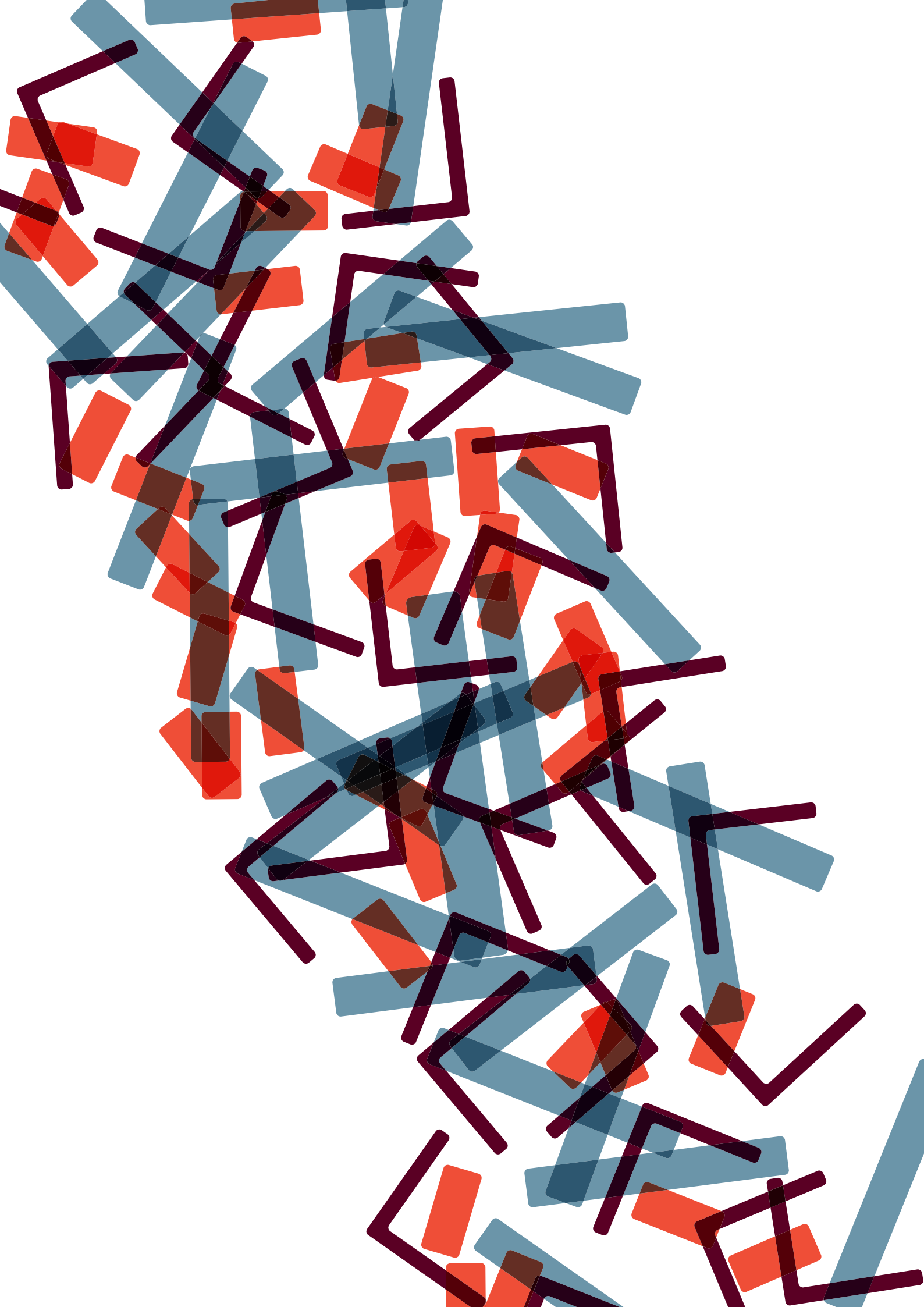


# LUXEMBOURG INSTITUTE OF HEALTH

RESEARCH DEDICATED TO LIFE

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ANNUAL REPORT 2017



# FOREWORD

## RESEARCH DEDICATED TO LIFE

The year 2017 marks the end of the four year period covered by the so-called Performance Contract 2014-2017 that was concluded with the Luxembourg Government. It draws to a close an important chapter in the evolution of LIH, which started with the merger of the former “Centre de Recherche Public de la Santé” (CRP-Santé) with IBBL-Integrated BioBank of Luxembourg at the end of 2014. Subsequent years have seen the restructuring of the departments within LIH and the appointment of two new Heads of Department - Prof Markus Ollert who has taken office in the Department of Infection and Immunity in 2014 and Dr Laetitia Huiart who became the Head of the Department of Population Health in 2017. The appointment of a new CEO Dr Ulf Nehrbass in late 2017 symbolises a natural starting point for the next step in the evolution of LIH.

I would like to acknowledge the outstanding achievements of LIH during this time, which are highlighted in part in this report. We have seen the steady increase of scientific output over the years from 228 publications in 2014 to 316 in 2017. Notable is not only the quantity per se but also the significant increase of contribution to high impact scientific journals, as we have seen a doubling of the share

(to 18%) of our publications figuring amongst the top journals (with impact factor >10). But in addition to the scientific excellence, the year 2017 has also been instrumental preparing strategic adjustments of LIH. Those allow Dr Nehrbass for a more translational positioning of the institute in the coming years, and a closer integration of IBBL in shared workflows.

I am deeply grateful to the Heads of Department for their constructive contribution and particularly to Dr Catherine Larue who as the CEO of IBBL has stepped in on a temporary basis to take over the leadership of the LIH in the last two years. At the end of year 2017 she has successfully passed the baton on to Dr Nehrbass and now continues to work for the shared translational objectives as CEO of IBBL.

  
Dr Gregor Baertz  
President of LIH's Board of Directors



*Board of Directors and Executive Management  
(from left to right): Karl-Heinz Dick (CFAO of LIH and IBBL),  
Xavier Poos (Commissaire de Gouvernement),  
Dr Viviane Bremer, Stéphanie Damgé, Patrizia Luchetta,  
Dr Gregor Baertz (president), Dr Nadine C. Martin (vice-president),  
Dr Ulf Nehrbass (CEO of LIH), Dr Catherine Larue (CEO of IBBL),  
Dr Hugues Malonne and Dr Robert Müller.  
Absent: Pierrot Schiltz, Prof Evelyn Schroeck.*

This is my first introduction to LIH's annual report, and while I cannot claim the accolades for this year's outstanding achievements, I can offer to share my "fresh" view on the institute and its operations. Before coming to Luxembourg, I have worked at a number of international research institutions, all of which came with a notion of "tradition". Tradition, however, is not a core value in today's fast moving health world. To the contrary:

*What matters is the ability to keep track of new concepts and approaches, to distinguish coming paradigm shifts from 'white tech-noise'. What matters is also the ability to accommodate and implement new concepts and ideas, and to make them resonate within the institute and the network of collaborators.*

All of these aspects seem to be very present in Luxembourg's dynamic research scene. Instead of tradition, then, there is outstanding competence, risk-taking and originality. Amongst research institutes here in Luxembourg there is an acute sense of opportunity and an ambition to achieve together, as a team.

This is also reflected within LIH. To start with, the science is of very high quality. In addition, LIH boasts the tools and building blocks of a next-generation translational institute. The institute appears to have been designed

with a clear anticipation of the challenges to come: biomedical research will increasingly depend on patient material and data. A future-oriented translational institute needs to cover the dimension of "population", it has to be able to "see" persons and patients in a holistic approach. It needs to connect bed to bench, with translational programmes retro-planned from a clinical perspective. It requires excellent biobanking facilities to unlock the patient dimension and produce quality data. Finally, of course, it needs to produce outstanding, high quality and original research.

LIH has all of that. The outstanding and original competences have been developed in their respective "incubators", the **Department of Population Health**, the **Department of Oncology**, the **Department of Immunity and Infection**, and **IBBL - Integrated BioBank of Luxembourg**. There obviously has been an element of splendid isolation, exacerbated through the physical fragmentation of LIH locations throughout the country. But I think LIH is now ready to present itself as a truly integrated institute. The diverse competences and expertise can be assembled in order to synergise around shared disease models. With a shared transversal medicine focus the diversity of LIH becomes a strength, able to cover large segments of a translational cycle that connects patients to research, and research results back to clinical applications.

LIH has the potential to become an internationally leading institute if it starts plying to its translational strength. Together with the partner institutions in Luxembourg, we will be able to make an impact on patients and their as yet unmet needs.

Dr Ulf Nehrass  
CEO of LIH





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## MISSION & VISION



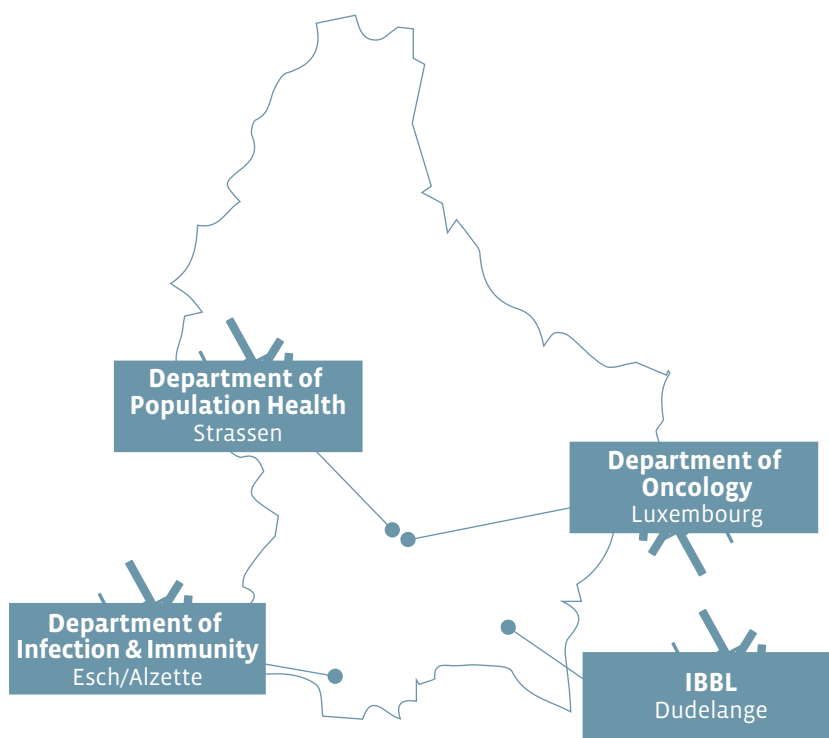


LH's **mission** is to impact on patients by performing and translating excellent biomedical research.

Its **vision** is to put Luxembourg at the forefront of biomedical research and create a translational hub in the heart of Europe.







## KEY FACTS

2017





# 3

RESEARCH  
DEPARTMENTS

# 1

BIOBANK



LUXEMBOURG  
INSTITUTE  
OF **HEALTH**  
RESEARCH DEDICATED TO LIFE

# 204


SCIENTISTS

# KEY FACTS\*

2017



**316**  
PUBLICATIONS



**12**  
NEW CLINICAL  
STUDIES



**205**  
AGREEMENTS  
SIGNED



**>270**  
ONGOING  
PROJECTS



**12.9** €  
MIO  
THIRD-PARTY  
INCOME

\*including IBBL



**22**

NEW PHD  
CANDIDATES



**36**

NATIONALITIES



**373**

EMPLOYEES



**41**

NEW PUBLIC-PRIVATE  
PARTNERSHIPS

# A NEW CEO FOR LIH

## Appointment of Dr Ulf Nehrbass

Since 1<sup>st</sup> October 2017, Dr Ulf Nehrbass, founder, Chief Executive Officer (CEO) and Scientific Director of Ksilink in Strasbourg, a French-German Translational Research Centre, has taken over the General Management of LIH. The new CEO plans to position the institute as an application-oriented research centre conducting research that impacts on patients.

Dr Nehrbass replaces Dr Catherine Larue who has guided the institute as CEO *ad interim* since January 2016 and who has returned to her former position of CEO of IBBL - Integrated BioBank of Luxembourg.

### Strong scientific background

After his biochemistry studies in Tübingen (Germany), and Cambridge (United Kingdom), Dr Nehrbass completed his PhD at the European Molecular Biology Laboratory in Heidelberg (Germany) in 1992. He was then offered the opportunity to work in the laboratory of the future Nobel Laureate, Prof Günter Blobel, at the Rockefeller University in New York (United States).

In 1998, he joined the “Institut Pasteur” in Paris (France) as Research Director to set up his own laboratory. Six years later, he became the Founder, CEO and Scientific Director of the brand new “Institut Pasteur” in Korea, specialised in infectious diseases and cancer research and aiming at translating research excellence towards therapies that impact on patients. The institute namely worked on a treatment against tuberculosis called Q203, the only new compound worldwide against totally drug-resistant tuberculosis bacteria.

Based on the success of the “Institut Pasteur” Korea, Dr Nehrbass was invited back to Europe to build a Franco-German institute with the same ethos. In 2013, he became the Founder, CEO and Scientific Director of Ksilink in Strasbourg, a centre created by seven

academic and public funding partners from France and Germany. Aiming for innovative therapeutic approaches, Ksilink is specialised in the modelling of diseases and personalised medicine, and aims at linking scientific and clinical excellence with biotechnology and pharmaceutical industry. The centre is well on its way to success.

