



Science providing **health** for all



PRIVATE FOUNDATION RECOGNISED AS BEING OF PUBLIC UTILITY SINCE 1898

Louis Pasteur and the regional industrial world

In 1854, Louis Pasteur was appointed Dean of the Faculty of Science of Lille which had just been created. He would remain in Lille until 1857.

Louis Pasteur's time in Lille would constitute a crucial period in his career, with his work on fermentation in relation with the local industrial world. He would go on studying abnormalities observed during alcoholic fermentation, and would demonstrate that the transformation of sugar into alcohol was due to the presence of a micro-organism. This marked the beginning of microbiology. After his publication on lactic fermentation at the Society of Science, Agriculture and Arts of Lille, Pasteur was appointed Administrator and Director of Scientific Studies at the Ecole Normale in Paris and left Lille in October 1857.

In the late 19th century, infectious diseases were raging worldwide in cities, with working people piling up in appalling hygiene conditions. The Nord-Pas de Calais region was no exception. In 1884, a diphtheria epidemic was raging in Lille. A delegation from the municipality travelled to Paris to meet with Louis Pasteur and discuss the way in which the new serum developed by Emile Roux could be implemented. Pasteur then recommended creating an institute for the preparation of serums and the study of infectious diseases and appointed Albert Calmette as director. The foundation stone of the institute to which Pasteur accepted to give his name was laid in 1895. The Institut Pasteur de Lille was inaugurated in 1899.

As soon as it was created, in the vicinity of a number of medical research axes, the Institut Pasteur played a significant role in collaboration with the regional industrial world in the fields of distillery, brewery and the sugar industry.

Today the Institut Pasteur de Lille includes 800 employees, dedicated to improving health every day through research and prevention. It also hosts a dozen start-up companies in research and innovation.



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Scientific news 2022

Jan.

Discovery of a natural molecule able to inactivate numerous viruses including coronaviruses Antimicrob Agents Chemother

Inserm U1019 - CNRS UMR 9017 - Institut Pasteur de Lille

New clinical trial phase for the intranasal Pertussis vaccine

Inserm U1019 - CNRS UMR 9017 Institut Pasteur de Lille - University of Lille

Dr Joel Haas awarded an ERC starting grant

Inserm U1011 - University of Lille - Institut Pasteur de Lille -Lille University Hospital - EGID

Antibiotic resistance: Identification of a new class of molecules able to potentiate the effect of antibiotics Nature Communications

Inserm U1019 - CNRS UMR9017 - University of Lille M2SV - Inserm U1177 - Institut Pasteur de Lille University of Lille

Discovery of pharmacological activators of the insuline-degrading enzyme Eur. J. Med. Chem.

Inserm U1117 - University of Lille - Institut Pasteur de Lille

Feb.

An innovative strategy to identify new genetic causes of obesity in man

Diabetes UMR1283 - Inserm -8199 CNRS - EGID University of Lille - Institut Pasteur de Lille - Lille University Hospital

Prof. François Pattou, winner at the 2022 Etoiles nordistes

A collaboration between Lille University Hospital – Inserm U1190 University of Lille – Institut Pasteur de Lille – EGID

March

Amélie Bonnefond, winner of an ERC Consolidator Grant

Team 1 – CNRS UMR 1283/8199 – University of Lille – Lille University Hospital – Institut Pasteur de Lille

Metabolic surgery: a new step towards precision medicine

Lancet Diabetes Endocrinol. U1190 "Translational research on diabetes" - Lille University Hospital - Inserm - University of Lille - Institut Pasteur de Lille

April

Alzheimer's disease: 75 genetic risk factors identified for a better understanding of the medical condition Nature Genetics

U1167 - Team 3 - Inserm - University of Lille - Lille University Hospital - Institut Pasteur de Lille

Targeting prematurely ageing cells due to radiotherapy to prevent the emergence of secondary cancer eLife

University of Lille - CNRS - Institut Pasteur de Lille - COL

The first Galapagos Award attributed for the discovery of a new anti-tuberculosis agent

U1019 - UMR9017 - "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille – Lille University Hospital U1177 "Drugs and molecules for living systems" University of Lille - Inserm - Institut Pasteur de Lille

New mutations of the MET receptor discovered in patients with hereditary kidney cancer

Hum Mutat.

UMR9020 – UMR1277 - Heterogeneity, plasticity and resistance to cancer therapy (Canther) - University of Lille CNRS - Inserm - Lille University Hospital - IRCL CLCC Lille - COL - Institut Pasteur de Lille

Маү

Identification of a new molecule capable of potentiating the effect of tuberculosis treatment

Science Translational Medicine

U1019 - UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille – Lille University Hospital U1177 "Drugs and molecules for living systems" University of Lille - Inserm - Institut Pasteur de Lille

Jul.

Philip Supply, a researcher at the Institut Pasteur de Lille, awarded the Gardner Middlebrook Lifetime Achievement Award

U1019 - UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille - Institut Pasteur de Lille Lille University Hospital

New molecular approach to diagnose and monitor leprosy The Lancet

U1019 - UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille - Institut Pasteur de Lille Lille University Hospital

Identification of a new mechanism potentially involved in cardiovascular diseases in obese patients

Hepatology

U1011 "Nuclear receptors, metabolic and cardiovascular diseases" Inserm - University of Lille -Institut Pasteur de Lille Lille University Hospital

COVID-19 and obesity: intestinal microbiota as an indicator of disease severity Gut Microbes

U1019 - UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille - Institut Pasteur de Lille Lille University Hospital

13 projects selected as part of the 2022 Generic Call for projects (AAPG 2022) by the National Research Agency (ANR)

Mapping and artificial intelligence for a better understanding and prediction of metabolic surgery results U1190 "Translational research on diabetes" Inserm - University of Lille - Lille University Hospital

August

Towards a better understanding of antidiabetic drug efficiency Cell Report

U1167 "Risk factors and molecular determinants of diseases linked to ageing" Inserm - University of Lille - Lille University Hospital Institut Pasteur de Lille

Discovery of new anti-malaria treatments **Open Biology**

U1019-UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille - Lille University Hospital Institut Pasteur de Lille

Sept.

Discovery of selective inhibitors of the ERAP2 protein, an enzyme whose deregulation may lead to cancer or autoimmune diseases Angew Chem Int Ed Engl.

U1177 "Drugs and molecules for living systems" Inserm University of Lille - Institut Pasteur de Lille

Oct.

Discovery of a major hepatic fibrosis regulator

Nat Commun.

U1011 "Nuclear receptors, metabolic and cardiovascular diseases" - Inserm - CNRS University of Lille Lille University Hospital - Institut Pasteur de Lille

Nov.

Discovery of a therapeutic approach to reduce the side effects of chemotherapy Journal of Clinical Investigation

UMR9020 CNRS - U1277 Inserm "Heterogeneity, plasticity and resistance to cancer therapy (Canther)" University of Lille - Lille University Hospital - Inserm - CNRS Institut Pasteur de Lille - CLCC Lille - COL

Discovery of new genes for which certain rare mutations increase the risk of developing Alzheimer's disease **Nature Genetics**

U1167 - Team 3 - Inserm - University of Lille Lille University Hospital - Institut Pasteur de Lille

A new screening tool for anti-SARS-CoV-2 drugs

Front Microbiol.

U1019-UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille - Lille University Hospital Institut Pasteur de Lille

Dec.

Identification and characterisation of Hepatitis E virus manufacturing facilities Cell Mol Life Sci.

U1019-UMR9017 "Lille Infection and Immunity Centre" Inserm - CNRS - University of Lille - Lille University Hospital Institut Pasteur de Lille

Points of view Excellence, spirit of Pasteur and project cross-functionality

Xavier Nassif, Managing Director of the Institut Pasteur de Lille, and Didier Bonneau, Deputy Managing Director, analyse the year's highlights. With scientific discoveries, expertise consolidation, innovation in terms of prevention and the ongoing transformation of the Foundation, 2022 was a productive year.

What is your outlook on 2022? > Prof. Xavier Nassif

In terms of research, what stands out is the success of the intranasal Pertussis vaccine phase 2 trial, which was conducted by an international research team led by Doctor Camille Locht, director of research Inserm. The Institut Pasteur de Lille, whose aura is measured by its top-level research and international attractiveness, is extremely proud of this success. I would also like to applaud the work conducted jointly by the teams of Professor Philippe Froguel, director of unit UMR8199, and Doctor Jean-Michel Lecerf, medical director at the Centre Prévention Santé Longévité (CPSL - Prevention, Health and Longevity Centre), as part of the PrevenDIAB research on diabetes. Thanks to their work, we have a better understanding of the biological, clinical and environmental causes of prediabetes, especially among precarious people. I am glad we were able to successfully create a bridge between research and prevention. As for the CPSL, 2022 was marked by the ongoing development of the territorial grid, as well as the deployment of an innovative assessment approach of preventive devices to help people, businesses and institutional players. These successes are working towards the CPSL's ambition to be the reference prevention centre in France.

Didier Bonneau

As for me, I would say 2022 was a disrupted year in terms of financial balance, with the war in Ukraine generating and exacerbating a double economic and energy crisis. However, the year has also marked a turning point for the IPL: enhancing the essentials of financial balance, i.e. formalising and deploying the Foundation project, developing the Campus Lille real estate project and enhancing human resources in charge of developments, in order to look to the future with confidence.

The IPL labelling process for the 2026 - 2031 cγcle was launched in 2022. What is its goal?

› Prof. Xavier Nassif

This label is to be granted to research teams based on scientific assessment criteria. It shall be used to contribute to the excellence of the "Institut Pasteur de Lille" brand. This labelling is essential today to assert our specificity and attractiveness, and shall be carried out by a universally recognised external scientific council. It will be chaired by Philippe Sansonetti, doctor and microbiologist, professor at the Collège de France and member of the most prestigious academies in the world. His team will include members of the French and European scientific community. Concomitantly with this approach, I have also recommended creating "Pasteur groups" within the labelled teams in partnership with the Inserm, the University of Lille, the CNRS and Lille University Hospital. These will help junior researchers in their choice to become more autonomous and prosper within our institution. This will help us in our ambition to recruit the best individuals to enhance our already excellent fundamental research, providing health for all.

Are the Foundation's strategic ambitions still in line with its economic goals?

Didier Bonneau

Absolutely! We aim to reach financial balance by 2026 by consolidating operations via their outreach and by deploying the real estate road map. We know the transformation must be achieved in order to confirm the stability of the Foundation. Our strategy remains identical: preparing the future by increasing the Foundation's resources to enhance support towards research. We have thus formalised the collection strategy with individuals, through a diversity of channels: implementation of a specific channel for "large donors", enhancement of targeted patronage and consolidation of bequests.



Prof. Xavier Nassif and Didier Bonneau

How does the IPL establish its position as a major player on the territory?

› Prof. Xavier Nassif

The Institut Pasteur de Lille is a major player on the territory thanks to its public health mission centred around its prevention centre: every year, 15,000 people go for a health check-up at the CPSL, a significant part of the Hauts-de-France territory. With its top-level research, the IPL is a regional pride. In fact, accelerating the promotion of research is a major concern for us. That is why in 2022, we signed a framework agreement with Inserm Transfert, a private subsidiary of the Inserm specialised in technology transfer. I am excited about the partnership, which will help support our researchers in the promotion of their work. Finally, with a strong institutional presence with our partners, notably the University of Lille as part of the new Etablissement Public Expérimental (EPE or Experimental Public Establishment), the Institut Pasteur de Lille has shown it is, more than ever, a full-blown player on the territory.

