199 CNRS - Institut Pasteur de Lille - Université de Lille - Pr Philippe Froguel
- UMR 8161 CNRS - Institut Pasteur de Lille - Université de Lille - Dr Yvan de Launoit
- U1177 Inserm - Institut Pasteur de Lille - Université de Lille - Pr Benoît Deprez

LABORATORIES AND EQUIPMENTS OF EXCELLENCE

- 3 LabEx : DISTALZ - EGID - ParaFrap
- 2 EquipEx : LIGAN - ImaginEx BioMed

2 HEALTH PREVENTION SERVICES

- The nutrition department : Dr Jean-Michel Lecerf
- The prevention and health education center : Dr Dominique Bonte

2 APPLIED RESEARCH UNITS

- Genetic toxicology laboratory : Dr Fabrice Nesslany
- Microbiological safety unit : Dr Michèle Vialette