### Spearhead next generation healthcare

At the forefront of technology development, Dr Nehrbass has witnessed first-hand the transformative potential it can have on healthcare. Luxembourg, through its intense investment over the last decade, is leading in key aspects of this technology trend. The next step will now be to translate scientific breakthroughs into actual improvement for patients. LIH will take a coherent translational approach to address unmet patient needs. According to Dr Nehrbass, Luxembourg's researchers and clinicians are already working in this direction and the country is ideally positioned to lead the way with its openness, flexibility and ingenuity.

## BIOGLOSSARY

The idea behind **personalised medicine** is that healthcare can be customised to fit the unique characteristics of each person's or group of individuals' disease.

**Translational research** is oriented towards application by using findings from basic science to improve human health and wellbeing.

**Tuberculosis** is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* that affects the lungs.

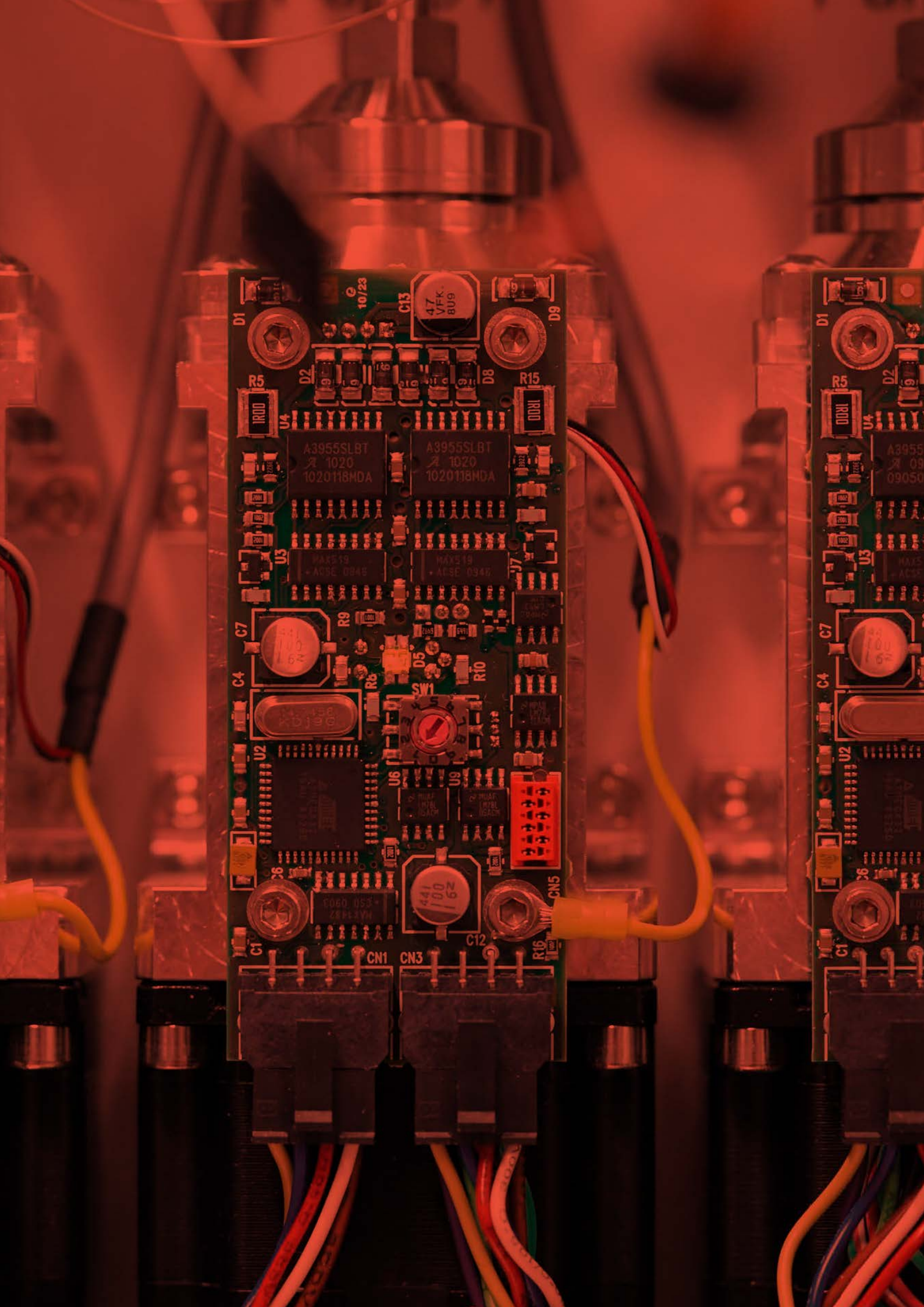
A portrait of Dr. Ulf Nehrbass, a middle-aged man with short brown hair, wearing a dark suit, light blue shirt, and a patterned tie. He is looking slightly to the right with a calm expression. The background is a solid blue color. Overlaid on the image are several large, abstract white and black geometric shapes, including a large white 'L' shape and various black polygons.

“

*I am convinced that LIH -  
in close collaboration with the other  
Luxembourgish research partners -  
will play an important role in building  
effective translational programmes,  
which will impact on patients.”*

*Dr Ulf Nehrbass, new CEO of LIH*







**SCIENTIFIC  
ADVANCEMENTS**







# A MASTER DETOX MOLECULE BOOSTS THE IMMUNE DEFENCE

Revealing an unknown immune mechanism

LIH scientists analysed the function of glutathione, a molecule produced amongst others by T cells and known for its role in cleaning the body from harmful metabolic waste. Their research uncovered that glutathione promotes the activation of the human immune system by stimulating the energy metabolism of T cells.

Glutathione is key in helping T cells getting enough energy to grow, divide and fight off intruders when in contact with pathogens. It is thus essential for an optimal immune response. This discovery offers starting points and perspectives to develop new therapeutic strategies for targeting cancer and autoimmune diseases.

## An antioxidant with a dual role

Immune cells such as T cells normally reside in a state of alert hibernation, with their energy consumption reduced to a minimum. If pathogens get in contact with the T cells, these wake up and boost their metabolism, to produce more energy. This necessarily creates greater amounts of metabolic waste products such as reactive oxygen species and free radicals, which can be toxic for the cells. When the concentration of these oxidants increases, the T cells have to produce more antioxidants so as not to be poisoned.

No previous research group had studied the mechanism of action of antioxidants in T cells to great detail before. In exploring this phenomenon, the scientists discovered that the antioxidant glutathione produced by T cells serves not only as a garbage collector to dispose of metabolic waste products, it is also a key switch for energy metabolism that controls the immune response, and is thus of high relevance to various diseases.

## Essential for T cell function

For their investigations, the scientists used mouse models having T cells unable to produce glutathione. Without glutathione, T cells do not become fully functional; they remain in their state of hibernation. The mice thus presented a marked immunodeficiency. They were unable to control viral infections but also to develop any autoimmune disease such as multiple sclerosis.

The research group sees the results of their study as a prelude to more in-depth investigation of the energy balance of immune cells. A number of different autoimmune diseases are related to malfunctions in various subgroups of T cells. By understanding the differences in the molecular mechanisms by which they stimulate their metabolism to get energy during defensive or autoimmune responses, it becomes possible to discover clues as to potential attack points for therapeutic agents regulating the immune response.



Prof Dirk Brenner

## Publication:

The study was published in the April 2017 issue of the world's most prestigious immunology journal *Immunity*. The publication, entitled "Glutathione Primes T Cell Metabolism for Inflammation", is co-first-authored by postdoctoral researcher Dr Melanie Grusdat and last-authored by Prof Dirk Brenner.

## Funding & Collaborations:

Prof Dirk Brenner holds an ATTRACT Consolidator grant from the Luxembourg National Research Fund (FNR).

The study was performed in close collaboration with the former FNR ATTRACT fellow Prof Karsten Hiller of the Metabolomics Group at the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg (now full Professor at the Integrated Centre of Systems Biology of the Braunschweig University of Technology, Germany) and with Prof Tak W. Mak, Director of the Campbell Family Institute for Breast Cancer Research at the University of Toronto (Canada).

## BIOCABULARY

An **autoimmune disease** is a disorder in which immune responses are directed against one's own healthy cells and tissues.

**Glutathione** is an antioxidant molecule present inside cells that is capable of preventing damage caused by reactive oxygen species to important cellular components.

**Immunodeficiency** disorders prevent the body from fighting infections and diseases.

**Immunotherapy** is a treatment that uses the body's own immune system to fight a disease.

A **pathogen** is a microorganism that can cause disease.

**T cells** are white blood cells that play a central role in the immune system.





## Master detox molecule boosts immune defence



T cells are a type of white blood cells that circulate around our body, scanning for cellular abnormalities and infections.



As all cells they produce a compound called glutathione, a master detox molecule ...



... which, among other things, cleans the body from harmful waste produced by the cells' functioning.



T cells normally reside in a state of alert hibernation, with their energy consumption reduced to a minimum.



When in contact with a pathogen, they wake up, consume more energy and produce therefore more glutathione to clean the waste surplus.



LIH researchers discovered a new additional role of glutathione: the molecule is also key in helping T cells getting enough energy to boost immune defence ...

... and fight off intruders!



This discovery offers starting points and perspectives to develop new therapeutic strategies for targeting cancer and autoimmune diseases.

©Communication LIH

Cartoon developed to promote the research results to the media and the lay public

“ These fascinating results form a basis for a targeted intervening in the metabolism of immune cells and for developing a new generation of immunotherapies treating auto-immune diseases, but also fighting off cancer! ”

Prof Dirk Brenner, Principal Investigator

# BRINGING NATURAL KILLER CELLS TO THE TUMOUR BATTLEFIELD

## Autophagy blockade in skin cancer

By studying melanoma, LIH researchers revealed a mechanism by which the immunosuppressive tumour environment can be switched to an immunosupportive one. When autophagy is blocked in tumour cells, Natural Killer (NK) cells can be massively recruited and efficiently kill malignant cells to let tumours shrink.

### Targeting autophagy

NK cells play a major role in the immune response against tumours. However, cancer cells can circumvent this immune defence by establishing a microenvironment that prevents the infiltration of NK cells and thus promotes tumour survival and growth. Therefore, a key issue in the field of anti-cancer immunotherapy is to develop strategies capable of driving immune cells into the tumour bed.

For several years already, it has been known that tumour growth can be reduced by suppressing autophagy in cancer cells. While autophagy blockade is believed to render tumours more sensitive to chemotherapy, its impact on anti-tumour immunity is not well understood. The scientists revealed that, when the autophagy process is blocked in tumour cells, a large amount of functional NK cells infiltrated into the tumour and this led to a significant reduction in tumour size.

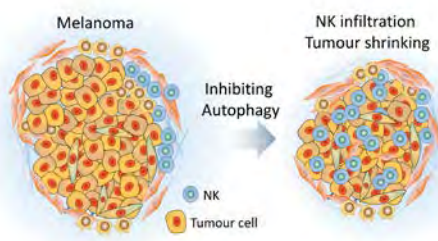


Illustration of the effect of autophagy inhibition on tumours

### Attraction to the tumour bed

The autophagy-defective tumour cells were found to produce an increased amount of CCL5, a small cytokine able to attract NK cells to the tumour bed. When CCL5 is depleted, the infiltration of NK cells and the subsequent regression of tumour volume were no longer observed, thus confirming the crucial role of CCL5 in driving NK cells into autophagy-defective tumours.

Using tumour biopsies from melanoma patients, the researchers could show that there is a positive correlation between the production of CCL5 and the infiltration of NK cells. The more CCL5 is produced, the stronger tumours are infiltrated with NK cells. A high level of production of CCL5 was also found to have a positive impact on the survival of melanoma patients.

This is the first time that a mechanistic link between autophagy and NK cell recruitment could be established. The researchers are now planning to address the impact of targeting autophagy on the immune landscape of melanomas by studying other immune cells in the tumour microenvironment. The ultimate goal of this research is to provide the proof of concept that targeting autophagy could improve the efficacy of current immunotherapies.



Dr Bassam Janji

“Our study provides a cutting edge advance in the field of cancer immunotherapy and could specifically pave the way for more effective NK cell-based treatments.”

Dr Bassam Janji, Principal Investigator

### Publication:

The publication titled “Targeting autophagy inhibits melanoma growth by enhancing NK cells infiltration in a CCL5-dependent manner” appeared in open access in the October 2017 issue of the acclaimed scientific journal *Proceedings of the National Academy of Sciences of the United States of America*. It was first-authored by PhD candidate Takouhie Mgrditchian and last-authored by Dr Bassam Janji.

### Funding & Collaborations:

The project was supported by grants from the Luxembourg National Research Fund, F.R.S-FNRS Télévie, the Luxembourg Cancer Foundation “Fondation Cancer”, the Calouste Gulbenkian Foundation, “Ligue contre le Cancer” and the French National Cancer Institute.

The research project was carried out by members of the Laboratory of Experimental Cancer Research working in close collaboration with other research entities in Luxembourg: the National Cytometry Platform within LIH’s Department of Infection and Immunity, the Life Sciences Research Unit of the University of Luxembourg, the “Laboratoire national de santé” and the “Centre Hospitalier de Luxembourg”. Valuable partners were as well the renowned Gustave Roussy Cancer Centre in Villejuif (France) and the University Hospital of Besançon (France).