What will be the highlights of 2023? • Didier Bonneau

There are many projects to come, in the continuity of 2022: deploying the Foundation project, accompanying teams as part of IPL labelling, implementing health checkups with the Artois population, deploying reference prevention programmes, reinforcing expertise business with our economic partners, proceeding with the real estate road map, implementing the development plan for the 2023-2026 collection, the energy sobriety plan and the IT regulatory compliance programme. If I had to sum up our conducting line in three words, these would be: excellence, spirit of Pasteur and project crossfunctionality.

A committed plaγer, providing health for all



Excelling at research to fight diseases and discovering the treatments of tomorrow

Cancer, diabetes, heart failure, respiratory diseases, infectious diseases, Alzheimer's disease, fighting antibiotic resistance, discovering new drugs: for over 120 years, the Institut Pasteur de Lille has been carrying out works to advance science and human health. Researchers conduct top-level research, guided by Louis Pasteur's motto: "Putting science to work for health".

Our strategic lines for research

Understanding diseases to fight them better Slowing down their growth

Creating the treatments of tomorrow

Our resources on the Pasteur Campus in Lille



Cardiovascular and neurodegenerative diseases

U1167 Inserm Prof. Philippe Amouyel



MANAGEMENT OF INFARCTION IN WOMEN

There has been progress but we can do better!

Cardiovascular diseases are the leading cause of death in women: nearly one out of three women die from a cardiovascular disease every year. A study of acute coronary syndrome (ACS) in men and women aged 35-74 having been hospitalised for an incident event for 12 months in 2006 or 6 months in 2016, evidenced the following: in 2006, women were older and had more atypical symptoms than men, while these differences were no longer detected in 2016. The reason: in 10 years, medical care improved in men and women alike. However, revascularisation treatments, prescriptions of antiplatelet drugs, statins and functional rehabilitation were still less frequently given to women than men in 2016, with all other factors being equal.

people suffer from

3 rd

cause of death in men, 2nd in women behind cancer and mγocardial infarction people suffer from a stroke everγ γear. Over 110,000 are hospitalised and 30,000 die

500 к

A link with inflammation?

Air pollution is responsible for 5.4% of deaths worldwide. The ELISABET survey, which was conducted between 2011 and 2013 in Lille and Dunkirk on a wide population sample, suggests a role of inflammation in the effects of air pollution on health. Its goal: searching for associations between shortterm and residential exposure to air pollution and a number of inflammatory biomarker rates. Observation: low-grade chronic inflammation (persistent and low-level, such as in a number of diseases including diabetes) may be one of the underlying mechanisms explaining the effects of air pollution on health.

French people live with the after-effects of cardiovascular and neurodegenerative diseases.

Highlights

THEY ARE THE INSTITUT PASTEUR DE LILLE

Marcos Costa Doctor in neurosciences

Specialising in induced pluripotent stem cells (iPSC), Dr Marcos Costa was recruited by the Inserm in 2022 to integrate the team of Dr Jean-Charles Lambert within the unit of Prof. Philippe Amouyel. The team is noted for having identified the majority of genes implicated in the occurrence of Alzheimer's disease. Today it is looking at understanding how these genes are implicated in the development of the physiopathological process, in order to come up with new therapeutic and preventive approaches.

The 43-year old Brazilian researcher was trained at the University of Rio de Janeiro. After leaving for Munich for a post-doctorate, he returned to his home country in 2009, in the city of Natal, where he became a neuroscience professor at the Brain Institute. He came to France ten years later with his own funds, after having been recruited by the Institut Pasteur de Lille as part of the CPER CTRL programme - Emerging team.

Dr Marcos Costa, at the head of new research techniques, took part in the design of a new 3D brain organoid model. This "mini-brain", which is a million times smaller than a



human brain, can be used as living material to mimic the disease, have a better understanding of the mechanisms and assess the efficiency of new treatments. "These 3D models will also be used to mimic interactions between immune cells and neuronal cells, to understand the neuro-inflammation mechanism and its role in the development of Alzheimer's disease and other infectious diseases affecting the brain", he declared.

Since childhood, Marcos Costa has always loved studying, observing, understanding and explaining things. "I have always been attracted to physics, to medicine, to the universe and the human being. I opted for the second, but remain an astrophysician at heart." »

ALZHEIMER'S DISEASE

75 new predisposition genes identified

Identifying genetic risk factors for Alzheimer's disease is a vital research challenge to have a better understanding of the mechanisms behind the occurrence of the disease. As part of the EADB (European Alzheimer's disease DNA Biobank) project involving 18 European countries and coordinated by our unit and by Dr Jean-Charles Lambert, researchers have identified 75 genome regions associated with Alzheimer's disease. Forty-two of these are new and had never been involved in the disease yet. These results, published in Nature Genetics, open the door to new treatment and diagnosis approaches.

TYPE 2 DIABETES

Towards more effective antidiabetic drugs

Type 2 diabetes affects over 400 million people worldwide. It is defined by an excessive blood sugar level due to insufficient insulin production, the hormone regulating our glycaemia level. A number of medical treatments use molecules targeting the route of the "glucagon-like peptide-1" receptor (GLP-1R), intestinal hormones involved in the regulation of blood sugar level, by acting on the pancreas, stomach and brain (Ozympic is an example of this type of medicine, which is currently massively recommended on social media to lose weight before summer). Within our unit, a new team, conducted by Dr Jean-Sébastien Annicotte, has discovered the key role of a protein called E2F1, which regulates the expression of the gene coding the GLP-1R receptors. Thus when the action of E2F1 is inhibited, the drug targeting the route of the GLP-1R receptor is no longer fixed to the cell: it is rendered ineffective and can no longer regulate insulin production. These works may lead to new therapeutic approaches, notably for patients who are not responding well to current treatments.

Cancer

UMR9020 CNRS UMR1277 Inserm Dr Isabelle Van Seuningen



CHEMOTHERAPY

A new drug with reduced side effects

Cisplatin is a reference chemotherapy used to treat tumours in a large number of cancers. However, it comes with detrimental neuropathic and nephrotoxic side effects which affect about a third of patients. Prof. Christelle Cauffiez's team (SenFib), in collaboration with Dr David Blum's team (Lille Neuroscience & Cognition) and researchers at the State University of Michigan (United States) have identified a new molecule, istradefylline, which may reduce the adverse effects of chemotherapy and increase its antitumour properties. The efficacy of the drug, which is already used in Parkinson's disease, will need to be confirmed by a clinical trial. The study was part of a publication in The Journal of Clinical Investigation.

NON-SMALL CELL LUNG CANCER

Discovery of an effective marker for patient treatment

Non-small cell lung cancer (NSCLC) is the most common form of lung cancer. A study conducted by the team of Dr David Tulasne (Target), in collaboration with the London Barts Cancer Institute, the pneumology department and the Biology Pathology Centre of Lille University Hospital, shows the muted form of the Met receptor on exon 14, responsible for these cancers, remains receptive to targeted anti-Met therapies but that it requires the presence and activation of its HGF ligand. This study shifts the paradigm saying a receptor's active form acts independently from its ligand. The HGF tumor expression could thus be used as a biomarker to stratify patients who can receive targeted therapies against the Met receptor. The study was published in Molecular Oncology.



RADIOTHERAPY

How can we reduce the risk of induced secondary cancer?

The ionising radiation delivered during radiotherapy operates by destroying the cancerous cells by causing DNA breaks. But these can sometimes mutate within non-cancerous cells which have survived radiation, and in the long run may induce a second cancer, different from a relapse of the cancer treated initially. Prof. Corinne Abbadie's team (SenFib), in collaboration with the Centre Oscar Lambret, has studied the cellular and molecular mechanisms leading to the formation of secondary cancers. Result: non-cancerous cells submitted to very low doses on the border of an irradiated territory develop DNA single-strand breaks and are subject to premature ageing (senescence mechanism), and some, very rarely, progress toward a cancerous state. Therefore, after radiotherapy, the use of senolytics, which are able to destroy ageing cells, may reduce the risk of developing secondary cancer. The study was part of a publication in eLife.

ONCOLille

Canther teams meet on the site of Lille University Hospital

The mixed research unit Canther (Cancer Heterogeneity, Plasticity and Resistance to therapies) is part of ONCOLille, Lille's Interdisciplinary cancer research institute created in December 2020, headed by Dr Isabelle Van Seuningen. In order to facilitate exchanges with other teams working on cancer, it was only natural for both teams, SenFib and Target, to integrate the institute located on Lille's university-hospital campus. This has now been effective since August 2022!

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new cases of cancer detected every day in France 3.8^M

million people in France



cause of death in men, 2nd in women

Cardio-metabolic diseases

U1011 Inserm Prof. Bart Staels



Dr Hélène Duez

METABOLISM

Our biological rhythms influence our health

There is a verified link between biological rhythm dysfunction due to shift work, frequent jet lag and nocturnal exposure to light, and a number of metabolic diseases. Work from Hélène Duez's team has shown that a disrupted biological clock increased the risk of developing metabolic diseases (obesity, type 2 diabetes, fatty liver disease), inflammatory diseases and cardiovascular diseases (atherosclerosis, myocardial infarction). It could be beneficial to reset our biological clocks to treat these conditions. Simultaneously, researchers are trying to understand how our biological clock controls our metabolism and inflammation, found in diabetes and cardiovascular diseases, and vice versa. The research may open the door to new therapeutic approaches.

LIVER DISEASES

Closely studied epigenetic mechanisms

While genetics refers to the study of genes, epigenetics studies a "layer" of additional information which defines how these genes are used or not by a cell. Jérôme Eeckhoute's team has studied the link between these epigenetic mechanisms and the development of liver diseases and a number of cancers. Understanding these molecular mechanisms in order to correct them to revert to a normal expression of genes would lead the way to new treatments.





HEPATIC STEATOSIS

A protein secreted by the liver at the source of cardiovascular diseases?

Nonalcoholic fatty liver disease (NAFLD), the most frequent chronic liver disease, mainly affects overweight people who drink little or no alcohol. It is defined by an abnormal accumulation of fat in the liver. NAFLD is often associated with a deregulation of blood fat levels (triglycerides and cholesterol) and with cardiovascular diseases. Dr Joel Haas's team has identified a protein secreted by the liver, Apolipoprotein F (ApoF), whose expression is halved in obese patients suffering from NAFLD. The study has shown that ApoF reduces circulating triglyceride levels by increasing capture by the liver. Therefore, reduced ApoF levels in obese patients could increase the risk of cardiovascular diseases. This major discovery could help fight the disease.

cardiac Risk The protective role of nuclear receptor REV-ERBα

The number of people suffering from a myocardial infarction and/or having to go through a coronary bypass or any other operation requiring cardioplegia has strongly increased in France: 150,000 people affected every year. Risks associated with these events, whether they are unexpected or programmed, are related to the heart ischaemia-reperfusion, which induces a series of molecular events. It can sometimes lead to cardiac tissue damage. A number of cardio-protection strategies have been tested, with mixed results. In this context, Philippe Lefebvre's team has evidenced that protein REV-ERB α , a vital component in the molecular clock, is a relevant pharmacological target as its pharmacological antagonism protects the heart from damage induced by ischaemia-reperfusion.

of liver cancers are caused

by NAFLD.



suffer from hepatic steatosis in France.

Discovering new drugs

U1177 Inserm Prof. Benoit Déprez



MULTIDRUG-RESISTANT TUBERCULOSIS

A new drug named Alpibectir bγ the WHO

With 1.4 million deaths every year, tuberculosis remains, more than ever, a major public health issue. Alpibectir is to be the name of the drug which should be marketed after the final phase of clinical trials, which began in late December 2022 in South Africa. It was discovered thanks to a successful collaboration between the teams of Prof. Benoit Déprez and Nicolas Willand (U1177) and of Dr Alain Baulard from the Centre d'Infection et d'Immunité de Lille (CIIL), biopharmaceutical company GSK and BioVersys, historical partner of the IPL Centre de Découverte des Médicaments (Drug Discovery Centre).