## BIOCABULARY

**Autophagy**, literally “self-eating”, is an essential physiological process for the degradation and recycling of cellular components.

**Cytokines** are small proteins released by cells that trigger cell signalling and affect the behaviour of surrounding cells.

**Immunotherapy** is a treatment that uses the body’s own immune system to fight a disease.

**Melanoma** is a highly malignant form of skin cancer that develops from the pigment-containing cells named melanocytes.

**Natural killer cells** are immune cells with strong cytotoxic activity, capable of killing abnormal and infected cells.

# IMPROVING STATISTICAL METHODOLOGY FOR SMALL POPULATION CLINICAL TRIALS

Completion of the European project IDeAl

Over 30 million European citizens suffer from rare diseases with an incidence of fewer than five in 10,000 people. The European project IDeAl for “Integrated Design and Analysis on small population group trials”, involving LIH as a partner, addressed the limitations of conventional statistical methodology in evaluating new therapies in clinical trials.

## Limited sample sizes for rare diseases

From 2000 to 2010 in Europe alone, over 60 orphan drugs have been approved with the majority based on studies with sample sizes below 50. Ethical limitations and age variability in paediatric clinical trials also limit sample size, as do studies on personalised medicine where efforts to tailor therapies to individual patients' needs significantly lower the participant number.

Statistical methodology is well accepted for validating the results of clinical trials and proving the efficacy and safety of new therapies. However, most statistical methods are suited for large population studies where assumptions on the validity of the methods are usually handled by increasing the sample size. This cannot be implemented in small group trials where the rarity of the disease or the sparse geographic distribution of patients hampers clinical trial recruitment numbers.

There is an imminent need for adopting innovative methodologies in the setting of small sample population group trials. To address this, the scientists of the IDeAl project proposed to refine statistical methodology for application in small population group trials such as those testing novel therapies for rare diseases. LIH's Competence Centre for Methodology and Statistics was leading one of the work packages of this project.

## Addressing the shortcomings of existing methods

When applied to small population size trials, conventional statistical methodology leads to reduced confidence. Furthermore, it cannot adequately address heterogeneity in patient outcome or the limited repeatability of clinical trials. To circumvent these issues, IDeAl researchers developed statistical methods to adapt the significance level and allow confirmatory decision-making in clinical trials with small populations.

In addition, they developed methodology for the selection of the best practice randomisation procedure, a key technique used in clinical trials to avoid bias. Importantly, the tools, software packages and the 33 recommendations generated during the IDeAl project will support clinical research of rare diseases and pave the way for medical and pharmaceutical advances.

“The methodological progress achieved by the IDeAl project will improve the design and analysis of clinical trials on treatments for rare diseases, leading to more cost-effective and reliable studies.”

*Prof Stephen Senn, IDeAl project partner and Head of the Competence Centre for Methodology and Statistics*



*Prof Stephen Senn*

## Funding & Collaborations:

IDeAl was funded by the 7<sup>th</sup> Framework Programme for Research and Technological Development of the European Commission. The multiparty research project, coordinated by the University Hospital Aachen (Germany) was successfully completed after having run for 3.5 years until mid-2017.

## BIOGLOSSARY

**Clinical trials** are research studies on human participants that evaluate a medical, surgical, or behavioural intervention. They are part of the drug development process.

An **orphan drug** is a drug developed to treat a specific rare disease.

**Randomisation** in clinical trials means dividing the participants by chance into separate groups to compare different treatments or interventions.

# IS THERE A LINK BETWEEN MIGRATION STATUS AND DEPRESSION BURDEN?

Nationwide study assessing depression symptoms

What is the proportion of people with depression in Luxembourg? This is the question that an LIH study aimed to answer and hereby revealed surprising differences between non-immigrants, first- and second-generation immigrants.

Depression is a multifaceted psychological disorder that is thought to affect about 350 million people on the globe. The World Health Organisation considers it as the leading cause of disability worldwide and a major contributor to the overall global burden of disease. A precise assessment of the prevalence of depressive symptoms and associated risk factors was missing in Luxembourg.

## More than 20% concerned

LIH initiated a nationwide study using cross-sectional data from the European Health Examination Survey conducted in Luxembourg from 2013 to 2015. This survey included almost 1,500 people aged between 25 and 64, a representative sample of the country's resident population. Participants completed a standardised Patient Health Questionnaire that assesses self-reported symptoms of depression based on nine diagnosis criteria for depressive disorders.

The prevalence of depressive symptoms was found to be 21.5% overall - 16.6% in men and 26.2% in women. These results are comparable with those of other studies conducted in different parts of the world. The study also investigated whether there were differences between non-immigrants and first and second generation immigrants.

## Second-generation immigrants at risk

A particularity of Luxembourg is its stable and attractive economy that favours immigration. In 2014, Luxembourg was the country with the highest immigration rate in the European Union. At the time of the study, 46% of the residents were non-Luxembourgers. Given this high proportion, the scientists decided to investigate whether there is an association between depressive symptoms and immigration status.

The research team observed differences between non-immigrants and immigrants, both in men and women. Immigrants, especially second-generation immigrants, meaning those born in Luxembourg with at least one parent born in a country other than Luxembourg, were found to be at higher risk for depressive symptoms compared to non-immigrants. The causes for these results would need to be investigated further.



Dr Maria Ruiz-Castell

“*Being from two cultures may lead to challenges of integration or emotional internal conflict - possible explanations for our findings on the prevalence of depression in the multicultural Luxembourg population.*”

Dr Maria Ruiz-Castell, project leader

## Publication:

The article titled “Depression burden in Luxembourg: Individual risk factors, geographic variations and the role of migration, 2013–2015 European Health Examination Survey” was published in the November 2017 issue of the *Journal of Affective Disorders*. It is first-authored by Dr Maria Ruiz-Castell.

## Funding & Collaborations:

This study was funded by the Directorate and the Ministry of Health.

It was conducted with collaborators from LIH's Competence Centre for Methodology and Statistics and the INSIDE Research Unit of the University of Luxembourg.

BIOGLOSSARY

**Cross-sectional data** are data that are collected from many participants at one time point.  
**Prevalence** refers to the proportion of people having a condition.



# GETTING INSIGHTS INTO THE METABOLIC CHAOS IN BRAIN TUMOURS

State-of-the art technologies for a look into the brain

Gliomas are heterogeneous brain tumours with a poor prognosis. To better understand their biology, LIH researchers characterised in depth the metabolic characteristics of gliomas carrying specific mutations that affect the function of a metabolic enzyme.

Lower grade gliomas frequently acquire mutations in the genes encoding the enzyme isocitrate dehydrogenase 1 and 2, shortly IDH, involved in the cell metabolism. The presence of IDH mutations is a major determinant in the classification of these gliomas. The mutations confer a more favourable disease evolution, with a significantly extended life expectancy for these patients. In parallel, it is known that IDH mutations lead to aberrant enzymatic activity and the extensive production of a metabolite named D-2-hydroxyglutarate, which interferes with cellular functions.

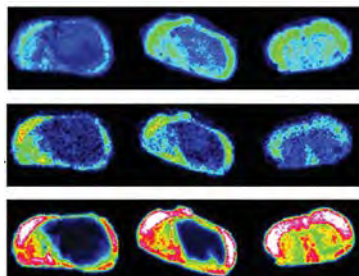
## Monitoring metabolite distribution

The alterations caused on cell metabolism remain poorly understood. Therefore, the researchers aimed to further investigate the metabolic consequences of IDH mutations, hoping to discover potential hints for new targets to interfere with cancer growth.

For this, they used small animal models (mice carrying glioma derived from human patients), as well as clinical glioma samples with and without IDH mutation.

Complementary technological approaches were used to visualise and analyse metabolite presence in the brain: mass spectrometry imaging and liquid chromatography coupled to mass spectrometry.

In glioma with IDH mutation they revealed the deregulation of numerous biological processes. The tumours showed an aberrant phospholipid metabolism, a reduced glucose turnover and lower energy potential, alterations in the abundance of amino acids and neuropeptides as well as differences in defence mechanisms against oxidative stress.



Metabolite distribution in brain tumours in mice models monitored by mass spectrometry imaging



Dr Fred Fack

“We identified important metabolic abnormalities in the tumours with the mutations, of which some could be targeted to develop anti-cancer treatments.”

Dr Fred Fack, project leader

## Publication:

The publication titled “Altered metabolic landscape in IDH-mutant gliomas affects phospholipid, energy, and oxidative stress pathways” appeared in open access in the prestigious journal *EMBO Molecular Medicine* in October 2017. Dr Fred Fack holds the joint first authorship and Prof Simone Niclou, Head of the NorLux Neuro-Oncology Laboratory, is the last and corresponding author.

## Funding & Collaborations:

The project was supported by the foundation Stiftelsen Kristian Gerhard Jebsen in Norway and intramural funding.

The research work stems from a collaboration with the Proteome and Genome Research Unit at LIH's Department of Oncology, the Beatson Institute for Cancer Research (Glasgow, United Kingdom), ImaBiotech (Loos, France), the Radboud University Medical Centre (Nijmegen, Netherlands) and the University of Bergen (Norway).

## BIOCABULARY

**Amino acids** are essential biomolecules in metabolic processes. They are also the building blocks of peptides and proteins.

An **enzyme** is a protein that can accelerate biochemical reactions in the cell.

**Glucose** is a sugar that constitutes an important source of energy for the cells.

**Liquid chromatography** is an analytical technique used to separate molecules in a sample.

**(Lower grade) gliomas** are aggressive and frequent tumours of the brain originating from a cell type named glial cells.

**Mass spectrometry** is an analytical technique that allows identifying and quantifying individual molecules based on their mass.

With **mass spectrometry imaging** one can visualise the distribution of molecules in a biological sample.

A **metabolite** is a molecule, generally small, formed in or necessary for metabolism.

A **mutation** is a permanent alteration in the DNA sequence that makes up a gene.

A **neuropeptide** is a molecule composed of amino acids used by neurons to communicate with each other.

**Oxidative stress** is caused by an imbalance between oxidants and antioxidants in the cell.

The **phospholipid metabolism** regulates the production of phospholipids, the major lipid type in cell membranes.

# AN ESTIMATION OF WORLDWIDE HEPATITIS C INFECTION

Luxembourg data served in global study

Can mankind get hepatitis C infection under control? The hepatitis C virus (HCV) can be transmitted from one human to another by the exposure to small quantities of blood. The population group being most at risk are drug users with unsafe drug injection practices.

A strategy presented in 2016 about the care and management of hepatitis infection at the World Health Assembly gives the objectives of the World Health Organisation (WHO): a 65% reduction in liver-related deaths, a 90% reduction of new hepatitis infections, and 90% of patients with hepatitis infections being diagnosed by 2030. It is in this context that LIH scientists contributed to two international studies on the global prevalence and the prevalence in Europe of hepatitis C infection.

## Large data collection

To get a global estimate on hepatitis C infection, a large consortium of researchers and clinicians provided data from 100 countries - including Luxembourg - representing more than 85% of the world's population. The data was collected from a systematic review of the literature on prevalence and genotype after the year 2013, complemented with interviews with 400 country experts to identify missing inputs and approve data.

The combination of all the data sets allowed estimating the prevalence of HCV to 0.1% in 2015, which corresponds to 71.1 million people. This percentage is lower than in previous less precise estimations. HCV genotypes 1 and 3 were found to be the most common cause of infection. This study is of high relevance for the development of strategies at country and regional level to control the hepatitis burden by 2030.

The European study assessed the burden of HCV infection in the 28 EU member states and evaluated the level of intervention required to achieve the WHO goals. A similar methodology was employed as for the global study. The prevalence for HCV was estimated to 0.63% in 2015, corresponding to 3.2 million infections. The authors claim that the WHO targets are achievable in Europe with a united effort.



Dr Carole Devaux

“As local experts on hepatitis C infection, it was key for us to bring our contribution to such large and crucial studies.”

Dr Carole Devaux, Principal Investigator

## Publications:

Both publications appeared in the journal *The Lancet Gastroenterology & Hepatology*. “Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study” was published in March 2017 and “Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study” in May 2017.

## Consortia:

The global study was conducted by a large consortium, the “Polaris Observatory HCV Collaborators”. The Polaris Observatory, an initiative of the non-profit CDA Foundation, was created in 2015 to monitor and forecast the disease burden for hepatitis B and C and provide decision analytics to support the worldwide elimination of hepatitis.

The European study was led by a consortium named “European Union HCV Collaborators”.

## Contributors:

Dr Carole Devaux and Daniel Struck provided the data sets for Luxembourg in both studies, and validated and optimised the input of the modelling as local HCV experts, with Dr Vic Arendt from the National Service for Infectious Diseases of the “Centre Hospitalier de Luxembourg”, Dr Joël Mossong from the “Laboratoire national de santé” and Patrick Hoffmann from the Ministry of Health.

## BIOGLOSSARY

The **genotype** is the entire genetic constitution/identity of an organism. The term can also refer just to a particular gene or set of genes.

**Hepatitis C** is a disease of viral origin that is characterised by an inflammation of the liver that can be acute or chronic. It may develop into chronic cirrhosis and liver cancer if not diagnosed early and treated adequately.

**Prevalence** refers to the proportion of people having a condition.

# HYPERMETABOLIC BLOOD CANCER CELLS RESIST TO CHEMOTHERAPY

LIH's genomics know-how valued

A study led by a team from the public research organism Inserm in France revealed new findings about the molecular mechanisms of drug resistance in blood cancer. LIH scientists could contribute with their recognised expertise in bioinformatics and genomic analysis.

Several months after an apparently successful chemotherapy, patients with human acute myeloid leukaemia often relapse. It was hypothesised that this is due to chemo-resistant immature leukemic stem cells that survive, but the present research work revisits this assumption.

## Refuting a hypothesis

In this study, the scientists used mouse models mimicking disease evolution from patients' cells. When treating the animals with chemotherapy medication, they observed that the treatment killed both resting and proliferating cancer cells and that the remaining chemo-resistant cells presented a high energetic status, meaning an increased function of their mitochondria. The resistance of leukemic cells thus seems to depend on their metabolic activity.

The scientists then tested pharmacological agents inhibiting mitochondrial metabolism in combination with chemotherapy and could show that treatment efficacy was enhanced. In the frame of this research work, scientists from LIH conducted some of the genomics experiments and performed data analysis. They could identify a gene signature able to predict patient response to chemotherapy.



Tony Kaoma

“ Our know-how was already valued in several collaborations with the French team. A follow-up study is planned that will include more patients and other data analysis in order to optimise our prediction model.”

Tony Kaoma, bioinformatician

## BIOCABULARY

**Hypermetabolism** is the physiological state of increased rate of metabolic activity.

**Genomics** (genomic analysis) is the large-scale study of the genome, the genetic material of an organism, in a biological sample (cell, tissue, organ, biological fluid or organism).

**Adult acute myeloid leukaemia** is a blood cancer that leads to the rapid growth of abnormally differentiated myeloid cells (myeloblasts, red blood cells, platelets). It builds up in the bone marrow and interferes with the production of normal blood cells.

A **stem cell** is an undifferentiated cell that can give rise to different cell types.

**Mitochondria** are structures inside the cell that generate the energy necessary to run all cellular functions.

A **gene signature** is an alteration in gene expression involving one or more genes that can be related to a biological process or pathogenic medical condition.

## Publication:

The article titled “Chemotherapy resistant human acute myeloid leukaemia cells are not enriched for leukemic stem cells but require oxidative metabolism” was published in *Cancer Discovery*, one of the top ten journals in oncology, in April 2017.

## Collaborations:

The project was led by the RESISTAML research group at the Cancer Research Centre of Toulouse (France) belonging to Inserm and involved several collaborations. The collaborators from LIH were Dr Laurent Vallar and Tony Kaoma.

# ADVANCED CYTOMETRY-BASED RESEARCH AND SERVICES

Technology that moves biomedicine forward

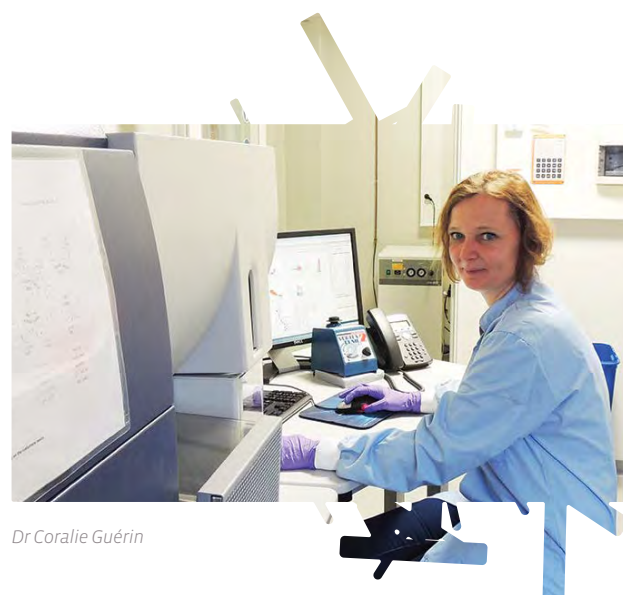
LIH comprises the National Cytometry Platform, shortly NCP. It is a shared resource facility that is available to assist scientists with the design of cytometry experiments, data acquisition, cell sorting and data analysis. It is equipped with state-of-the-art flow, image and mass cytometry instruments. In 2017, the platform contributed with its expertise to internal and external research works that led to three major publications.

The NCP was involved in a research project led by the Laboratory of Experimental Cancer Research in LIH's Department of Oncology featured earlier in this annual report (page 24). The article published in *Proceedings of the National Academy of Sciences of the United States of America* in October 2017 reports on a mechanism blocking the progression of skin cancer.

Another research work involving the NCP was conducted by groups from University Paris-Descartes and Inserm (Paris, France). The scientists analysed a therapeutic strategy to promote vascularisation and muscular recovery in critical limb ischemia. The results were published in the *Journal of Thrombosis and Homeostasis* in October 2017.

In a third remarkable study from different research groups and universities in Paris, the NCP contributed to novel insights into the pathogenesis of a kidney disease called focal segmental glomerulosclerosis. These findings were published in the *Journal of the American Society of Nephrology* in December 2017.

In addition to these valuable contributions, the NCP also succeeded in obtaining an ISO 9001:2008 certification for quality management. The platform underwent an evaluation process that included the development of a quality management system, a management system documentation review, a pre-audit and an initial assessment. Thanks to the certification, the internal and external users of the NCP can be confident that the platform is dedicated to maintaining the highest efficiency and responsiveness in achieving quality services.



Dr Coralie Guérin

“ The National Cytometry Platform, embedded within a highly advanced research environment, gives us multiple opportunities for international collaboration with academic and private partners.”

Dr Coralie Guérin

## BIOGLOSSARY

**Cytometry** is a technology that allows measuring the physical and chemical characteristics of cells. There are variations of the technology (flow, mass or imaging cytometry) serving different applications.

**Focal segmental glomerulosclerosis** is a rare disease that attacks the kidney's filtering units causing serious scarring which leads to permanent kidney damage or even failure.

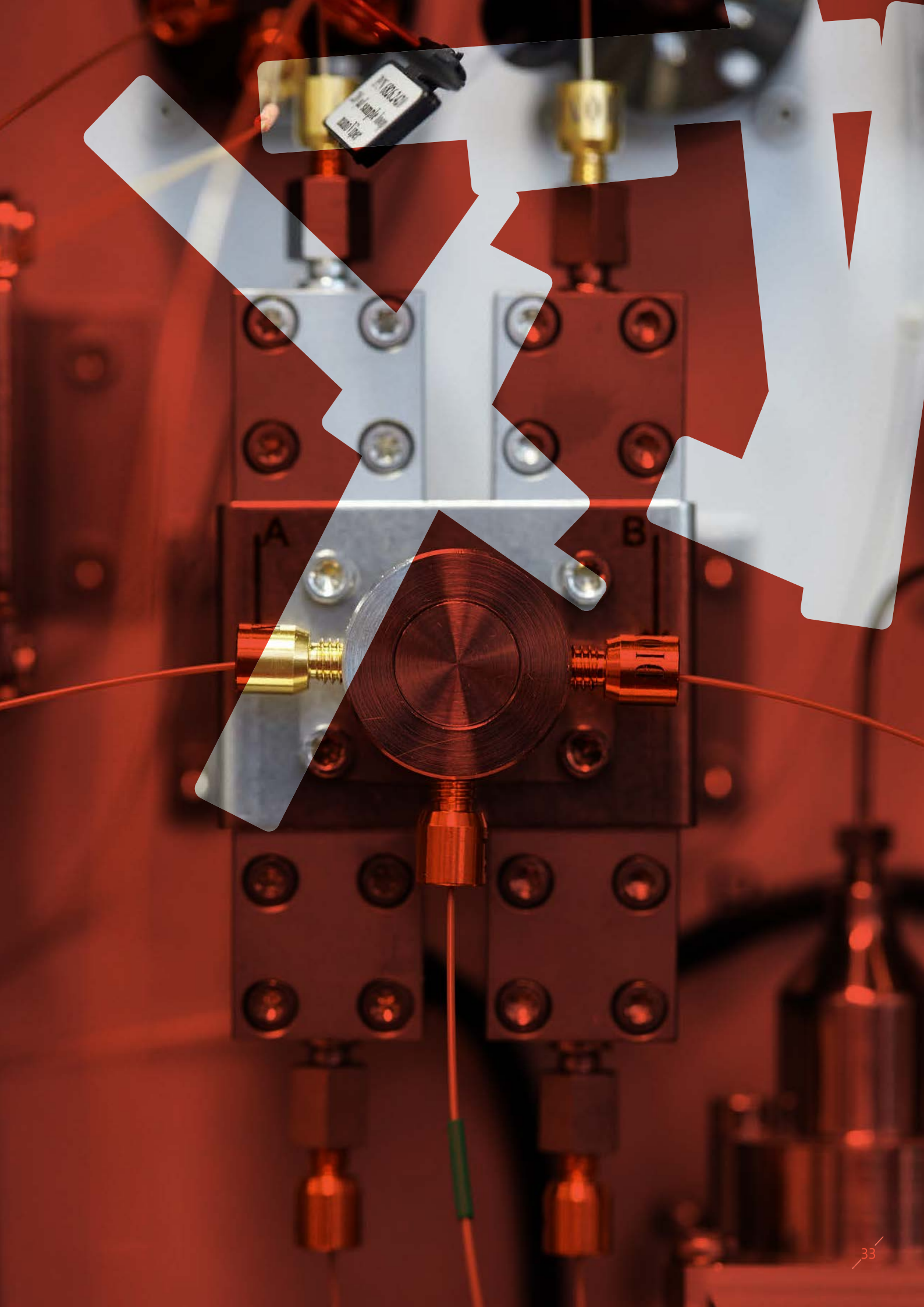
**Critical limb ischemia**, an advanced stage of peripheral artery disease, is a severe obstruction of the arteries considerably reducing the blood flow to the body's extremities.



## NEW RESEARCH CHALLENGES









# CLINICAL TRIALS ON A DRUG FOR A RARE MUSCULAR DISEASE

Leading role in the VISION-DMD project

VISION-DMD is a European project, which has been initiated to advance the clinical development of the orphan drug vamorolone for the treatment of Duchenne muscular dystrophy (DMD). LIH's Clinical and Epidemiological Investigation Centre (CIEC) plays a key role in the project as it has been designated to coordinate part of the clinical trials in six European countries, with the ultimate goal of introducing the drug on the market.

The rare genetic disease DMD affects approximately one in 3,500 to 5,000 male births. Untreated, boys become progressively weaker during childhood, losing independent ambulation, with an early death. The disorder still remains incurable. Long-term use of glucocorticoids is widely, yet not universally accepted as standard of care. This treatment is however associated with severe side effects.

## Clinical trials coordinated internationally

Vamorolone is an innovative first generation steroid drug specifically designed to retain or improve the benefits of glucocorticoids as treatment in DMD whilst aiming to reduce the side effects that currently restrict their use. With VISION-DMD, a series of Phase 2b trials with the new drug shall be conducted in Europe, the United States, Canada, Israel and Australia.

CIEC is a Scientific Partner in the European Clinical Research Infrastructure Network (ECRIN). Thanks to its strong expertise in coordinating clinical trials and its involvement in ECRIN, CIEC was chosen as the Lead Clinical Trial Unit for the clinical Phase 2b trial in more than ten reference sites across Belgium, Czech Republic, Germany, Italy, Poland and the Netherlands.



Dr Nancy De Breaecker

“ We are proud that our Luxembourgish centre was given a coordinating role in an international consortium.”

Dr Nancy De Breaecker, project leader of VISION-DMD at CIEC

## Project consortium:

VISION-DMD brings together leading international teams in the DMD field including Newcastle University's John Walton Muscular Dystrophy Research Centre (United Kingdom), the international academic clinical trial network Cooperative International Neuromuscular Research Group with its coordinating centre Therapeutics Research in Neuromuscular Disorders Solutions (United States), and ECRIN (France). The involvement of United Parent Projects Muscular Dystrophy (Netherlands) ensures that DMD patient groups have input into the project. ReveraGen Biopharma is the drug sponsor of vamorolone and holds the orphan drug designations. Ceratium Ltd (United Kingdom) and University Hospital Motol (Czech Republic) complete the project consortium.

## Funding:

Drug development is enabled thanks to innovative venture philanthropy through patient group funding and public investment. Amongst other funding sources, VISION-DMD has received support from the European Union's Horizon 2020 Research and Innovation Programme.

## BIOCABULARY

**Clinical trials** are research studies on human participants that evaluate a medical, surgical, or behavioural intervention. They are part of the drug development process.

**Duchenne muscular dystrophy** is an incurable genetic disorder, mainly affecting males, characterised by progressive muscle degeneration and weakness.

**Glucocorticoids** are of steroid drugs.

An **orphan drug** is a drug developed to treat a specific rare disease.

**Phase 2b** is a stage within a clinical trial. Its objective is the identification of the optimum dose at which a drug shows biological activity with minimal side effects.

A **steroid drug** is an active component that is structurally similar or identical to a steroid, which is a type of hormone.