Thanks to this work, they were awarded the prestigious Galapagos prize in 2022, handed out during the European EFMC symposium.

https://pasteur-lille.fr/2022/04/27/le-premier-prix-galapagos-attribuepour-la-decouverte-dun-nouvel-agent-antituberculeux/

DISTINCTION

Prof. Benoit Déprez elected at the National Academγ of Pharmacy

Benoit Déprez, a pharmacist, doctor in therapeutic chemistry and University professor, was scientific director at the Institut Pasteur de Lille from 2019 to 2022, followed by scientific advisor. He founded and is currently at the head of research unit "Drugs and molecules for living systems" (IPL, Inserm, University of Lille). He also founded and is a scientific advisor at company APTEEUS, winner of the 2017 Concours Mondial d'Innovation (Global Innovation Contest), in the category "individualised medicine". A corresponding member of the National Pharmacy Academy since 2006, he was appointed titular member by presidential decree in June 2022. Such a high distinction shows peer recognition of his expertise in the field of pharmaceutical innovation.



200 ^к

molecules and compounds making up the leading academic chemical library in Europe.

CANCER AND AUTOIMMUNE DISEASES

Discovery of powerful protein ERAP2 inhibitors

Enzyme ERAP2 is a protein involved in the immune response against viruses and cancer. Genetic studies have shown a link betweenthisenzymeandariskofdevelopingautoimmunediseases such as ankylosing spondylitis, birdshot uveitis and psoriasis. This protein is also associated with some cancers. The team of Prof. Rebecca Déprez has discovered powerful, selective ERAP2 inhibitors using an innovative strategy called KTGS (Kinetic Target-Guided Synthesis). It uses the target protein to irreversibly select inhibitors from biocompatible precursor molecules. These works, conducted in collaboration with the NSCRD Demokritos, the University of Athens and the University of Chicago, provide promising perspectives in terms of human health. They were published in Angewandte Chemie.



CORONAVIRUS

The hope of an oral treatment

Work conducted in 2020 by the Covid-19 Task Force has paid off: anti-coronavirus molecules operating more strongly and thus at lower doses were developed in 2022 by Prof. Benoit Déprez's research team. Thanks to these molecules, we have a better understanding of the dynamics of one of the virus's key enzymes as well as how they interact. This work could lead to a patent being issued and to an anti-coronavirus drug being developed.

THEY ARE THE INSTITUT PASTEUR DE LILLE

Nicolas Willand Organic and medicinal chemistry professor

Prof. Nicolas Willand, 47, is a teacher-researcher and leads a group of medicinal chemists within Prof. Benoit Déprez's laboratory. Since 2004, Prof. Benoit Déprez has constituted a team of about thirty high-level researchers on the Pasteur Campus in Lille - chemists, biologists, analysts. Their work leads to discovering, creating and selecting new drugs. They are behind the discovery of a drug candidate to fight multidrug-resistant tuberculosis, among others. "Research has become cross-functional: a researcher can no longer work on their own. Furthermore, the tools used to probe biological systems are more complex and require increasingly specific expertise. New therapeutic approaches can be explored and used thanks to team work, which includes doctors, biologists, crystallographers and chemists", says the researcher.

Nicolas Willand says he became passionate about chemistry although he was initially destined, at 20, for a career as a multiskilled engineer. After going back to school at Lille 2 University, he left the North of



France to go to the Midlands in England, in Coventry where he studied for a Master's degree in medicinal chemistry. He conducted a research project on the chemistry of sugar, at the crossroads between chemistry and biology. "I liked the idea of finding other applications for chemistry, of being able to "play with biology" in a way, by finding practical applications for it", he said.

In 2004, he became a lecturer at the Faculty of Pharmacy (Lille 2 University) and simultaneously began a career as a teacher and researcher in the Inserm team which was created at that time by Benoit Déprez. A professor in organic chemistry since 2013, Nicolas Willand simultaneously conducts research: "I find it exciting to be able to teach, to be in contact with students and to pass on knowledge while contributing to advancing research".

Diabetes

UMR8199 CNRS U1283 Inserm Prof. Philippe Froguel

INTERNATIONAL RECOGNITION

Genomic platform LIGAN receives ISO 15189 accreditation

The LIGAN platform, which is located in the facilities of the European Genomic Institutes for Diabetes (EGID) on the site of Lille University Hospital, is dedicated to next-generation sequencing and cutting-edge genomics for personalised medicine. In September 2022, LIGAN received the Cofrac accreditation in accordance with the ISO 15189 standard, an international standard specifying the applicable requirements in terms of quality and expertise for medical biology laboratories. LIGAN is the first French laboratory to receive the international recognition, allowing it to build partnerships with foreign laboratories.



PREVENTION OF DIABETES AND OBESITY

A unique cooperation between research and prevention

Two large-scale studies were launched in Lille for the prevention of diabetes in precarious individuals and obesity in children, as part of the translational and clinical research project in precision medicine for diabetes (PreciDIAB - see page 33). The latter develops highly original and innovative prevention programmes conducted outside the hospital.

PrevenDIAB with the CPSL

The study is conducted at the health check-up centre (CPSL) at the Institut Pasteur de Lille. It aims to have

a better understanding of the biological, clinical and environmental causes of prediabetes, especially among vulnerable, precarious individuals. 2,200 people will have contributed to the study by the end of 2023.

ELIPSE

This programme aims to promote children well-being by preventing excess weight from settling in and becoming permanent. The study was conducted by PreciDIAB and Lille University Hospital in 2022 with the 800 children in CP classes in Lille and Hellemmes. Result: one third showed an abnormal body weight curve. ELIPSE offers an educational programme to the families of the children concerned, which includes fun workshops on healthy eating, physical activity and wellbeing in order to increase their knowledge, for effective prevention from an early age.

RESEARCH GRANT ERC

Dr Amélie Bonnefond, 2022 winner!

Amélie Bonnefond, research director at the Inserm within unit "Metabolic functional genomics and molecular mechanisms involved in type 2 diabetes and associated diseases", is the 2022 winner of the ERC Consolidator Grant (OpiO). The project deals with the correlation between the consumption of opioids and metabolic disorders. The European Research Council grant recognises scientists for their top-level works. The Lille researcher had already received an ERC Advanced in 2017.





CHILDHOOD OBESITY

PreciDIAB at the heart of European project OBELISK

Prof. Philippe Froguel and Dr Amélie Bonnefond are coleaders on the project (\in 12M) which, from 2023 to 2028, will include 14 research teams in 10 European countries. Its goal: reducing the number of overweight European children and teenagers by 35%. The project will develop obesity prediction tools from birth and will be testing innovative obesity prevention programmes, particularly with teenagers. It will also look into determining the genetic and environmental factors of childhood obesity and will test the performance of new drugs to fight obesity in highly overweight children with genetic abnormalities interfering with their appetite. In 2022, nearly a third of European teenagers were overweight. An alarming finding, especially since childhood obesity has greatly increased over the last years in Europe, notably due to the Covid-19 lockdowns.



diabetics in France.



adults worldwide potentially affected by the disease by 2045.

Infectious and inflammatory diseases

U1019 Inserm UMR9017 CNRS CIIL

Dr Jean Dubuisson

WHOOPING COUGH

A promising intranasal vaccine

Whooping cough is a highly contagious respiratory infectious disease caused by the bacterium *Bordetella pertussis*. It can be severe and fatal, especially in young children. In spite of a wide vaccination coverage, there are frequent whooping cough epidemics, demonstrating the limitations of these vaccines. Dr Camille Locht's team has developed a live intranasal vaccine which mimics the natural infection without causing the symptoms of whooping cough. Phase 1 clinical trials in preclinical models have shown its efficacy. The phase 2 clinical trial conducted in 2022 on some 300 adult volunteers evidenced for the first time the proof of concept in man that a single intranasal administration of the live attenuated vaccine could prevent infection by *B. pertussis*. These promising results were published in The Lancet. They make it possible to continue developing the new-generation vaccine.

10.6 ^M

people developed tuberculosis worldwide in 2021 according to the WHO, i.e. + 4.5% compared to 2020.

66 ~

lives saved between 2000 and 2020 thanks to breakthroughs in research.

1.5 M people die from tuberculosis

every year.

people are infected by

every year.

multidrug-resistant bacteria

10

deaths everγ γear could be caused by antibiotic resistance by 2050.

TUBERCULOSIS AND ANTIBIOTIC RESISTANCE

Increasingly effective pro-antibiotics

In the treatment of tuberculosis, drugs called proantibiotics must necessarily be bio-activated by enzymes of Koch's bacillus, which are responsible for the disease. Mutations inactivating the bioactivation process are behind the pro-antibiotic resistance phenomenon. The team of Professors Déprez and Willand, medical chemists, has developed a compound, called Smart751, used to stimulate a cryptic enzymatic pathway without any mutation leading to ethionamide resistance, an antibiotic prescribed in the treatment of tuberculosis. Phase 2 of the clinical trial, conducted in December 2022 in South Africa, should lead to a drug being marketed under the name of Alpibectir (see page 18).

INTESTINAL INFECTIONS

A 15th research at the CIIL

Dr Alexandre Grassart received financing from ATIP-Avenir to develop a new topic called "Mechanobiology of host-microbe interactions". His team will be studying the way in which the micro-environment and physical forces control host-microbe interactions, with an emphasis on intestinal infections. The highly interdisciplinary research will be combining microbiology, cell biology and bioengineering. After a thesis in cell and molecular biology conducted at the Institut Pasteur de Paris (2006-2010), Alexandre Grassart joined the University of California in Berkeley as a post-doctorate researcher (2010-2014). After 5 years at the Institut Pasteur de Paris, he then set up his research laboratory at the Institut Pasteur de Shanghai (China) as a Professor at the Science Academy of China, before joining the CIIL in 2022.

YOUNG RESEARCHER OF PASTEUR DE LILLE

A dγnamic, human, Campus for a well-built future



In a world dominated by IT and virtual networking, the YPL association (Young researcher of Pasteur de Lille) headed by Layal MASSARA aims at creating a professional and friendly connection between young researchers on the Campus. Actions are implemented both internally and externally, on a scientific and social front. Internally, the association promotes interaction and encourages connections between young researchers through events including after-work meet-ups, breakfast catch-ups and the Mealtech to enhance the scientific connection and help young researchers build their future. Externally, the association promotes contacts with alumni and post-doctoral students, nominates ambassadors to develop an international reputation, open new horizons for potential collaborations, and implement a mentoring system with alumni willing to share their experience and expertise. The association also develops Campus visibility by involving young researchers in scientific popularisation efforts.

Translational research on diabetes

U1190 Inserm Prof. François Pattou

ISLET TRANSPLANTATION

World premier: a hope of treatment for Type 1 diabetes

The "islet of Langerhans" transplant, or cell therapy for diabetes, is used to replace destroyed cells in the pancreas in order to restore a regulated production of insulin. Thanks to this technique, it is possible to normalise the glycaemic control of patients and even discontinue insulin therapy in some cases. Work conducted for the last 15 years by the team of Prof. François Pattou, Marie-Christine Vanthighem and Julie Kerr-Conte led to the first pancreatic cell transplant at Lille University Hospital. Lille University Hospital has thus become the first institution in France to benefit from authorisations to take a donor's pancreas, cultivate the islets of Langerhans in a laboratory, and then transplant them in a recipient patient. This procedure is now reimbursed by Health Insurance, following authorisations issued by the French National Authority for Health (Haute Autorité de Santé) and the ARS (Regional Health Agency). A dozen transplants have already been carried out.



of the population are medically treated for diabetes, i.e. over 3.5 million people.