# IMPROVING TREATMENT OUTCOMES FOR GLIOBLASTOMA PATIENTS

## Involvement in the European project GLIOTRAIN

A four-year doctoral research and training programme named GLIOTRAIN was launched in September 2017 and aims at improving treatment outcomes for patients while contributing to the training of the next generation of brain cancer researchers. LIH is part of this multiparty European project led by the Royal College of Surgeons in Ireland.

GLIOTRAIN will focus on glioblastoma, a brain cancer that has a universally fatal prognosis, with 85% of patients dying within two years. New treatment options for glioblastoma patients and effective personalised treatments are urgently required. The project therefore aims to identify novel therapeutic strategies, and will use state of the art genomics and systems biology approaches to unravel disease resistance mechanisms.



Prof Simone Niclou

“GLIOTRAIN will allow doctoral candidates to benefit from excellent training conditions and get in contact with both the academic and the industry work environment.”

Prof Simone Niclou, Head of the NorLux Neuro-Oncology Laboratory

The consortium brings together leading European and international academics, clinicians, private sector and not-for-profit partners. In this context, 15 PhD candidates shall be trained across the fields of tumour biology, medical oncology, systems biology, genomics, cancer drug delivery and immunotherapy. Two PhD projects are planned to be conducted in Luxembourg, one at the NorLux Neuro-Oncology Laboratory, the other at ITTM Solutions, a spin-off of the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg. Both projects will stimulate the collaboration between the two organisms.

### Project consortium:

The project, coordinated by the Royal College of Surgeons (Ireland), involves major partners across Europe, including collaborators in Ireland (Cancer Trials Ireland); Germany (University of Stuttgart, Hannover Medical School, GeneXplain, Insilico Biotechnology, Yumab); Luxembourg (LIH, ITTM Solutions); Belgium (VIB, University of Leuven, Oncurios, Agilent Technologies); France (ICM Brain and Spinal Institute Paris, Bristol Myers Squibb, CarThera); the Netherlands (Erasmus Medical Centre, Teva Pharmaceuticals, Mimetas, Pepscope) and the United Kingdom (International Brain Tumour Alliance), as well as a partner in the United States (Champions Oncology).

### Funding:

GLIOTRAIN is supported by the European Commission's Horizon 2020 Marie Skłodowska-Curie Actions Programme as an Innovative Training Network.

## BIOGLOSSARY

**Glioblastoma** is the most frequent, aggressive and lethal of all brain tumours.

**Genomics** is the large-scale study of the genome, the genetic material of an organism in a biological sample (cell, tissue, organ, biological fluid or organism).

**Immunotherapy** is a treatment that uses the body's own immune system to fight a disease.

**Systems biology** is the computational and mathematical modelling of dynamic systems of biological components, which may be molecules, cells, organisms or entire species.

# GOOD RUNNING SHOES, FEWER INJURIES?

A new large-scale sports medicine study

What is the link between running shoes and injury risk? To address this question, the Sports Medicine Research Laboratory launched a major study in September 2017, closely monitoring 800 volunteer regular runners during a period of six months.

The majority of running injuries are overload injuries of the lower limbs that occur due to excessive or inappropriate biomechanical constraints, for example during over-intensive training, and develop progressively. It is therefore important to determine whether the running technique has an impact on injury risk. It has been proven that the running shoe, and in particular its cushioning, can influence the running technique.

## Wanted: 800 volunteer runners

The new project of LIH's sports medicine researchers aims at analysing these two aspects in a single study with 800 participants. Volunteer runners need to wear cushioned shoes specially designed for this research purpose for each running session they perform during a period of six months. Anyone aged between 18 and 65 who is in good health, regardless of weight, physical condition or experience, and willing to practice regular running activities, is considered eligible to participate in this study.

Participation starts with a preliminary visit to the laboratory where people receive a pair of running shoes. During six months, participants are required to run at least once a week using only the shoes

provided for the study. They then need to register all training sessions and competitions as well as the occurrence of pain or injury on an electronic platform developed by the research unit.

State-of-the-art technologies that are only available in very few sports medicine laboratories in Europe are used for the study. With this project, Luxembourg does pioneering research work. The scientists hope to find out amongst other whether the runners' weight has an influence on the risk of getting injured and/or on the running technique and whether one should choose running shoes according to one's weight.



Dr Laurent Malisoux



“ Our study is the first worldwide to investigate both running technique and injury risk in such a large cohort and over such a long period of time.”

Dr Laurent Malisoux, project leader

# FINDING THE EPIGENETIC ORIGINS OF DISEASE

A bilateral research project in epigenetics

Maternal diabetes can lead to the development of both diabetes and emotional disorders in the offspring. To understand how, the Immune Endocrine and Epigenetics Research Group has developed a joint research project with scientists from the University of Bordeaux and the University Paris Diderot in France.

It is broadly accepted that negative early life events have consequences on health that persist through the lifespan. Recent epidemiological studies suggest that maternal diabetes increases the risk for their offspring to develop mental disorders such as autism or schizophrenia.

## Inheritance of disease risk

There is growing evidence that regions in the genome relevant for disease development are regulated by epigenetic modifications. These hallmarks can be transmitted from one generation to the next and play a significant role in disease development.

In the new project named MADAM, epigenetic processes - in particular DNA methylation - will be closely examined to understand the links between the exposure to maternal diabetes and the development of both diabetes and emotional disorders in the offspring at a molecular level.



Dr Jonathan Turner

“With this project, we hope to improve our understanding of the epigenetic origins of both diabetes and depression to be able to better prevent and treat the two associated disorders.”

Dr Jonathan Turner, Principal Investigator

## Funding:

The bilateral research project MADAM is jointly funded by the Luxembourg National Research Fund and the “Agence Nationale de la Recherche” in France through the INTER funding scheme. In 2017, only five out of 33 proposals involving Luxembourg partners were retained for this competitive funding.

## BIOGLOSSARY

**DNA methylation** is an epigenetic modification of DNA that can have an effect on gene expression. **Epigenetics** is the study of changes in organisms caused by modification of gene expression not involving changes to the underlying DNA sequence of genes.

# HOW SMALL VESICLES INFLUENCE BLOOD CANCER

A bilateral research project in oncology

Extracellular vesicles, released by cells into tissues and body fluids, are small biological containers filled with a complex mixture of molecules serving for the communication between cells and inducing changes in their environment. The research community becomes increasingly interested in their function as they are thought to play an important role in the crosstalk between healthy and malignant cells in cancer.

Extracellular vesicles have diverse roles in intercellular communication and are involved in many physiological and pathological processes. To understand how they shape and modulate the tumour microenvironment, the Laboratory of Experimental Cancer Research developed a research project to have a closer look at these vesicles in blood cancer.

The project focuses on B cell lymphoma, a non-curable blood cancer, and intends to analyse the content of extracellular vesicles. The researchers will in particular examine the complex mixture of RNAs in the vesicles and study their function.



Dr Etienne Moussay

“We hope to be able to characterise extracellular vesicles in depth and shed light on how they influence the tumour microenvironment and impact on disease development.”

Dr Etienne Moussay, Principal Investigator

## BIOCABULARY

**B cell lymphoma** is a type of blood cancer affecting white blood cells called B cells or B lymphocytes. **Extracellular vesicles**, filled with a complex mixture of molecules, are released by cells into tissues and body fluids. They can serve for the communication between cells and induce changes in their environment.

**RNA** (ribonucleic acid) is a nucleic acid, similar to DNA. The polymeric molecule has numerous essential roles in the cell, being amongst others involved in regulating gene expression.

The **tumour microenvironment** is the immediate cellular and molecular environment around tumour cells.

### Funding & Collaborations:

The bilateral research project is jointly funded by the Luxembourg National Research Fund and the German Research Foundation “Deutsche Forschungsgemeinschaft” through the INTER funding scheme.

It involves collaborations with the German Cancer Research Centre in Heidelberg and the University of Ulm (Germany).





# PROMOTING PHYSICAL ACTIVITY IN CANCER PATIENTS

## The power of motivational interviews

Physical activity can prevent several cancer types, but also have a beneficial role in cancer treatment if used as a therapeutic adjuvant. How can patients be motivated to do more sports? LIH researchers initiated a new project to test the effectiveness of a method to promote physical activity in cancer patients.

### Proven benefits of physical activity

Many scientific studies suggest a preventive role of physical activity on the risk of recurrence and death from cancer in patients under treatment. The benefits of physical activity on prognosis, meaning cancer progression, development of new primary tumours or relapse, was shown for many cancer types.

Physical activity promotes the maintenance and development of cardiopulmonary capacity, muscle strength, bone density, flexibility and balance. It also helps to better manage body weight and reduces tiredness. In addition, it has positive psychological effects, improving sleep, increasing self-esteem, and reducing depression and addiction. Overall, physical activity contributes significantly to improving the quality of life of cancer patients.

### Getting patients motivated

Despite the demonstrated benefits of sports and its prescription by physicians, the participation rate in therapeutic sports courses remains generally low. Prescribing alone does not seem to be sufficient to influence the behaviour of patients towards a more active lifestyle.

The project MIPAClux aims to change this situation. It will study the feasibility and effectiveness of motivational interviews to permanently alter the behaviour of cancer patients with regard to physical activity. Motivational interviewing is an approach that uses open discussions between an advisor, such as a trained nurse, and a patient to develop the latter's motivation for a durable change in life style. Such interviews were shown to be effective in increasing the level of physical activity of patients with chronic diseases.

The project will focus on patients with breast, colon or endometrial cancer. Two randomly selected groups of patients are planned to be analysed: one group shall receive, in parallel to their treatment, one motivational interview per week during 12 weeks, and a second group, serving as control, shall only receive the treatment. Several measurements will be taken in both groups before and after the trial, and six months later.

### Funding:

The MIPAClux project is supported by a grant from the Luxembourg Cancer Foundation "Fondation Cancer".

*“The results of our pilot study will evaluate the value of introducing motivational interviews with cancer patients into clinical practice.”*

Dr Alexis Lion, project leader



The Cancer Foundation supports the MIPAClux project.  
From left to right: Dr Carlo Bock (President of the Cancer Foundation), Prof Daniel Theisen (Head of the Sports Medicine Research Laboratory, LIH), Dr Alexis Lion (project leader, Sports Medicine Research Laboratory, LIH), Karl-Heinz Dick (Chief Financial and Administrative Officer of LIH) and Lucienne Thommes (Director of the Cancer Foundation)

## BIOCABULARY

**Endometrial cancer** is a cancer that arises in the lining of the uterus.

**Motivational interviewing** is a counselling method that helps people find the internal motivation for a change in their behaviour.

# FIVE FNR CORE PROJECTS IN THE STARTING BLOCKS

Five research projects submitted by LIH have been selected by international expert committees to be supported with the CORE funding instrument of the Luxembourg National Research Fund (FNR) in 2017.

## Zoom on these projects:



### PACA

The PACA project will explore new biomarkers to predict the outcome after cardiac arrest. It purposes to identify and validate a set of long non-coding RNAs and circular RNAs that have a prognostic value for the health outcome of patients having survived a cardiac arrest. Data from several cohorts of patients with cardiac arrest will be used for an extensive and independent biomarker validation. Collaborators in this project are the “Centre Hospitalier de Luxembourg” and the Helsingborg Hospital in Sweden.



*Results will constitute the basis for the development of a diagnostic test - a step forward towards the implementation of personalised medicine in the field of cardiovascular disease.”*

**Dr Yvan Devaux,**  
Head of the Cardiovascular Research Unit,  
Department of Population Health



*This study will lead to a better understanding of the regulation of gene expression and will identify new regulatory pathways, which can be exploited for targeted cancer therapies.”*

**Dr Gunnar Dittmar,**  
Head of the Proteome and Genome Research Unit,  
Department of Oncology

### PrISMaHif

The PrISMaHif project will study the molecular interactions of a transcription factor named HIF-1 that plays an essential role in the cell metabolism. When cells lack oxygen, which is the case inside tumours, HIF-1 can switch biochemical pathways in the cell. To better understand the function of the transcription factor, the project aims to analyse its structure and the set of proteins with which it interacts. A newly developed protein interaction screening technology will be used to characterise these interactions and their regulation.



### IRGal

The IRGal project aims to study immune reactions to the allergy-causing carbohydrate alpha-Gal. Tick bites are thought to induce the generation of specific antibodies directed at this carbohydrate. They can cause a delayed form of anaphylaxis triggered upon consumption of red meat or innards - the so-called alpha-Gal syndrome. The project will characterise the molecules involved the allergic reaction and the mechanisms underlying the sensitisation process. IRGal involves a collaboration with the "Centre Hospitalier de Luxembourg", the Eberhard-Karls-University in Tübingen (Germany) and the Technical University Munich (Germany), and is also supported by the German Research Foundation "Deutsche Forschungsgemeinschaft".

*"With this project we hope to improve our basic knowledge on immune responses to carbohydrates and provide new targets for therapeutic intervention."*

**Dr Christiane Hilger,**  
Principal Investigator in the Molecular and Translational Allergology Research Group, Department of Infection and Immunity



*"In addition to improved patient classification, our methodology will provide new insights into processes taking place in distinct cell types and their regulation, and ultimately point to new therapeutic targets."*

**Dr Petr Nazarov,**  
Scientist at the Proteome and Genome Research Unit, Department of Oncology

### DEMICS

The objective of the DEMICS project is to improve the classification of heterogeneous tumour samples from patients by using computational methods. The majority of biological samples analysed with omics techniques are heterogeneous at the cellular level. This is especially true for tumour samples containing numerous subtypes of cancer cells as well as healthy cells. To allow for a better patient classification, data from samples will be decomposed with a computational method called "independent component analysis". The project involves a collaboration with the Institut Curie Research Centre in Paris (France).



### iMPACT.lu

The iMPACT.lu project shall advance the understanding of the effect of environmental pollutants and dietary-derived constituents like micronutrients on cardiometabolic disease and associated risk factors such as obesity, hypertension, lipid disorders or diabetes in Luxembourg. The funding will enable to analyse data from the European Health Examination Survey in Luxembourg, a cross-sectional population-based survey conducted by LIH in 2013-2015, including almost 1500 residents aged between 25 and 64.

*"We hope that our results will impact on public health policies targeting environmental conditions and diet as a key strategy to improve health."*

**Dr Maria Ruiz-Castell,**  
Scientist at the Epidemiology and Public Health Research Unit, Department of Population Health

## BIOGLOSSARY

An **allergy** is an excessive reaction of the immune system to harmless substances of the environment. **Allergic sensitisation** is the initial production of a specific antibody against an allergy-causing substance. **Anaphylaxis** is a serious, life-threatening allergic reaction affecting the whole body. An **antibody** is a Y-shaped protein that is produced by immune cells to neutralise pathogens and trigger other immune responses. A **biomarker** is a biological characteristic that is objectively measured and evaluated as an indicator of physiological or pathological processes, or of a response to a therapeutic intervention. The **carbohydrate alpha-Gal** is a sugar molecule that is found in mammalian meat. **Circular RNAs** and **long non-coding RNAs** belong to the family of non-coding ribonucleic acids. Those are biomolecules encoded in the genome that are not translated into proteins, as is the case for another more commonly known type of RNAs. A **cross-sectional survey** collects data to make inferences about a population of interest at given point in time. The idea behind **personalised medicine** is that healthcare can be customised to fit the unique characteristics of each person's or group of individuals' disease. **Omics** refers to the collective characterisation and quantification of pools of biological molecules that translate into the structure, function and dynamics of an organism (e.g. proteomics, genomics, metabolomics). **Targeted cancer therapies** block cancer growth by interfering with specific molecules. **Transcription factors** are proteins involved in the process of converting the genetic information contained in DNA.

# FOR A BETTER PREVENTION AND TREATMENT OF FOOD ALLERGIES

## Pump priming for application-targeted research

Food allergies are becoming an increasingly important public health issue. In Europe, more than 17 million people are affected by allergic reactions to harmless food proteins. At the annual retreat of Luxembourg's Personalised Medicine Consortium, a collaborative project on the molecular characterisation of food allergies led by LIH was presented and announced to receive pump priming.

The breakdown and absorption of food allergens by the body's digestive system is believed to be different in allergic versus tolerant individuals. The project aims to test the hypothesis that food-allergic and food-tolerant individuals have different immunologically active allergen-derived peptides circulating in their bloodstream.



Dr Annette Kuehn

“To be able to develop approaches for successful treatment and future disease prevention, we need to better understand food allergies at the molecular and immunological level.”

Dr Annette Kuehn, Principal Investigator

The project entitled “Peptide signatures in allergic versus tolerant individuals: paving the way for novel personalised medicine approaches to diagnose and cure food allergies” will include the recruitment of 15 patients with peanut or fish allergy who will be compared to 15 tolerant control persons. To identify specific peptide signatures, the participants will be exposed to different food challenges. Their blood samples will then be characterised for allergen residues, specific antibodies and immune cells.

### Funding & Collaborations:

This project is supported by the Pump Prime Fund of Luxembourg's Personalised Medicine Consortium. If the results of this study are promising, a further grant application may be submitted elsewhere to extend the scope of the project.

The project involves a collaboration with the “Centre Hospitalier de Luxembourg” and clinical partners from Denmark and Norway for sample collection, IBBL - Integrated BioBank of Luxembourg for sample storage, and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg for data analysis.

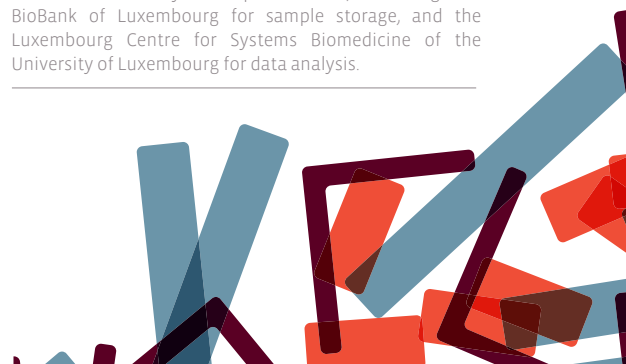
## BIOCABULARY

An **allergy** is an excessive reaction of the immune system to harmless substances of the environment.

**Peptides** are short chains of amino acids, whereas proteins are long chains of amino acids.

A **peptide signature** is a mix of specific peptide sequences that can be associated to particular biological functions.

**Pump priming** is a small funding that allows to conduct preliminary experiments for a new project, allowing later on for a robust grant application to further develop the project.



# WHAT ARE THE MOLECULAR CAUSES OF THE GOOD'S SYNDROME?

Understanding the cause of a rare disease

LIH is active in the field of rare diseases, specifically with a newly launched project researching Good's Syndrome, a disease with only a few hundred described cases worldwide.

Good's Syndrome is a rare disease defined as an adult-onset immunodeficiency accompanied by a tumour in the thymus, a thymoma. The disorder leaves patients very susceptible to many types of infections, mainly of the sinus and lungs. They also suffer from autoimmune syndromes and chronic diarrhoea. The survival rates are 70% five years after diagnosis and 33% ten years after diagnosis, with severe infections being the main cause of death. The origin of the disease is currently unknown.

To better understand this disorder, an exploratory research project was initiated, titled "Immunodeficiency with autoimmunity: unravelling the molecular origin of Good's syndrome" or shortly GOODSYN. Its objective is to carry out in-depth investigations on the white blood cells of Good's Syndrome patients to a degree never done before, as well as to identify genetic factors that may be involved in the pathogenesis of the disease.



Dr Jacques Zimmer

*“We hope that this project will help uncover what goes wrong on molecular and cellular levels in patients affected by the Good's syndrome.”*

*Dr Jacques Zimmer, Principal Investigator*

While advancing the understanding of the disease, the project will also generate important data beyond the context of the Good's Syndrome, regarding the knowledge of primary immunodeficiency, susceptibility to pulmonary infections and autoimmunity.

## BIOCABULARY

**Autoimmunity** is a disease in which immune responses are directed against one's own healthy cells and tissues.

**Immunodeficiency** disorders prevent the body from fighting infections and diseases.

A **sinus** is a cavity within a bone or other tissue. The term commonly refers to the cavities in the bones of the skull connecting with the nasal cavities.

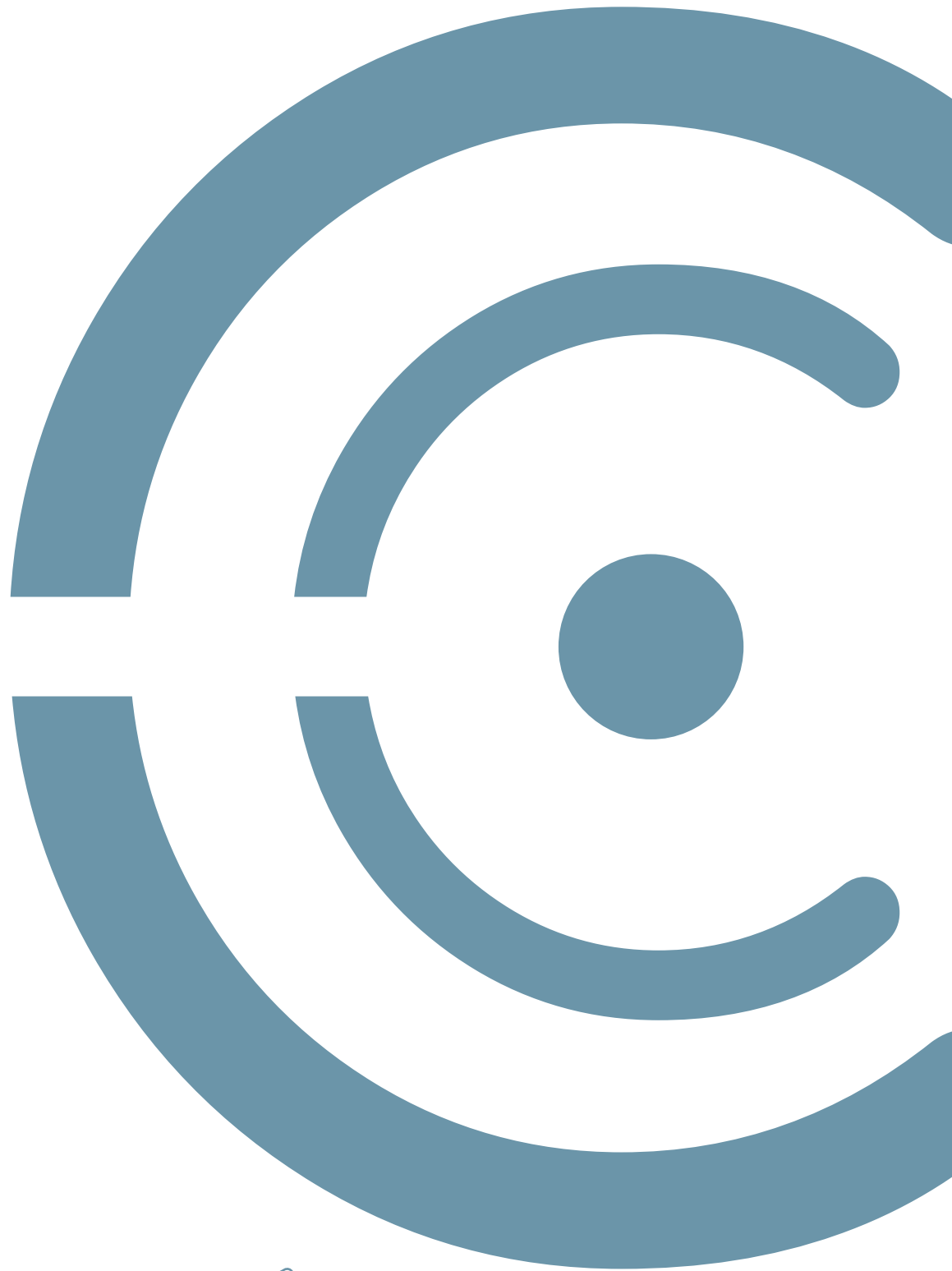
The **thymus** is a gland located closely to the lungs. Its primary function is the maturation of a specific type of immune cells.

### Funding:

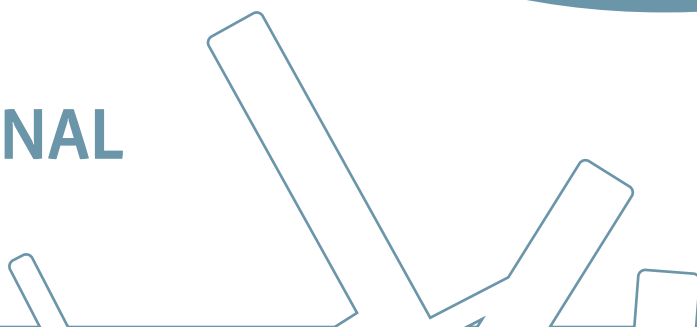
The GOODSYN project is supported by the Luxembourg National Research Fund.







**ENABLING  
TRANSLATIONAL  
RESEARCH**







# A CENTRE OF EXCELLENCE IN DIGITAL HEALTH AND PERSONALISED HEALTHCARE

Kick-off of the CLINNOVA project



In its endeavour to conduct application-targeted research, the Luxembourg biomedical research community has plans to create a Centre of Excellence in Digital Health and Personalised Healthcare in cooperation with leading research institutions abroad.

Digitalisation has the potential to increase the efficiency and transparency in healthcare, as well as to improve patient care. Around ten years ago, the Luxembourgish Government decided on a diversification strategy, which encompasses the life sciences and healthcare domains. The strategic development and the investments in personalised medicine were strong contributors to the expansion of the biomedical research entities in Luxembourg. To continue in this direction, a plan for the establishment of a Centre of Excellence in Digital Health and Personalised Healthcare is now being set up.

## Successful first step

A consortium coordinated by the Luxembourg National Research Fund, and including LIH, IBBL - Integrated BioBank of Luxembourg and the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg as national partners, was successful in Phase 1 of the European Commission's Horizon 2020 programme TEAMING by proposing the establishment of this centre in a project named CLINNOVA. It is one of only 30 projects to pass Phase 1 of the selection process, out of 208 projects submitted to the Commission.

On 26<sup>th</sup> September 2017, the official kick-off meeting of the CLINNOVA consortium was held with various invited stakeholders. Present at the meeting was Luxembourg's Minister of Health, Mrs Lydia Mutsch, and representatives from ministries, hospitals, industry and research, as well as representatives from the international partners.