TYPE 2 DIABETES

Treating patients with metabolic surgery

Obesity surgery involves modifying the anatomy of the digestive system, reducing the amount of food consumed and/ or the assimilation of food by the body. In patients with type 2 diabetes, metabolic surgery also leads to a rapid decrease in blood sugar level. In clinical practice, indications for this effective but invasive approach are still debated for type 2 diabetes. Prof. François Pattou's team, with Prof. Ricardo Cohen and Dr Violetta Raverdy, identified a subgroup of patients associated with the best results after metabolic surgery, both in terms of improving diabetes and renal function. These results, which were validated in Sao Paulo by a team of Brazilian researchers and published in the prestigious journal Lancet Diabetes Endocrinol, have opened the door to precision medicine in metabolic surgery for the first time.



COVID-19

The link between obesity and the risk of Covid-19 complications is confirmed

Just behind age, obesity is considered as the second highest risk factor for developing a serious infection with SARS-CoV-2. The team led by Dr Mikael Chetboun and Prof. Mercè Jourdain was the first to establish a link between obesity and the severity of Covid-19. This study, which appeared in the journal Obesity, was part of a 2020 publication which was among the most cited publications internationally. It revealed that over 47% of infected patients entering a resuscitation unit were obese. In addition, having a BMI over 35 significantly increased the risk of being placed on invasive mechanical ventilation, regardless of age, high blood pressure and diabetes. A multicentre study conducted in 2021 confirmed these results and showed that patients who had obesity surgery before a potential SARS-CoV-2 infection were less severely affected.

over 4.5 M

people in France have diabetes, but around one million are unaware of it.



type 2 diabetics.It is strongly increasing and is the most frequent worldwide.

CPER-CTRL Outcome of the 4th call for projects



On 12 January 2023, the Institut Pasteur de Lille hosted the closing seminar of the CPER-CTRL programme (State-Region Planning Contract – Transdisciplinary Research Centre on Longevity) funded by the State, the Hauts-de-France region, the Métropole Européenne de Lille (MEL) and ERDF funds.

Over 60 researchers, representatives of funders and partner establishments (University of Lille, Inserm, CNRS, Lille University Hospital) gathered to review and reflect on the structure and results of the programme, which

began in 2016. Conference and poster sessions were organised to host discussions and highlight the programme achievements: scientific discoveries, support for scientific platforms and infrastructures, public communications and enhancing the therapeutic innovation ecosystem.

	M TITLE IN FRENCH	TEA	MS
ACRONYM		First name, Surname	Unit
(Epi)genomics of muscle biopsies OBEPI-muscle in insulin resistance associated with obesity	(Epi)genomics of muscle biopsies	Amna Khamis	UMR 8199
	François Pattou	UMR 1190	
Manipulation of t apeline interaction antibacterial immu subject	Manipulation of the Rev-erba/ apeline interaction to restore	François Trottein	CIIL t12
	antibacterial immunity in elderly subjects	Hélène Duez	UMR 1011
Consequences of cerebral inflammation caused by the parasite Toxoplasma gondii on the exacerbation of pathological processes in tauopathies.	Sabrina Marion		
	the exacerbation of pathological processes in tauopathies.	David Blum	UMR-S 1172
NL4TB-2	New generation of leads to combat tuberculosis - 2	Baptiste Villemagne	U1177
		Ruben Hartkoorn	













Globally recognised top-level research





AWARD

Prof. François Pattou, winner at the 2022 Etoiles nordistes

Congratulations to Prof. François Pattou, head of the Translational Research on Diabetes unit at the Institut Pasteur de Lille and head of department at Lille University Hospital, winner at the 2022 Etoiles nordistes by La Voix du Nord in the "Science and research" category.

Congratulations to Dr Philip Supply

director of research CNRS - National Centre for Scientific Research at the Centre for Infection and Immunity of Lille, winner of the Gardner Middlebrook Lifetime Achievement Award.

The prestigious award recognises outstanding contribution in the field of tuberculosis diagnosis and treatment. It has been awarded to a small group of microbiologists including Philip Supply. In close collaboration with company GenoScreen, the researcher developed and perfected the first diagnosis test by DNA sequencing to detect antibiotic resistance of the *Mycobacterium tuberculosis* bacteria. The molecular diagnosis is already used by the WHO in over thirty countries.

Their work has led to the identification of a new antituberculosis agent, BVL-GSK098, targeting a new mechanism called "EthR".

RANKINGS

Research.com

International research network **Research.com** has just published its 2022 global ranking of the "best scientists" and the Institut Pasteur de Lille is particularly well featured this year! Congratulations to Professor Bart Staels (head of unit U1011) #EGID for being ranked first for France in the field of Medicine (177th place in the global ranking)

In medical research, Professor Philippe Froguel (Head of EGID - U1283-UMR8199), is ranked 121st in the global ranking.







Scientific publications

Publications in international journals such as Nature, Nature Genetics, the Lancet, PLoS One, PLoS Medicine, Gut, the New England Journal of Medicine, etc. reflect output excellence. Bibliometrics, which includes a quantitative assessment of impact factors in prestigious journals, reflects the interest of the scientific community in discoveries, which are thus mentioned and cited.

Bibliometrics evaluates research activity by applying statistical methods to scientific publications (bibliography of articles, signatures of articles, keywords and authors, etc.). It measures the scientific output and notoriety of a researcher, laboratory, institution, country or field of research.



Year NB InCites AVERAGE CNCI Top 1% Top 10% 2022 642 2.44 24 106

NB InCites: number of articles found in InCites, a database containing citation-based impact indicators.

Average CNCI: Category Normalised Citation Impact - normalised citation index. It takes into account the year of publication, the disciplinary field and the type of documents. A CNCI of 2 indicates that publications are, on average, twice as cited as the world average.

In 2022:

44 %

overall leadership on publications

40 %

leadership on publications in the most prestigious journals



Our researchers' articles are more cited than the world average. **Congratulations!**

16% in the top 10% of the most cited articles

4% in the top 1% of the most cited articles

Articles are 2.44 x more cited than the world average

Becoming the reference *in terms of health prevention to live better and longer*



LONGEVITY NETWORK The Route to Longevitγ[®] is up-and-running in Toulouse

After materialising in late 2021 with the signing of a letter of intent with the ADIMEP, a preventive medicine association in Toulouse, and with the financial support of LCL, spin-off project Route to Longevity® really began in September 2022 with the inauguration of the Toulouse centre. The programme is open to active persons, pensioners, soon-tobe-pensioners, family caregivers and young people aged 16 to 25. Created in 2017, the unique preventive medicine device consists of a comprehensive health check-up, personalised support and a one-year follow-up to allow everyone to play an active part in their own health. There are other spin-off projects of the programme on other territories, including a digital version for use in local primary care structures. The Centre Prévention Santé Longevité (CPSL -Prevention, Health and Longevity Centre) concentrates all health and prevention components of the Institut Pasteur de Lille.

- INNOVATIVE PATHWAYS IN PREVENTIVE MEDICINE AND HEALTH EDUCATION.
 PUBLIC HEALTH ACTIONS ON THE FIELD CLOSE TO THE PEOPLE.
- RECOGNISED EXPERTISE IN VACCINATION AND TRAVEL MEDICINE.
- SCIENTIFIC EXPERTISE TO HELP PREVENTION RESEARCH.

> An assessed ambitious prevention approach targeted at people, public players and companies.



"The ambition of the CPSL is to be a reference centre for preventive health, in order to help people live a healthier, longer life. Our challenge is to develop true research around evaluated prevention, by developing cross-border projects with research units at the Institut Pasteur de Lille. We also want to digitalise a number of fields of expertise and enhance accessibility in the field of health prevention in the Hauts-de-France region. »

> **Dr Jean-Michel Lecerf,** Medical Director of the CPSL

12,250

Health Prevention Check-ups (EPS) carried out for the CPAM, including 57% for those in vulnerable/precarious situations 425

check-ups outside CPAM including 135 Routes to Longevity®



HEALTH CHECK-UPS

Inauguration of a health check-up centre in Béthune

After Arras and Lens, the health check-up centre in Béthune is the 3rd delocalised CPSL branch, designed to bring an answer to the healthcare fracture, by going on the field close to the people. The centre offers check-ups and medical assessments to vulnerable people who are often way outside care pathways. A dedicated team was put in place. Goal: to carry out 3,500 check-ups every year for Artois patients. "The strength of the Prevention, Health and Longevity Centre is being able to uniquely combine every type of health prevention expertise, as well as being backed by a research centre. Our health prevention experience on the field for 120 years and our high



local anchorage mean we have a precise knowledge of population issues in the Hauts-de-France. Today the challenge lies in pursuing innovation and the experimentation of new prevention devices, assessing them and sharing them to improve life expectancy in good health for as many people as possible".

Perrine Quivron,

Administrative Director of the CPSL

HEALTH EDUCATION

Bonus Santé Operation

With financial support from the Hauts-de-France region over three years, Bonus Santé is one of the many health education projects conducted this year. It was developed in four priority territories in 2022: the Artois, the Douai territory, the Saint-Quentin territory and the Valenciennes territory. It aims at promoting healthy behaviours in a region that is strongly affected by overweight and obesity: in the Hauts-de-France region, 20% of people are obese, compared to 17% in France. The aim was to target fragile and vulnerable people including women aged 30 to 40, who are more prone to suffer from cardio-vascular diseases, as well as young people aged 16 to 25. They take part via social networks, local missions and other local social structures.

- 12 workshops were included in each territory around three themes: diet, suitable physical activity and stress management.
- A special event took place at the Louvre-Lens in June 2022 to complete actions on the territory.

vaccines administered including 3,400 for influenza

8,770

consultations in travel medicine

THEY ARE THE INSTITUT PASTEUR DE LILLE

Coralie Marlier

Prevention nurse

Coralie Marlier, who has been a nurse at the CPSL since 2014, is conducting health prevention check-ups for all



types of public, including the poorest. These consist in a blood sample and check-ups to assess a person's health: height, weight, blood pressure, electrocardiogram, eye test and hearing test. "We also conduct preventive actions with young people on a variety of topics including "sex and love life" and "pleasure and dependency", said the 34 yearold nurse.

After graduating in 2013, Coralie Marlier started her career as a nurse filling in for temporary absences in nursing homes, before joining the CPSL team at the Institut Pasteur de Lille a few years later. In July 2022, in order to complete her training, she successfully took a diploma in addictology nursing, meaning she is now able to conduct tobaccology consultations. She is also currently training for "travel medicine" in order to integrate the vaccination centre at the Institut Pasteur de Lille.

While she initially wanted to be a child care worker, she has found personal and professional fulfilment in being a nurse. "What I like most about my job, is meeting a wide variety of people, and above all being able to establish a relationship with them."

HEALTH IN THE WORKPLACE

Launch of the Équilibre digital programme

How to manage stress, diet, sleep and physical activity? This is the aim of the digital programme which was launched in partnership with Sharecare, a company specialising in educational digital applications. As a first step, the comprehensive prevention programme is offered to businesses for their employees. It relies on an informative, educational device deployed online and in the workplace. For every participant, only 5 minutes a day are required, twice a week, for 8 weeks, to start, continue and finalise the 4 programmes available. This project results from a combination of skills from all CPSL expertise fields.

> www.programme-equilibre.fr



An experimentation of the Route to Longevity[®], financed by AGR2 La Mondiale, has been conducted on a number of employees in the agri-food industry in view of its potential deployment as part of inter-branch collective agreements.

> 80 routes carried out in companies of all sizes, from Meert (approx. 10 employees) to the Lesaffre group (some 40 handlers working in flexitime).

Specific training courses

These sessions, which are targeted at companies' occupational health departments and/or HR and CSR managers, prepare for the development of health actions in the workplace around various themes.

> 3 sessions / 2 days of training





The themes developed over the two days of the 23rd edition were: **"A little metabolism for practice" and "Obesities, medicine and surgery: the role of lifestyle".**



PREVENTION RESEARCH

Alreadγ over 700 volunteers recruited for the PrevenDiab surveγ

The PrevenDiab survey, which is conducted as part of the diabetes precision medicine translational and clinical research project, is a prevention research project. Within the CPSL, a dedicated team is in charge of recruiting volunteerstocollectclinical,sociologicalandanthropometricdata,i.e. 1,500 data per patient.

- > 708 volunteers included, including 34% in precarious situations. Goal: 2,200 at the end of 2023.
- > Lynn Abou Jaoudé, a PhD student at the University of Lille, integrated the PrevenDiab project to complete a thesis called "Understanding and developing a diabetes prevention programme with a disaffiliated population", in partnership with the Faculté d'Ingénierie et Management de la Santé (ILIS).

they are the INSTITUT PASTEUR DE LILLE **Bérengère Legendre** Clinical study technician.

<u>Clinical resea</u>rch associate

Bérengère Legendre, 41, joined the Institut Pasteur de Lille clinical study department as part of the CPSL in June 2022 and contributes to the conception, implementation and conduct of clinical studies aimed at assessing the nutritional effects and health benefits of food supplements.



35

of an association for the prevention of cardiovascular diseases and diabetes, travelling across the Lille metropolis, the dietetian and sport medicine instructor decided to take a vocational training course at University. She graduated as a Clinical research associate (CRA). She performed her end-of-course internship at Oscar Lambret Centre, where she stayed for 8 years, managing among other things clinical studies on breast cancer treatments in women with gene mutations. Then came a desire to explore new fields: *"I've always wanted* to work in prevention, particularly in the field of nutrition and physical activity. That is why I decided to apply for a job at the CPSL in order to use my previously-acquired skills for the project".



 workshops dedicated to the general public and professionals.

Supporting industrials in the deployment of their innovations for the environment and health

Simultaneously to its research and prevention activities, the Institut Pasteur de Lille has developed specific expertise in terms of microbiological safety, environmental microbiology and genetic toxicology.

- Internationally recognised expertise.
- Close to the practical applications of research.
- Supporting industrials.

> Contributing to a healthier, more sustainable environment and better health for all.



ENVIRONMENTAL MICROBIOLOGY AND VIROLOGY

Laboratory dedicated to preventing infectious risks

Respiratory viruses are mainly transmitted in the air but also by contact with surfaces when contaminated droplets are deposited on them. Other infectious agents in the environment (bacteria, viruses, fungi) may also contaminate the air we breathe and the surfaces we touch. More than ever since the Covid-19 pandemic, industrials are looking into designing products and materials which take into account the microbiological risk: air purifiers for homes, offices and lifts; functional textile with antimicrobial properties for train seats, surfaces for underground poles and so on.

The Microbiology Safety Unit (USM) is an applied research laboratory created in 2003 by Dr Michèle Vialette.

- Its role: to test and assess the effectiveness of a product or process against a pathogenic micro-organism in the environment.
- Laboratories dedicated to every type of micro-organism: bacteria, viruses, fungi.
- A team of 5 people supporting industrials.
- Practical applications in all business sectors: health, transport, cosmetics, agri-food, sustainable development and so on.
- International deployment: partnering with the leading industrial research centres in Europe, industrial groups, SMEs and start-ups worldwide.
- > Wherever there is a microbiological risk, the USM brings its expertise in environmental microbiology to enable industrials to develop new products, processes and technologies.
- > New development opportunities with regards to sustainable development and infectious risk management in the hospital will be developed.



Michèle Vialette, founder and head of department at the USM

"We have been working on interior air quality for over ten years by creating contaminated atmospheres in our laboratories. During the Covid-19 pandemic, a number of industrials realised the risks associated with respiratory viruses spreading in the air and contacted us; in 2022, we were able to broaden our offer via new structures and for new viruses. We have rare environmental bacteriology and virology expertise in France and we support industrials and innovators from the conception throughout their projects. By carrying out customised studies or studies inspired by existing standards, we try to be as close as we can to reality. We develop the structures and materials to help them evaluate their innovations in laboratory conditions while being as close as possible to actual conditions of use".



GENETIC TOXICOLOGY

One of the largest genotoxicity centres in France

The **Genetic Toxicology Laboratory,** which was created in 1981 by Prof. Daniel Marzin and is headed by Dr Sophie Simar, is among the largest genotoxicity centres in France.

- Its role: conducting studies to assess the genotoxic and mutagenic potential of chemical, pharmaceutical, cosmetic, biotechnological and agrochemical substances, in compliance with international guidelines.
- A unique expertise in France in the study of nanomaterial and nanoparticle toxicity.
- Attached to the Labelled Research Unit ULR 4483-IMPECS (IMPact of the Chemical Environment on Health) of the University of Lille.
- GLP accredited (Good Laboratory Practices) by the Ansm, the Anses and the Cofrac.
- R&D activities used to enhance the connection between expertise and research.

Thanks to research, and notably the influence of publications and the use of new technologies developed in R&D, 2022 was marked by a change in the type of tests, from in vivo tests to in vitro/in silico models, high throughput tests, and a change in endocrine disruptor tests towards a GLP status, opening up to new types of clients.

Since genetic toxicology is a cross-functional science, the laboratory continues investing in the field of environmental health, with the study of emerging pollutants and/or new health concerns, notably in the field of air contaminants.

Studies on all fronts of research

Monito-CoV-ageing study: The study, which is led by Lille University Hospital and labelled "National Research Priority" by CAPNET, focuses on the assessment of the quality of anti-SARS-CoV-2 vaccine response in elderly subjects residing in residential care facilities for dependent elderly persons (EHPAD), compared to young and immunocompetent subjects such as caregivers.

Therapide trial: The CMU took part in the Therapide trial labelled "National Research Priority" by CAPNET, by developing an RT-PCR method for the quantification of the SARS-CoV-2 genome. The unit organised the circuit of biological samples from the samplers' offices to the Institut Pasteur de Lille, analysed the biological samples and submitted the analysis reports.

CritiSARS2: The study, led by Prof. K. Faure (University Hospital – CIIL) and submitted as part of the Flash COVID call for projects in March 2020, aimed to identify new viral, inflammatory and immune markers for critical forms of Covid-19. The CMU is responsible for two work packages, allowing funding of €32,000 (ANR – Hauts-de-France region funding).

AAP Infinite 2021: The study consists in testing highpressure viral inactivation capacities on breast milk. The consortium is made up of a group led by J. Lesage, Infinite, specialised in the study of breast milk specificities, and the CMU-Virology for coronavirus tests and the MCV-HEV group for HEV tests. Analyses are in progress.

POMADE-CoV study: As part of an I-SITE – ULNE call for projects to fund doctoral theses, the CMU received co-funding for the supervision of a foreign student, whose mission was to develop custom porous materials able to quickly capture and inactivate coronaviruses. This doctoral student is co-supervised by Prof. C. Volkringer (École Centrale de Lille) and Prof. Anne Goffard. His virology work is conducted under the supervision of Peggy Bouquet.

Not forgetting...

Since 2020, the Clinical Microbiology Unit (CMU) has been asked by manufacturers for expertise to test antiviral products for SARS-CoV-2 or to assess the neutralising power of monoclonal antibodies.

FOCUS ON

Collaboration between research and expertise in the fight against Covid-19

Following the COVID-19 health crisis, the Institut Pasteur de Lille was requested to test a number of antiviral products and monoclonal antibodies. In order to face the challenge of handling SARS-CoV-2, which is classified as highly pathogenic and must be handled in a high-security P3 laboratory, a collaboration was set up between the Clinical Microbiology research Unit (CMU) headed by Prof. Anne Goffard, and Dr Vialette's expert service.

During 2022, the CMU was able to test the neutralising power of monoclonal antibodies and the efficacy of antivirals against SARS-CoV-2, thanks to Peggy Bouquet's expertise and under the coordination of Prof. Anne Goffard.





CLINICAL MICROBIOLOGY

A laboratory dedicated to antibiotic resistance

A major medical discovery, antibiotics have saved, and continue to save million of lives every year worldwide. However, they are starting to become less effective due to increased antibiotic resistance.

What risk does it pose?

The risk is for bacterial strains to become massively multidrugresistant, leading to an increase in bacterial infectious diseases. This would mean that infections we are able to treat today could once more become fatal.

Antibiotic resistance, which is rightly considered by the World Health Organisation (WHO) as one of the biggest current health threats, could lead to the death of 10 million people every year worldwide by 2050.

The challenge of research teams is to understand the mechanisms of (multi) antibiotic resistance and to find innovative molecules in order to put in place effective, sustainable therapies.

Fighting superbugs

A team at the Institut Pasteur de Lille benefits from Professor Patrice Nordmann's unique expertise in that field. The team has chosen the major world health issue as its research subject:

"Antibiotic-resistant bacteria travel worldwide in the intestinal flora and spread unnoticed. In order to fight these superbugs, we must first use antibiotics appropriately, but also develop new methods to quickly diagnose carriers and prevent the spread of threatening bacteria, while we continue research to come up with new antibiotics. »

Resources *dedicated to* **projects**





Supporting researchers regarding the administrative and financial aspects in the building of their project

"In order to finance their research programme, a researcher has to file a number of funding requests through regional, national, European and international calls for projects. To do so, the researcher has to draft a scientific project with the best chances of being selected. The role of the Department for Research Administration and Contract Management is to help build the project, particularly regarding the administrative and financial aspect.

Over fifty new projects are filed every year and about 200 projects financed are managed by the department. "

Fabienne Jean, Director of research administration

Research, innovation and promotion administration

Turning discoveries into practical innovations for society

INNOVATION / PROMOTION

Enhancing research promotion and enabling technology transfer is a major concern for the Institut Pasteur de Lille, which has deployed an entire ecosystem around research units.



patent families in portfolio

- A dedicated team for research administration and contract management. A key player within the campus, it supports teams looking for essential funding to carry out their projects. Its missions: identification of potential funding on a regional, national, European and international level, support in the building, management and financial justification of contracts obtained, file monitoring in collaboration with partner institutions.
- A legal department for the research units, responsible for the Foundation's institutional and collective interests, in a tightened regulatory context and an enhanced competitive environment.
- Support for innovation carried out in partnership with the Technology Transfer Acceleration Companies (SATT - sociétés d'accélération de transfert de technologie) and the various departments for the promotion of academic partners of the Institut Pasteur de Lille: Inserm, CNRS, University of Lille.

patents pending in 2022

IPL LABELLING

The process has been launched!

In order to make implementation easier, a web portal was created to send labelling applications. Team and/ or group managers can send their applications until the end of April 2023, when they will be transferred to be assessed by the international scientific council of the Institut Pasteur de Lille.

> See "Points of view" page 08

Weighing the risk between doing and not doing

"We offer our legal skills to researchers and doctors to help them develop their work and help them protect and promote their discoveries. That is why in the very early stages of a project, we find it important to identify its valuation potential in order for us to protect data early on, before they are leaked by a publication or a funding outcome. By securing the results of a project and protecting it, we are able to offer it to an industrial at the right moment in view of developing it. It is also important to do so in conditions that do not jeopardise the Foundation. In other words, it means weighing the risk between doing and not doing, in acceptable conditions. As part of this valuation logic, we are currently setting up agreements with every one of our co-supervisors, in order to have, if not a common strategy, specific operating procedures for the Pasteur Campus in Lille. Thus we aim to achieve simplification of procedures and therefore a mitigation of risks which may impact the sustainability of the Foundation."

> Florence Boulangé, Legal director



ANR CALL FOR PROJECTS A productive γear in 2022

13 projects, including 8 in coordination with 10 research teams, were selected as part of the 2022 Generic Call for projects (AAPG 2022) by the National Research Agency (ANR). It targets all scientific communities and all public and private players involved in research in France, and involves several funding instruments, each with their specific features. The success rate is outstanding and shows the quality of research teams at the IPL.