The latter are the University of Southern Denmark and the Odense University Hospital that will allow the consortium to benefit from the experience Denmark has in setting up modern eHealth infrastructures, and the National Centre for Tumour Diseases of the German Cancer Research Centre having strong expertise in oncology.

The centre will build on the previous investments into fundamental biomedical research and form a bridge to the hospitals in Luxembourg, ensuring that laboratory innovations reach clinical implementation and benefit patients. Having passed phase 1 of H2020 TEAMING, CLINNOVA has received funding from the EU Commission to develop a sound business plan for the phase 2 proposal. If the project is also successful in this phase, financial support will be awarded by Horizon 2020 to make CLINNOVA a reality.



Kick-off meeting with the stakeholders of the CLINNOVA project

“*Clinnova could be a next step in the Luxembourg life sciences and healthcare development and a way into a new era of connecting research and care. This work will without a doubt increase our knowledge, and we will certainly identify patterns and make connections we were never able to make in the past.*”

Mrs Lydia Mutsch, Luxembourg Minister for Health

## BIOGLOSSARY

**Digital health** converges modern digital technology with health monitoring and healthcare. The idea behind **personalised medicine** is that healthcare can be customised to fit the unique characteristics of each person's or group of individuals' disease.



# ARTIFICIAL ANTIBODIES BOOST IMMUNE DEFENCES AGAINST CANCER

Proof of concept studies for a new technology

LIH researchers have developed innovative artificial antibodies for cancer immunotherapy. The molecules bind selectively to cancer cells and lead to their destruction by the activation of the complement system. Preclinical studies shall be conducted to take this drug development project “from bench to bedside”.

## Marking cancer cells to kill them

With conventional antibody-based immunotherapies, antibody binding is often below the threshold needed to trigger the assembly of the complement on the cell surface leading to cell killing. Dr Xavier Dervillez has developed artificial antibodies, called “CoMiX” for “complement multimeric immunotherapeutic complexes”, which can overcome this limitation.

The chemical composition of CoMiX facilitates the complement assembly on cancer cells. In addition, these molecules can initiate several types of immune responses in a simultaneous and rapid manner, a novelty compared to existing treatments. The molecules are composed of a scaffold on which several fragments can be bound. The most efficient molecule variants comprise a “targeting function” for the recognition of cancer cells and two “effector functions” that trigger two distinct immune responses.



Structure of a CoMiX molecule

## A long development process

Since the beginning of the research project, the composition and features of the molecules have evolved. The first generation was bifunctional, the second is trifunctional, allowing the simultaneous activation of several immune responses, which conventional antibodies are unable to achieve in anti-cancer therapy. A patent was filed in 2016 to protect the invention.

The molecules were successfully tested in cell culture for two types of cancer: breast cancer (representative of a “solid” cancer) and lymphoma (representative of a “liquid” cancer), indicating that the therapeutic strategy could be applied to several types of cancer. After more than four years of developing multiple types of CoMiX and verifying their efficiency in cell culture, the technology is now mature enough to move to the next stage of the drug development process: the preclinical phase. The effectiveness and safety of the molecules will be confirmed *in vivo* in mouse models.

The project has already attracted the attention of the pharmaceutical industry. Project leader Dr Carole Devaux hopes that following the results of the preclinical studies, companies will formally engage in the project to drive it towards clinical application.



Dr Xavier Dervillez

“CoMiX are modular and multifunctional, and can efficiently hit cancer cells in different ways, which is a true novelty.”

Dr Xavier Dervillez, inventor of the CoMiX technology

## Funding & Collaborations:

The Luxembourg National Research Fund supports the project with almost 500,000 Euros via its Proof-of-Concept (PoC) programme (renamed JUMP). This funding instrument aims to enable research institutes to validate and commercialise their scientific results. It is the first time that LIH is granted such a funding type.

The research work is conducted in collaboration with Prof Iris Behrmann from the Life Sciences Research Unit of the University of Luxembourg and Prof Jacques Cohen from the Nanosciences Research Laboratory of the University of Reims Champagne-Ardenne (France).

## BIOCABULARY

An **antibody** is a Y-shaped protein that is produced by immune cells to neutralise invading microorganisms and trigger other immune responses.

The **complement system** is a complex set of serum proteins that can cause cell killing either directly by assembling on the surface of microorganisms and abnormal cells or by triggering other immune responses.

“**From bench to bedside**” is a phrase used to describe the process by which the research results generated in the laboratory are directly used to develop new ways to treat patients.

**Immunotherapy** is a treatment that uses the body’s own immune system to fight a disease.

The term ***in vivo*** (Latin for “within the living”) refers to experiments conducted on whole living organisms or cells.

**Lymphoma** is a cancer of the lymph nodes.

**Preclinical studies** consist of testing medical treatments in animal models with the aim of collecting data in support of the safety of the new treatment. Such studies are required before trials in humans can be started.

# CREATING ECONOMIC AND SOCIETAL VALUE FROM RESEARCH

Support in business development

LIH has been successful with the submission of a proposal for the Knowledge and Innovation Transfer Support (KITS) funding scheme of the Luxembourg National Research Fund. This grant will help the institute in its effort to translate research results into concrete applications impacting on patients.

The objective of the KITS programme is to provide competitive funding to public research institutions in Luxembourg that will allow them to attract and integrate highly skilled professionals in the area of knowledge transfer.

Among the two projects accepted for funding in December 2017 is “Project DEvelopment”, shortly ProDEV, conceived by LIH’s Business Development Office (formerly named Research Knowledge Transfer Office). The institution already benefits from the KITS programme through the ACTOR project funded since September 2016, which aims at integrating the dimension of valorisation already in the conception stage of research projects. ProDEV will bring this sensitivity to the next level by maturing applied projects and developing platforms that will give the institute distinguishing features.

The funding will allow the hiring of a project developer for a period of two years to strengthen the team of the Business Development Office.



Dr Fabrice Mouche

“ We will be able to provide strong professional support in business development to our researchers.”

Dr Fabrice Mouche, Head of the Business Development Office

## BIOCABULARY

**Valorisation** is the use of research results for socio-economic purposes. It represents society's direct and indirect return on the public sector's investment in research and development.





**PUBLIC HEALTH  
EXPERTISE**







# IMPROVE HEALTH AND CHANGE LIFESTYLES

Vision of Department Director Prof Laetitia Huiart



Prof Laetitia Huiart

Since August 2017, LIH has a new director to lead its Department of Population Health - a cornerstone of the institute and its development towards translational research. Prof Laetitia Huiart is expert in public health, epidemiology as well as methodology and statistics for clinical research, and has a special interest in oncology.

By joining the institute to manage the Department of Population Health, Prof Huiart, who previously worked in a management and clinical position at the University Hospital Centre of Reunion Island, has set herself a new challenge. What mainly attracted her to Luxembourg is the dynamism of the country and its openness to develop research and innovation in specific areas.

## Developing population health research...

The Department of Population Health has a unique expertise in Luxembourg for the design and coordination of clinical trials in close connection with hospitals. In addition, it conducts research aimed at preventing and targeting the main causes of disease and mortality. It communicates public health information to the principal health actors in Luxembourg to enable evidence-based decision-making.

Prof Huiart plans to restructure the department in accordance with its three main activities: clinical research, population health research and expertise in public health. This will enable it to play a decisive role in the development of translational research by bringing the innovations that arise from basic research to the patients.

To valorise the researchers' expertise and have more impact, the new department director would like to further strengthen the exchange with stakeholders in health and healthcare. She has the vision that the studies performed at LIH could profoundly change lifestyles and habits, in particular with regard to diet and physical activity.

## ...with an impact on society

Prof Huiart is convinced that innovation in public health is possible at a national level namely with the use of national databases. According to her, e-health technologies enable for a more efficient analysis and exchange of health data. Digital health platforms are an interface between healthcare professionals and patients that allow a better medical follow-up and personalised patient advice.

Beyond the exchange with healthcare actors, Prof Huiart also aims to involve the general public. Her goal is to conduct research for the population - with the population. This involves collecting and integrating the opinions of individuals, especially patients and patient organisations, into research.

## Collaboration is key

The strategy of Prof Huiart should foster the collaboration between the different research units within LIH, increase the visibility of Luxembourg as a research site for population health and clinical research, and have a true influence on the health behaviour and lifestyle of the local population.

To be more involved in the international scientific community, the new director intends to initiate new collaborations and join European research networks. She also aims to strengthen existing partnerships with universities having curricula and research themes focused on public health such as the University of Lorraine (France) and the University of Maastricht (Netherlands).

“ Our scientific questions should not be disconnected from people's lives. Research must serve society, respond to its needs.”

Prof Laetitia Huiart, Director of the Department of Population Health

## BIOCABULARY

**Digital health** or **e-health** converges modern digital technology with health monitoring and healthcare.

**Translational research** is oriented towards application by using findings from basic science to improve human health and wellbeing.

# RETRACE - inform to prevent

Luxembourg's injury surveillance system rated excellent

The current implementation of Luxembourg's injury surveillance system operated within LIH was rated excellent and sustainable in an evaluation performed in the context of the European project BRIDGE-Health.

Accidents and intentional injuries are one of the major causes of death, hospital admissions and disabilities in Luxembourg. Therefore, the Ministry of Health, in the framework of the European Injury Data Base (IDB) network and in collaboration with LIH, has committed itself to an injury prevention policy.

## An exemplary system of data collection

BRIDGE-Health, standing for "BRidging Information and Data Generation for Evidence-based Health policy and research" is a large-scale project funded by the European Commission to work towards a European health information and data generation network covering major EU health policy areas by promoting the coordination and convergence of existing key projects in health information. LIH, with its objective to implement a quality injury surveillance system, is part of the BRIDGE-Health network encompassing 31 partners in 16 European countries.

In accordance with the common European IDB methodology, Luxembourg's injury surveillance system named RETRACE for "Recueil de données sur les traumatismes et accidents" collects information on injury causes and circumstances at the emergency departments of all hospitals with the purpose to conceive injury prevention measures.

The implementation of RETRACE was evaluated in a scorecard report. Different criteria, such as participation in data exchange at European level, data delivery over the past five years, geo-coverage of the collected data, prospects for data collection in the current year and capacities of the project team for injury data analysis were scored. RETRACE received the maximum number of points for each criterion and stood out as an exemplary national injury surveillance system.

## Second RETRACE report published

The data collected with RETRACE are published in reports to render them accessible to the public. A first RETRACE report, co-authored by the Ministry of Health and LIH appeared in 2015, presenting the national statistics on accidents and injuries from 2013 and comparing them at the international level. A second report with data from 2014 was published in October 2017.

The new report is available for download on the Health Portal [www.sante.lu](http://www.sante.lu). It informs that in 2014, 4,516 people were hospitalised for injury and 60,400 were treated as outpatients in the hospital's emergency departments. Children, teenagers and the elderly were identified as the most vulnerable population groups for injuries and accidents.



Dritan Bejko

*“Injury monitoring on a national level is eased by the small size of the Grand Duchy.”*

*Dritan Bejko, coordinator of RETRACE*



Second RETRACE report

# AVIAN INFLUENZA APPEARANCE IN LUXEMBOURG

LIH demonstrated preparedness for diagnosis

In May 2017, eight months after the Food and Agriculture Organisation of the United Nations raised awareness on the potential reintroduction of avian influenza in Europe, the viral disease struck Luxembourg. LIH's experts in infectious diseases were able to swiftly identify the viruses and thus helped the country to efficiently react to the outbreak.

Avian influenza is the most dreaded bird disease and can have dramatic consequences for the poultry industry, as all animals of an infected flock must be destroyed to stop the disease from spreading. Highly pathogenic avian influenza viruses originating from Asia had already been introduced in Europe several times. When birds are infected in their breeding grounds in the circum-polar region, they can carry the virus along their migratory routes to Europe and beyond, where they may infect domestic birds.

## Swift viral characterisation

At LIH, experts in virology have screened birds for various viruses in collaboration with the Veterinary Medicine Laboratory "Laboratoire de Médecine Vétérinaire de l'Etat" since the advent of bird flu in 2006. Timely diagnosis and virus characterisation by the team at LIH allowed rapid interventions by the Ministry of Agriculture to stop disease spreading.

The virus was characterised overnight within hours and revealed itself as the highly pathogenic H5N8 subtype that has already appeared in other European countries. The identification of the virus as H5N8 was in addition confirmed by the Veterinary and Agrochemical Research Centre in Brussels (Belgium).

The team participates every year to a Proficiency Panel testing scheme and had perfect results since the beginning in 2006, demonstrating its preparedness. Besides virovigilance and rapid diagnosis for the Luxembourg Ministry of Agriculture, the team investigates viruses in humans and animals in numerous regions of the world. Its research focuses on a better understanding of routes of infection, animals as virus hosts or reservoirs, and risk factors for people being exposed to those viruses. These activities help preventing disease spread and human exposure.



Dr Chantal Snoeck



**“ With the dynamic influenza virus you must always expect the unexpected. Preparedness and research are crucial to prevent disease spread amongst domestic animals and transmission to humans.”**

*Dr Chantal Snoeck, responsible scientist for avian influenza diagnosis*

## BIOCABULARY

**Avian influenza**, commonly known as bird flu, is a viral infection spreading among birds. Many different viral strains or subtypes exist which are classified according to their ability to cause disease and death.