PROMOTION

Inserm Transfert at our researchers' side

Externalising research promotion was a goal for general management, who signed a partnership with Inserm Transfert in order to support IPL researchers in the protection and promotion of their research. The private Inserm subsidiary, which was created in 2000, deals with the economic and social promotion and the transfer of knowledge from Inserm and partner research laboratories. Since November 2022, permanences with Inserm Transfert "patent engineers" have been organised twice a month on the Pasteur Campus in Lille. And it's been full ever since!

Over 40 projects financed over 2017-2022

High-level platforms *in support of top-level research*

PLATFORMS

The Pasteur Campus in Lille hosts several technological platforms, including seven of Lille's eight biology and health platforms from the PLBS Support and Research Unit (UAR 2014-US 41). They are dedicated to academic research in Lille, and are also accessible to the entire scientific community, especially biotechnology companies and those specialising in pharmaceutical research.

EUROPEAN RESEARCH

Platforms engaged in large-scale scientific projects

GO(@L, P3M and Bilille are taking part in European project H2O2O FAIR (Flagellin Aerosol therapy as an Immunomodulatory Adjunct to the antibiotic treatment of drug-Resistant bacterial pneumonia). ARIADNE is contributing to a European Recovery Plan (REACT-EU) project to deal with the consequences of the health crisis and to the ANR project Programme Investissements d'Avenir Mustart (Multiparametric strategies against antibiotic resistance in tuberculosis).



13

technology platforms overall:

- including 7 of the 8 PLBS platforms in Lille metropolis: BICeL / GO@L / PAGés-P3M / Bilille / ARIADNE / PLEHTA / LIIFE / SINBIOS
- 6 PLBS platforms are also labelled IBISA: ARIADNE / BICeL / PAGés-P3M / Bilille / LIIFE / GO@L



Dr Frank Lafont

BICEL 2023

An imaging platform contributing to national technology networks

The Biolmaging Centre in Lille has existed since 2010 and, in 2020, was included in the PLBS unit (Lille's biology and healthcare platforms). This is an inter-site platform (Health Campus, Scientific City and Pasteur Campus). BICeL contributes to national technology networks: RIME (Réseau d'Imagerie en Microscopie Electronique, Imaging Network in Electronic Microscopy) and Rtmfm (Réseau technologique en microscopie de fluorescence multimodale, Technological network in multimodal fluorescence microscopy) and is labelled GIS IBISA.

Instrumentation highlights in 2022:

- Installation of a high-speed spinning disk CrestOptics XLightV3 video-microscope (Pasteur purchase €250 K) in the Calmette, L2 culture U1167 building.
- Installation of a colour camera on the Prime video (University of Lille purchase €10 K), enabling average output histological section scans.
- Installation of multiphoton confocal microscope Leica Sp8 in the premises of the new animal housing facility. The new premises have been specifically arranged close to the A2 area, with independent access, an area dedicated to handling and an adjoining housing area so that the MP confocal microscope may be used in A1 and A2 containment, and may be accessed by any user inside or outside the IPL campus.

Communication activities in 2022 focused on 4 days demonstrating the STELLARIS confocal microscope by Leica, as well as the 2022 Fête de la science on the topic of Climate Awakening. The BICeL provides user training in microscopy and image analysis at different levels. In 2022, this amounted to 35 new autonomous users for phototonic or electronic microscopes on the campus, and 45 trainees taking part in permanent regional and national training in phototonic microscopy and image analysis. »

NMR - NUCLEAR MAGNETIC RESONANCE

SARS-CoV-2: a fragment with identified antiviral properties

The protease known as 3CLpro is an essential enzyme of SARS-CoV-2, as it cuts the precursor polyproteins pp1a and pp1ab into different active proteins which will then allow for the replication of the virus. Therefore, it is an important therapeutic target.

A library with 960 molecular fragments from laboratory U1177 (Prof. Benoit Déprez) was screened against the 3CLpro protease using proton (1H) and fluorine (19F) NMR spectroscopy. At the end of the screening, carried out in 2 steps, 38 fragments were identified, including one with antiviral properties.

INNOVATION

From full protein synthesis to the discovery of a potential drug



After long years of research and development in chemistry and biology, Drs Oleg Melnyk and Jérôme Vicogne (UMR CNRS 9017) and their team, in collaboration with the University of Pavia, developed a molecule called K1K1, which was patented in 2015, and has potential therapeutic properties thanks to its ability to induce anti-fibrotic, regenerative and anti-inflammatory responses by activating the signal depending on the Hepatocyte Growth Factor Receptor (c-MET or HGFR). Deriving from genetic engineering, the K1K1 protein consists of two kringle 1 (K1) domain copies of the Hepatocyte Growth Factor/Scattor Factor (HGF/SF), the natural agonist of c-MET.

Simultaneously to the signature of a licence agreement with Boehringer Ingelheim, the SATT Nord (Société d'Accélération de Transfert de Technologies, Technology Transfer Acceleration Company) and its partners at the CNRS, the University of Lille, the Institut Pasteur de Lille, the University of Paris-Cité and Italian partners at the University of Pavia, started collaborating with this major player of the pharmaceutical industry in order to develop an innovative treatment in clinical research to treat patients suffering from pulmonary fibrosis.

Ref: EP15152027.7, 21 January 2015. WO2016/116577 A1 « Met receptor agonist proteins." Applicants: University of Science and Technology of Lille – Lille 1, CNRS, Institut Pasteur de Lille, University of Lille 2 Law and Health, Universita' Degli Studi Di Pavia. Exclusive licence Boehringer Ingelheim, December 2022.





BRC - NUCLEAR BIOLOGICAL RESOURCE CENTRE

Collaborations on the THERAPIDE collection

With Prof. Benoit Déprez's research team, the BRC took part in the reception, provision and preservation of the THERAPIDE collection. The collection originates from a clinical trial to measure the efficacy of a therapeutic molecule against SARS-CoV-2 versus a placebo. Two other projects were initiated in collaboration with the CPSL teams led by Dr Jean-Michel Lecerf. The first project deals with the reception and preservation of biological samples in order to evaluate the beneficial effect of a dietary supplement on the oxidability of LDL versus placebo. In the second project, the BRC is in charge of receiving, preparing and preserving biological samples for the study of the prevalence of diabetes and prediabetes.

Not forgetting...

In 2021, the BRC platform saw its NF $\,$ 96-900 certification renewed for 3 years.

A few figures

- Over 500,000 biological samples, some of which have been stored for over 30 years.
- Biological samples of all kinds: whole blood, plasma, serum, red blood cells, buffy coat, DNA, RNA, urine, cerebrospinal fluids, expired air condensates, hair, stool, nasopharyngeal samples.

BILILLE

Life sciences: shared digital spaces

Since late 2020, bioinformatics platform Bilille (UAR 2014 - US 41 - PLBS) has been taking part in the only EquipEx+ programme in Biology and Healthcare in the Lille metropolis, led by the Institut Français de Bioinformatique (IFB). The MuDiS4LS (Mutualised Digital Space for FAIR Data in Life and Health Sciences) project aims to build shared digital spaces for life sciences at a national level and promotes open science by providing scientists with all the keys to make their data Findable, Accessible, Interoperable and Reusable (FAIR).







SINBIOS PLATFORM

SINBIOS joins PLBS platforms

In February 2022, the SINBIOS platform, headed by Karl Oulmi, joined Lille's biology and healthcare platforms (PLBS), offering access to the equipment and expertise required to support Lille units in their activity. SINBIOS meets the IT needs of scientists within the 24 academic research units in life sciences, biology and health throughout Lille territory. The team provides expertise and proximity IT support in association with a great variety of research projects, making them more relevant, efficient and speedy. For instance, SINBIOS helps set up customised collaborative work environments as part of research projects and provides teams with support in terms of scientific data management, storage, accessibility and security.









ARIADNE

National platform ARIADNE-Criblage (Screening) brings together a set of expertise and high-technology equipment dedicated to supporting discovery programmes for biological disruptors and drug candidates. ARIADNE possesses a chemical library which includes 100,000 compounds, including a large number of original molecules deriving from regional research, as well as a human and murine siRNA library. Three automated or semi-robotised technological platforms are used to screen these molecules on in vitro, in bacterio and in cellulo biological models. ARIADNE is one of the few European structures to offer this type of approach in a continuum of containment levels BSL1-BSL2-BSL3. ARIADNE-Criblage is backed by platform ARIADNE-ADME, used by teams to profile and improve the pharmacological properties of hits originating from screening campaigns. The entire ARIADNE structure is backed by teams of medicinal chemists, cell biologists and microbiologists, all sharing the same ambition of developing innovative and effective drugs. The ARIADNE platform is a partner for a number of projects including European project ERA4tb (European Regimen Accelerator for Tuberculosis), a public-private initiative aimed at speeding up the development of new therapeutic schemes to fight tuberculosis, and project CPER Resist-Omics (Resistance, Complications, vulnerability factors and holistic approach for Therapeutic Innovations in Inflammatory and Infectious Diseases).

HUMAN RESOURCES

Human resources

Promoting the human capital and placing it at the heart of the Foundation project

Men and women at the Institut Pasteur de Lille contribute to making every project a success.



Placing humans at the heart of the Foundation project means:

- Developing the employer brand to promote the Institut Pasteur de Lille globally and attract the best talents.
- Building a sustainable Human Resource strategγ in line with emploγee expectations and work organisation evolutions.
- Accompanying employees in their career bγ developing their skills and providing meaning to their action to ensure personal fulfilment.
- Enhancing adherence of all to the companγ project, its goals and values.
- Consolidating employee loγalty towards the Foundation and their sense of belonging to a collaborative unit.

• The foundations of our HR project:

- Developing HR communication and emploγer branding.
- Having a solid HR base.
- Accompanying change management by guiding managers, our daily partners, and employees in the project implementation.

> A strong ambition to promote the Institut Pasteur de Lille globally!





"The Institut Pasteur de Lille pursues the transformation of its management culture. The Foundation project was defined, explained and presented in late 2022 before the administrators, managers and employees. The project lies on shared values of excellence, solidarity, discipline, ethics at the heart of decisions and well-being in the workplace. More than ever, the human capital is at the heart of the Foundation project. In 2022, we took the first steps towards employer branding and a more communicative, facilitating and cross-border HR department".

> Mélanie Lestoquoi, Human Resources and Social Relations Manager

MANAGERS

Launch of a codevelopment group.

Individuals trained as part of the "manager training" cycle can now continue the exchange as part of a co-development group. These work sessions, which are hosted in house, are used to exchange on issues related to the Foundation HR project. 2023 In 2023, a community

of managers was created

A socially engaged player that is present on the **territory**

A human, federative and meaningful project bringing collective fulfilment

In 2022, the campus real estate transformation accelerated, taking shape before our eyes. It was necessary to carry out the large-scale key programme for the future of the Foundation: it is experienced and built today for tomorrow. Within the next 3 years, our scientific installations will be modernised, the well-being of professionals working here will be improved, exchanges with our ecosystem will be facilitated and we will be able to welcome new workers in renovated, spacious, sustainable premises. In addition to being a daily technical challenge, it is a wonderfully human, federative and meaningful project bringing collective fulfilment and enabling the Institut Pasteur de Lille to meet future scientific and health challenges even more efficiently".

Didier Bonneau, Deputy Managing Director



Campus 2026: *a federative project for the entire campus*

The Institut Pasteur de Lille welcomes over 800 employees every day on its campus: 320 Pasteur Institute employees as well as agents from the CNRS, the Inserm, the University of Lille and Lille University Hospital, working in the joint research units or in the toxicology and microbiological safety departments, prevention workers at the CPSL, as well as employees of tenant companies from the world of research and innovation.

800

dailγ employees on the Pasteur Campus in Lille, including 320 Pasteur Institute employees as well as agents from the CNRS, the Inserm, the Universitγ of Lille and Lille Universitγ Hospital, working in the joint research units or at the CPSL. It also hosts a dozen start-up companies in research and innovation.

Campus transformation

Since 2016, the Pasteur Campus in Lille has been undergoing a full transformation to become more attractive, more responsible, exemplary and sustainable. By 2026, the real estate project provides for the rehabilitation of old buildings, offices and laboratories, as well as the development and marketing of a new rental investment programme.



REHABILITATION

Works on the Guérin building

Rehabilitation is under way for the buildings used for the activities of the Institut Pasteur de Lille, in particular the Guérin and Calmette buildings. Renovation of the Guérin building will provide the research teams present on the Campus with modern, performing and scalable laboratories.

In February 2021, the first phase of deconstruction, asbestos removal and lead abatement for levels 1, 2, 3 and 4 was initiated. Works began in May 2022.

The rehabilitated Calmette building will be able to accommodate the CPSL teams. It will also be made compliant with regard to safety and the reception of persons with reduced mobility.



REHABILITATION

A new experimentation platform for the PLEHTA

After several years of works, the PLEHTA has invested the new building which was rehabilitated in July 2022. The new tool ensures units have the ideal conditions to continue their projects. Breeding is now carried out by the PLEHTA. The new high technology laboratory meets the need for rederivation and cryopreservation. The A2 capacity was significantly increased. The entire team is ready to meet upcoming challenges.

CAMPUS

The Winners' Club takes a look at the campus transformation projects

Members of the Winners' Club were able to take a look at the campus transformation projects. The programme included a recap of the history of Louis Pasteur in Lille by Dr Jean-Michel Lecerf, followed by a presentation of the transformation project by Virginie Drelon and Didier Bonneau. The event was rounded off with a tour of the work site and a cocktail reception!



50,000 sqm



of surface to be optimised including 10,400 sqm currently being optimised and 4,600 sqm vacant.

<u>65</u>€M

total real estate project amount

2026 vend of works.



RENTAL INVESTMENT PROGRAMME

"24 Boulevard Louis XIV" is unveiled

Launch of the rental investment programme on the corner of Boulevard Louis XIV and Boulevard Maréchal Vaillant. The works, which are to last 18 months, began in July with the demolition of the old buildings. The project will continue with the construction of a corner building dedicated to offices and shops, followed by another, called "Le Pavillon", offering a new area for congresses in Lille Metropolis. It will also be a place for meetings and exchanges for the teams and tenants on the Campus.

Real estate road map





CALMETTE BUILDING Ground floor

Rehabilitation work for the reception of the Synlab medical analysis laboratory.

2016













CALMETTE BUILDING

Development work for the Prevention, Health and Longevity Centre



NEW BUILDING

At the corner of Boulevard Louis XIV and Boulevard Maréchal Vaillant.

REHABILITATION

Guérin building.



NEW BUILDING

Rue du Professeur Calmette.



The Pasteur Campus in Lille, a breeding ground for innovative biotechs

Biotechnology is revolutionising the health sector. At the heart of the campus, the Institut Pasteur de Lille supports the development of biotechnology and innovative health projects, start-ups and companies. A common goal: to develop promising therapeutic treatments, new services and products for analysis or diagnosis, directly resulting from fundamental research conducted in Lille.

APTEEUS

Repositioning of existing drugs

"Apteeus's mission is to identify new uses for existing drugs. With an ability to simulate diseases and test every drug in the world in a short time, our team has already succeeded in improving the life of several children affected by extremely rare genetic diseases. In 2022, two of our research projects particularly grew in magnitude. The first one, stemming from a public-private partnership with researchers at the Institut Pasteur de Lille, will involve an Apteeus subsidiary to redevelop a drug to treat pneumonia. The second one, currently subject to fundraising, aims to redevelop a drug which could save the lives of a hundred children every year in Europe. Such significant development perspectives for Apteeus are the result of a varied research activity in Pasteur Campus in Lille, an exceptional environment that is internationally recognised".

BIOTECHS

Terence Beghin

apteeus



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BACTERIAL RESISTANCE

BioVersγs for new antibiotic treatments.

The Swiss biopharmaceutical company, established in Lille since 2018, announced the first subjects treated in the phase 1 clinical trial of BVL-GSK098 and in the additional phase 1 clinical trials of BV100. It also received a second CARB-X grant of up to \$15.34 million for the BV300 project. Several clinical trials began in 2021 (antibiotic for *Acinetobacter baumannii* infections, and a small molecule that potentiates anti-tuberculosis antibiotics). Other research projects involving conventional (new class of broad-spectrum antibiotics) or non-conventional approaches (anti-virulence agents for the treatment of infections caused by *Staphylococcus aureus*) are currently being conducted.





A NEW KIT IS BORN

Launch of the Deeplex[®] Myc-Lep kit

2022 marked the commercial launch of the Deeplex® Myc-Lep diagnosis kit, used to identify and trace the leprosy germ with great precision and diagnose its antibiotic resistance. With this kit, the company ambitions to significantly contribute to eradicating the disease, which still infects 200,000 people in the world every year.

PLATFORM SERVICES ARE UPDATED AND ARE ALWAYS RELEVANT

GenoScreen services, based on sequencing and bioinformatics and biostatistics analyses, are still available and have been enriched with the latest sequencing technologies to meet the increasingly specific needs of academic and industrial research teams. These services are shown in a catalogue which can be downloaded at www.genoscreen.fr



A GLOBAL SUCCESS

2022: sales deploγment of the Deeplex[®] Mγc-TB kit worldwide

The 1st kit in a developing series, this kit, which aims at predicting antibiotic resistance of the bacteria responsible for tuberculosis, has been selling in over 40 countries. Such success can be explained by numerous scientific and medical validations, as well as sales agreements with established distributors worldwide. In order to speed up the sale of this kit, at the end of the year GenoScreen signed a major co-marketing agreement with ILLUMINA.

LAUNCH OF A METAGENOMICS BRAND

Launch of the GenoBiome[®] range, for the study of microbiomes

With a dozen years' experience in metagenomics, 2022 was marked by interesting service and expertise requests from industrial companies in various business sectors, from the agri-food industry to the cosmetics industry. In order to offer solutions rather than mere analyses, GenoScreen offers a workflow called GenoBiome®, to accompany and guide our clients throughout their entire microbiome characterisation project, from experimental design to the presentation of results. As these approaches often give rise to applications, they lead to fascinating and rewarding collaborations.



SAL: MedTech of type LaaS (Longevity as a Service).

With a longer life expectancy, ageing well has become the social challenge of the future.

Under the management of Dr Thierry Mathieu, StarkAge Longevity (SAL) has developed a dedicated platform for health and the prevention of age-related diseases.

It is a clear, reliable platform to be informed on the latest scientific breakthroughs in terms of ageing, with articles written by experts in the field.

This year, SAL also launched a platform for calculating one's epigenetic biological age, making it possible to implement targeted prevention measures.

The calculation is based on an algorithm developed by SAL and a collaboration with Steve Horvath's Clock Foundation, a reference international organisation in the field.

Results come with a specialised medical consultation and personalised advice for ageing well.

The company is also working on a score to predict age-related diseases (Arpa-Score), based on Artificial Intelligence and its proprietary algorithm. In the long term, SAL will be launching "Genomic Longevity Routes" in collaboration with the IPL. The high added-value, 360° personalised preventive medicine programme will help fight the effects of ageing in the best way.

Not forgetting...



Lifebloom developed a medical device to provide physical assistance to dependent people, allowing them to get up and walk on their own. Users can continue conducting their life.

STARKAGE_ THERAPEUTICS

SATX: Biotech.

Cell ageing (senescence) is a natural phenomenon behind a number of age-related diseases, due to an accumulation of senescent cells within tissues. A number of pathologies including cancer, fibroses and neurodegenerative diseases are linked to a lack of elimination of senescent cells by the immune system.

StarkAge Therapeutics (SATX) is a BioTech aimed at selectively destroying senescent cells by developing targeted therapies (antibodies, ADCs, CAR-T,..).



With the help of innovative methods such as surface protein analysis (surfaceome), senescent cell-specific membrane markers were identified for the first time. A patent family has just been accepted in the USA and a series of patents are being applied for.

The first therapeutic indication for the development of antibody anti-DPP4 is idiopathic pulmonary fibrosis for the targeting of senescent fibroblasts. More recently, another line of research was opened for cancer with the conclusion of a partnership with Oscar Lambret Centre to combine our anti-DPP4 antibody with radiotherapy or chemotherapy to destroy senescent cancer cells responsible for resistance to treatments and patient relapse. With the arrival of new investors, we will be able to finance the pre-clinical development of different programmes.



CSR commitments

The activities of the Institut Pasteur de Lille are part of a Corporate Social Responsibility (CSR) approach. Initiated in 2017 and conducted by General Management, this approach involves daily practical actions by all employees of the campus, and falls into three categories: social, societal and environmental.

Social Creating human values on the campus

DEVELOPING EMPLOYABILITY

 $2\ \text{workstations}$ ergonomically adapted for health reasons in 2022

TRAINING BUDGET 1.3% of payroll in 2022 + 1% training tax

EQUAL OPPORTUNITIES

Training of two HR employees as Disabled Persons Contacts

PROFESSIONAL EQUALITY INDEX

96/100 (2021-2022 Index published in 2023)

RATE OF WORKERS WITH DISABILITIES 7.14%



Societal Rendering a public health service to the population

The IPL Prevention, Health and Longevity Centre carries out over 12,500 Health Prevention Check-ups (EPS) by delegation of the Health Insurance, including nearly 60% dedicated to precarious populations. As part of these check-ups, the IPL notably delivers health education actions (diet and physical activity, sex and love life, addictions) to groups of vulnerable young people, thanks to partnerships with social centres, local missions, communal social action centres, etc. Health education actions can also be carried out outside of the IPL. Residents of Priority City Districts benefit from health prevention actions (diet, physical activity, stress management, sleep, etc.) and relays such as health mediators are trained by our teams. Every year, about 600 beneficiaries are involved in these actions, and some 300 professionals on the field are supported by our teams. Part of our health prevention research is dedicated to understanding public health factors, including the link between health and poverty. The prevention component of the Precidiab research programme studies the prevalence of pre-diabetes in the Hauts-de-France region and aims, among other things, at updating the links between diabetes and poverty. The societal and public health commitment is part of the ongoing history of the Institut Pasteur de Lille, which began over 120 years ago with the creation of a dispensary for diphtheria vaccinations.

CSR

• Environmental 2022, the γear of awareness

During the year, and particularly during Sustainable Development Weeks, some twenty workshops were made available to all personnel on the campus to raise awareness and share best practices around topics of health and safety in the workplace, impact on the environment and mobility, to complete the work conducted daily by prevention assistants. Over 250 employees took part in at least one workshop, which included:

- climate mural, waste sorting, ecodriving,
- taking part in the Mobility Challenge,
- health and safety awareness: stress management, mindfulness meditation, first-aid training.

Completion of the first greenhouse gas emission assessment for the campus in order to orientate our environmental strategy better.

In late 2022, an energy sobriety plan was defined as part of the national effort towards sobriety, resulting in technical actions as well as awareness being raised by campus ecocorrespondents regarding eco-friendly gestures which can be followed by all.

SAFE WORKING CONDITIONS

In 2022, only one accident related to a same-level fall resulted in work stoppage, confirming risks are controlled on the site.

Frequency rate: 1.8 Severity rate: 0.04

The risk prevention policy is materialised through a multiyear action programme centred around 4 pillars:

- improving working conditions,
- developing prevention culture on site,
- **controlling** risks in our professions,
- reacting as efficiently as possible when faced with an emergency.

Staff awareness and training is a major lever to maintain and improve our performance in terms of risk prevention and health & safety.

SIMPLIFICATION AND OPTIMISATION OF PROCEDURES

A computer software to digitise the quality approaches of several services has been deployed. It has simplified, and even optimised, a number of activities while maintaining the certifications acquired.

FOUNDATION

The Institut Pasteur de Lille acts for women's heart

CPSL teams were present when the Women's Heart Bus stopped in Lille, offering free diagnosis tests for cardiovascular diseases, the first cause of death in women in France.

The goal? Directing these women towards Health Prevention Check-ups and raising awareness on diet, physical activity and stress management to protect their heart.

L'Oréal: "For girls and for Science"



The L'Oréal Foundation launched its programme For girls and for Science in the region, aimed at encouraging female first-year pupils in French lycées to choose scientific branches and jobs. Alicia Mayeuf-Louchart, from the Pasteur Institute, winner of the 2018 For Women in Science programme, sponsored the regional edition.

ECONOMIC % INDICATOR

Percentage of turnover redistributed for the benefit of the local economy.

Percentage of turnover distributed locally

> Percentage of turnover distributed in France

Philanthropy **Today's donations** make the discoveries of tomorrow

Giving to the Foundation means giving researchers at the Institut Pasteur de Lille the opportunity to go faster and further in their research and discovery of new treatments against diseases.

Medical research can only be considered over time. Every donation, whether general or targeted, recurring or one-off, counts and contributes to the influence of the Foundation, the development of research projects, the equipment in our laboratories and the dissemination of knowledge.

Every donation helps: anyone can donate within their means.

The momentum must go on

2020 and 2021 were marked by outstanding generosity, from private individuals and companies, in a context of global health crisis. Two outstanding years, both in terms of donor engagement and in terms of funds collected. The momentum was not replicated in 2022. However, we continue fighting infectious diseases and other conditions such as cancer, diabetes, cardiovascular diseases, Alzheimer's disease...



Which helped to finance:

- Laboratory equipment and specialised technological platforms and dedicated teams.
- Teams of researchers, engineers and technicians.
- Support resources used to execute and promote our research mission.

Why make a donation?

The Institut Pasteur de Lille is a private foundation: resources dedicated to research are only financed by public funds up to 25%. This means that 75% of all human and material means allocated to our community of researchers and scientists solely depend on public generosity and support from companies and institutions, through sponsorship and responses to calls for projects.

"Without these resources, we will not be able to support research programmes, even with regards to major society issues. By supporting the IPL, you are supporting our commitment to society, which is to provide every individual with the means to live longer and in good health. Beyond a support to research, it is a way of providing a chance for all to share happy times with family and friends for longer."

> **Ghislain Fauquet,** Director of Communication and Philanthropy Development



An ambitious plan for 2032

Supporting individual collection

Through a more targeted communication encouraging individual donors to choose standing orders. Standing orders only accounted for 18% of donations in 2022, which is too low!



"Standing orders offer long-term visibility and reduce our processing charges. They also guarantee regularity and a lasting commitment so that our researchers can secure and complete their research on diseases."

Eugénie Devendeville, In charge of individual collection

Enhancing corporate sponsorship

By offering sponsoring companies the possibility of becoming special partners for specific, targeted research programmes and/or projects. In 2023, the IPL will also be launching skills-based sponsorship.

"Corporate sponsorship goes far beyond financial support for our Foundation. By working closely on long-term projects, we establish strong relationships with companies which share our values and help us have a sustainable impact. The fiscal advantage is a lever for corporate commitment but it is not the main motivation. According to

a survey conducted by association Admical, only a third of companies in France use their tax receipt after a donation. The main motivation behind sponsorship is the embodiment of corporate values."



Léa Dessaigne, Philanthropy manager



Consolidating bequests

By enhancing communication with our donors and the general public.

"Along with life insurance policies and donations, bequests are a way of transferring assets, free of inheritance tax. Bequests are used to designate the beneficiary(ies) of all or part of a person's estate after their death, on a will which can be filed with a notary. However it is still taboo to speak about death in France. That is

a notary. However it is still taboo to speak about death in France. That is why our support is essential for people interested in the device, who are often elderly people with no heirs. Our role is to listen to them, give them advice, and sometimes gain their confidence, as part of a relationship based on trust and honesty."



Sγlvie Frémaux, Bequest development and testator relations manager

SOLIDARITY SALE

"Guinguette" at the Institut de Genech

Four BTS students from the Institut de Genech decided to have a food and drink stand on the open house day of their institute on 19 March 2022, and distribute profits to the IPL to support the fight against diseases. Philanthropy is ageless!

Gaïa's dreams: exhibitsale of painter Jihemdé

The opening of the tribute exhibit-sale for painter Jihemdé took place on 30 April 2022. 70% of profits from sales were distributed to the Institut Pasteur de Lille to support research.



race The Foulées du Bruaγsis

The city of Bruay-La-Buissiere reaffirmed its support towards the Institut Pasteur de Lille during the 28th edition of the Foulées du Bruaysis which took place on Saturday 2 April 2022.

A donation box was made available to people registering and 1 euro was distributed for every inscription on the 10-km race.



ARTIST

Franck Thilliez celebrates 20 years!

The patron of our Foundation celebrated 20 years of writing n 2022!

Franck Thilliez, the third most read author in France, worked with researchers at the Institut Pasteur de Lille to make his successful novel "Pandemia" as accurate as possible and guarantee scientific soundness.

The writer, who is passionate about science, remains highly committed to the Institute to this day.

We send him our congratulations for his 20-year career and thank him for his highly appreciated support.

SPORTS CHALLENGE

A Pasteur supporter cut from steel!

Simon Spychala, a sport medicine instructor at the Institut Pasteur de Lille, took part in the IRONMAN races in Nice and Vichy respectively on 26 June and 21 August 2022. We thank him for both of these challenges, as part of which he collected funds for research.



FOUNDATION



Louis Pasteur bicentenary

2022 marked the bicentenary of Louis Pasteur's birth. Born on 27 December 1822, Louis Pasteur is behind a number of scientific discoveries and the creation of the first Pasteur Institutes, including the Institut Pasteur de Lille in 1894. A number of events were held throughout the year to celebrate the bicentenary. The Institut Pasteur de Lille was part of the general Pasteur 2022 bicentenary committee.

Your Lilo drops of water help build great rivers



Support the projects of the Institut Pasteur de Lille for free by using Lilo, a French search engine based on solidarity.

For every search, you will be credited a drop of water, and you can redistribute all or part of your drops to a project at any time.

You may even choose to donate your drops automatically to a project if you wish. Find out more: https://www.lilo.org/



FOUNDATION

The Institut Pasteur de Lille signs the Universal Declaration of Humanitγ's Rights

By signing the Universal Declaration of Humanity's Rights on Friday 18 November 2022, the Institut Pasteur de Lille reasserted its commitment towards protecting current and future generations, which is mirrored on a daily basis through its research and prevention activities in favour of longevity and to fight infectious diseases.

Force Awards: awards ceremony

The SMARt-Lab project received the people's choice award at the ForceAwards. SMARt-Lab, which is coordinated by Prof. Nicolas Willand in partnership with Drs Marilyne Bourotte and Olivier Defert (for BioVersys) and Drs Alain Baulard and Ruben Hartkoorn (CIIL), is the result of a collaboration between U1177, the Institut Pasteur de Lille, the University of Lille, the Inserm, the Faculty of Pharmacy (UFR3S), Lille Infection and Immunity Centre and BioVersys AG, which began in 2019.



Chronodrive: when loyalty creates solidarity

Since October 2021, Chronodrive has been offering its customers the opportunity to turn their loyalty points into donations to help research to fight diseases.

To date, over 500 clients have shown their generosity in support of research and the Institut Pasteur de Lille. We thank Chronodrive for a great initiative and their customers for their support.



As part of Giving Tuesday, LCL supported the Institut Pasteur de Lille by encouraging employees and clients to make donations via social media, their website and various communication tools. We thank them for a wonderful solidarity initiative.

ROTARY

Fighting diseases with tulips



For the 2nd year in a row, the Lions Club in Aire-sur-la-Lys has shown support for the Institut Pasteur de Lille with "Tulips to fight cancer".

By selling flowers for charity, the Lions Club was able to distribute proceeds to three institutes specialising in cancer research and the treatment of patients, including the Institut Pasteur de Lille, for \in 6,000 each.

Many thanks to them.



GENEROSITY FOR OTHER CAUSES

Giving Tuesday 2022: collecting second-hand clothing

As part of Giving Tuesday, the IPL collected clothing and blankets for the Red Cross at the end of the year, for the benefit of people in need.

HEALTH EDUCATION



PREVENTIVE MEDICINE

[THE ROUTE TO LONGEVITY[®]]

Today the partnership between the Institut Pasteur de Lille and the Adimep is being made official with the deployment of the Route to Longevity[®] on the Toulouse territory, with the support of LCL. Created in 2017, the Route to Longevity[®] is a unique preventive medicine device consisting of a health check-up, personalised support and a one-year follow-up to allow everyone to play an active part in their own health.

AG2R La Mondiale supports the Nutrition & Physical Activity Department at the Institut Pasteur de Lille

Since 2015, AG2R La Mondiale has been supporting the Nutrition & Physical Activity Department at the Institut Pasteur de Lille in the conduct of health education projects via nutrition: this year, AG2R La Mondiale is supporting the "Nutrition & Fragility" project, aimed at offering health education via nutrition workshops to caregivers and recipients as well as handicapped people. The project also includes training on the subject for professionals in the structures, in order to launch a dynamic within the territories.



Every donation, every gesture counts *How can you support us?*

Donations, bequests and life insurance policies, events, solidarity races, online collections, corporate sponsorships and so on... Every contribution is essential to providing the Foundation with the means to advance research and develop the treatments of tomorrow.



As a donor and testator

A donation to the Institut Pasteur de Lille provides direct support to the research teams in their fight against diseases. Bequests, donations and life insurance policies also ensure the sustainability of our research.

Bequests and life insurance policies made up nearly 41% of Institut Pasteur de Lille private resources in 2022. Whatever its amount, a bequest, donation or life insurance policy forever unites the history of the benefactor (or testator) to the destiny of the Foundation. This act of transmission simultaneously helps to beautify the world and reveals the deep aspirations of our testators.

The Institut Pasteur de Lille is a foundation recognised for its public utility; as such, it is exempt from inheritance tax. Each bequest granted to the Institut Pasteur de Lille is worthy of tremendous respect, remembrance and recognition.

As a sponsoring company

Private funds are a major funding resource for the Foundation. The support of sponsoring companies is therefore essential to carry out the Foundation's ambitious research projects.

As a fundraiser

Anyone can commit, at their level and within their means, by initiating a solidarity action to raise funds to support our research work.

In 2022, a number of fundraising events were organised by individuals wishing to support research.

As a committed sponsor and volunteer

Putting one's popularity at the service of a good cause or giving a little of one's time alongside our teams is also a way of supporting our Foundation.

Thank you to our **57,000 donors!**

Thank γou to our corporate sponsors

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They made a bequest for research

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The Board of Directors of the Institut Pasteur de Lille ensures compliance with the fundamental values of the foundation and its statutes. It defines the organisation strategy and economic model, and controls implementation by the Managing Director.

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Bart STAELS - Director of unit U1011 "Nuclear receptors, cardiovascular diseases and diabetes"





Resources €39.1^M

€8.9 M resources collected from the public

Resources allocated to **2022** social missions in € €18 M products not related to public generosity

€12.2 M subsidies and other public funding

The Institut Pasteur de Lille contributes to fundamental research worldwide









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2022 ANNUAL REPORT

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Accelerate research and act for tomorrow's health.

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