**Pathogenic** means causing disease.

# MONITORING HOSPITAL-ACQUIRED INFECTIONS

## Point prevalence survey

Every two years, LIH conducts a point prevalence survey (PPS) on nosocomial infections and antimicrobial use in healthcare facilities in collaboration with the Ministry of Health and the European Centre for Disease Prevention and Control (ECDC). In 2017, a national validation study was carried out in parallel, verifying the accuracy of the collected data.

The ECDC developed a methodology for repeated surveys with the main objective to estimate the total burden of nosocomial infections and the prescription of antibiotics in acute care hospitals in the European Union. LIH is strongly involved in the nationwide implementation of the PPS. Aurélie Fischer from the Clinical and Epidemiological Investigation Centre is responsible for data assembly and analysis as well as for the training of hospital nurses and hygienists on study protocol and data collection. Data on nosocomial infections is provided from all the hospital sites in Luxembourg.



Aurélie Fischer

“ Conducting point prevalence surveys allows health authorities to establish recommendations for the improvement of hygiene and antibiotic use in healthcare facilities.”

Aurélie Fischer, Clinical Research Coordinator

The ECDC expected all involved countries to perform a validation study in 2016 or 2017. The main objective of this study was to assess the validity, reliability and inter-country comparability of the data collected during the national or regional PPS. In the Grand Duchy, the validation study was conducted at all hospital sites by the re-examination of 30 patients per hospital. No deviation could be detected, which demonstrates that data collection in Luxembourg is accurate.

## BIOGLOSSARY

**Nosocomial infections** are infections acquired in a healthcare facility such as a hospital.  
**Point prevalence** is the proportion of persons with disease at a specific time point.







A large, abstract graphic composed of several thick, blue, geometric shapes. It resembles a stylized letter 'K' or a series of overlapping bars, with a long diagonal bar on the left and several horizontal and vertical bars on the right.

**TALKING SCIENCE**





# LUXEMBOURG AT THE CENTRE OF MOLECULAR ALLERGOLOGY

Co-organisation of ISMA 2017

For the first time, the allergy research community gathered for an international and worldwide known meeting in Luxembourg. The 7<sup>th</sup> edition of the International Symposium on Molecular Allergology (ISMA) was held from 9<sup>th</sup> to 11<sup>th</sup> November 2017 at the European Convention Centre in Kirchberg with about 300 allergy experts from 42 countries.

ISMA is one of several focused meetings of the European Academy of Allergy and Clinical Immunology (EAACI) targeting the research community in allergology. ISMA 2017 was jointly organised by EAACI and LIH, as the institute has a strong expertise in allergy research.

Prof Markus Ollert, Director of the Department of Infection and Immunity, was the driving force in bringing the symposium to Luxembourg after previous editions had been held in other capitals such as Lisbon, Vienna and Rome. He was invited to act as a chair for the event, while Dr Christiane Hilger and Dr Annette Kuehn, Principal Investigators at the Department of Infection and Immunity, were nominated to be part of the local Scientific and Organising Committee.



Prof Markus Ollert

## Fostering scientific interaction

EAACI, together with the Scientific Programme Committee, decided to offer a partially novel format for ISMA in 2017: plenary sessions summarising state-of-the-art knowledge delivered by leading scientists in the field, alternating with parallel symposia presenting selected topics in-depth. Besides the themes for which the meeting has built its disruptive and early mover reputation since the first ISMA in 2006, such as the analysis of molecular allergen structures and the challenges in molecular diagnosis and therapy of allergic diseases, a new second track covered emerging research topics relevant to the field of allergy and clinical immunology.

The event was conceived in a way to promote the establishment of strong scientific links between scientists at an international level and enhance the intensity of scientific debate. Cutting-edge results were presented both in lectures and on posters. There was a very active scientific exchange in all sessions inspiring the ISMA 2017 delegates and faculty members. A total of 78 scientific abstracts were presented, eight of them as oral presentations and 70 as posters. Eight travel grants and six poster prizes were attributed to merited participants. Two of the posters prizes went to scientists from LIH.

## BIOCABULARY

An **allergen** is a substance capable of triggering an allergic reaction.

**Allergology** is the study of the causes and treatment of allergies.

An **allergy** is an excessive reaction of the immune system to harmless substances of the environment.

“ We were proud to contribute directly to the organisation and success of this international symposium that gives Luxembourg more visibility and exposes its growing positioning in biomedical research.”

*Prof Markus Ollert, Director of the Department of Infection and Immunity and chair of ISMA 2017*

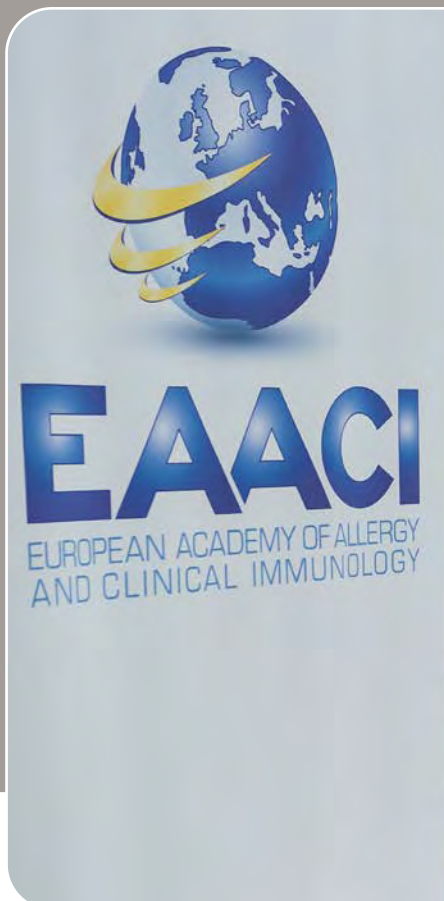


Photo © Oliver Dessy

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**Funding:**

ISMA 2017 was supported by a RESCOM grant from the Luxembourg National Research Fund.

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# FOUR SCIENTIFIC LECTURE SERIES WITH INTERNATIONAL SPEAKERS

Gathering the research community

In 2017, four annual lecture series on different scientific topics with renowned international speakers were initiated at the institute, two of them for the first time. LIH's lecture series are aimed at addressing current hot research topics and promote scientific exchange and networking.



## Cancer Research

The lecture series in *Cancer Research* organised for the third time comprised six seminars in 2017. Each seminar was followed by a "Meet & Eat" session during which a restricted group of early-stage researchers could informally exchange with the speakers about their research topic and their career path. This lecture series, jointly set up by LIH's Department of Oncology and the Life Sciences Research Unit of the University of Luxembourg, continues in 2018 with five more events.

## Infection and Immunity

The fourth edition of the lecture series in *Infection and Immunity* organised by the Department of Infection and Immunity offered the opportunity to listen to 13 international speakers working in different fields related to immunology. Each lecture was followed by a "Meet & Eat" session targeting mainly the early-stage researchers. These sessions allowed for more intense exchange with the speakers around a light lunch.

## BIOCABULARY

**Clinical trials** are research studies on human participants that evaluate a medical, surgical, or behavioural intervention. They are part of the drug development process.

**Systems biomedicine** is the computational and mathematical modelling of dynamic systems of biological components (molecules, cells, organisms) applied to advance biomedical knowledge.

**Translational bioinformatics** is an emerging research field that applies informatics methodology to biomedical data to formulate knowledge and medical tools and improve human health.

**Translational research** is oriented towards application by using findings from basic science to improve human health and wellbeing.

## Biomedical research - from discovery to patients

A new lecture series entitled *Biomedical research - from discovery to patients* started in May 2017 and runs until June 2018. It focuses on the actors and major challenges of biomedical research and innovation through testimonials from researchers-entrepreneurs. The programme, set up by LIH's Research Knowledge Transfer Office, foresees 12 lectures.

This lecture series is divided into two main parts: Part A termed "Research results at the centre of the therapeutic revolution" presents how results from academic research can be transferred into clinical applications and explain the general process behind that transfer. Part B provides scientists with key tools to define, mature and implement their applied research projects.

The inaugural lecture was held on 19<sup>th</sup> May 2017, chaired by Prof Markus Ollert, Director of the Department of Infection and Immunity. LIH had the pleasure of welcoming Prof Agnes Bernet, professor at the University Claude Bernard in Lyon (France) and co-founder of the start-up Netris Pharma. She shared her fascinating entrepreneurial experience from first discoveries in the laboratory to first patient inclusions in clinical trials.

## Translational bioinformatics and systems biomedicine

Another novel lecture series named *Translational bioinformatics and systems biomedicine* was launched in June 2017 and shall run until mid-2018. The programme includes nine lectures by outstanding researchers followed by "Meet the speaker" sessions.

These scientific events provide a unique opportunity for learning about the latest advances in computational methods and their application to biomedical research, with an emphasis on challenges of potential clinical relevance. Transdisciplinary and translational research programmes that rely on the application of mathematical and computational methods have become crucial to advance biomedical research. This is in particular necessary to make sense of the large amounts of available biological and medical data in a broad range of patient-oriented applications.

The scientific organisation committee for the lecture series includes researchers from the Departments of Oncology and Infection and Immunity at LIH, and the Life Sciences Research Unit and the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg.

The first lecture was held on 19<sup>th</sup> June 2017 and chaired by Dr Feng He from the Department of Infection and Immunity. The audience had the pleasure of listening to a presentation by Prof Luonan Chen, who is the Director of the Key Laboratory of Systems Biology at the Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.

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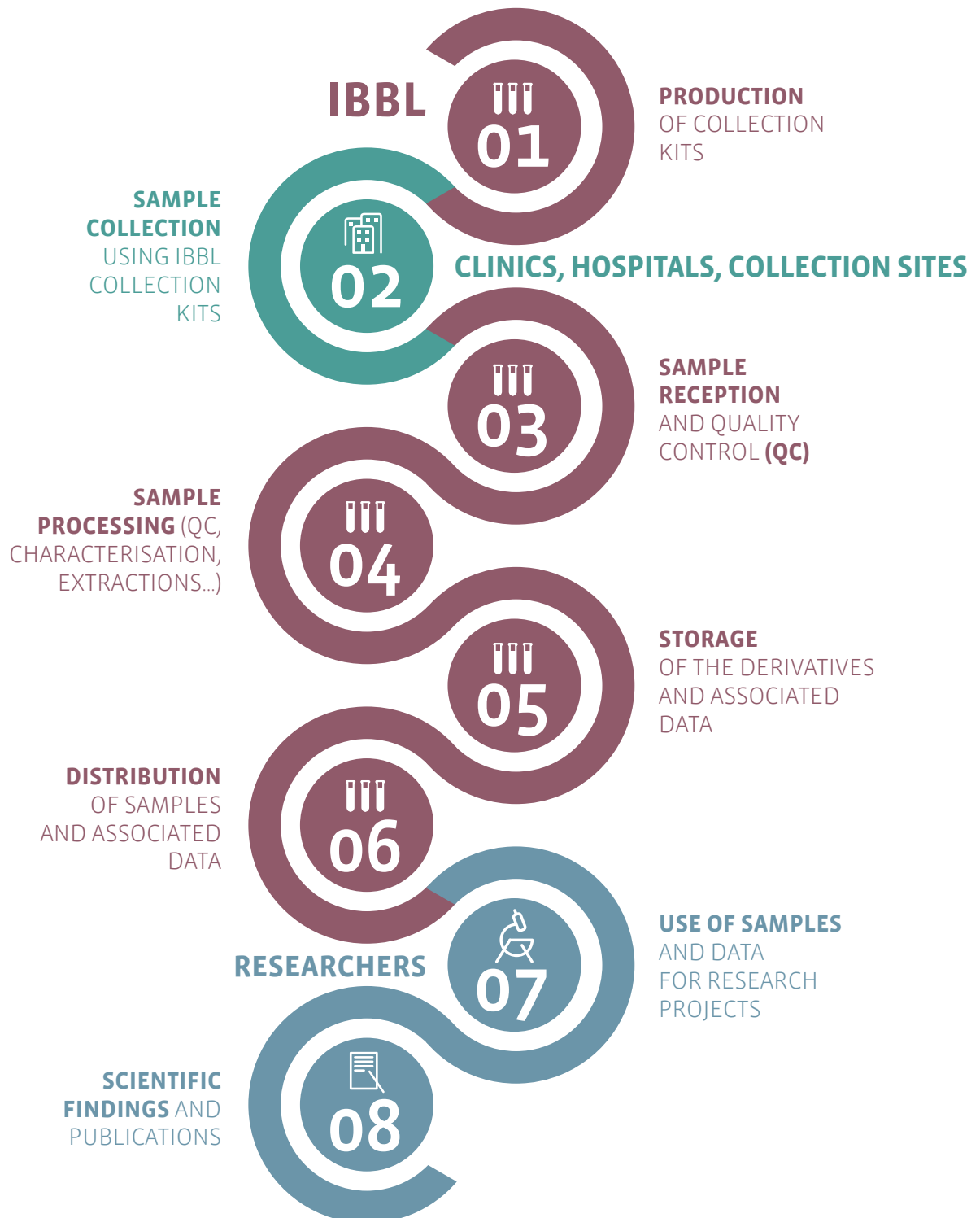
### Funding:

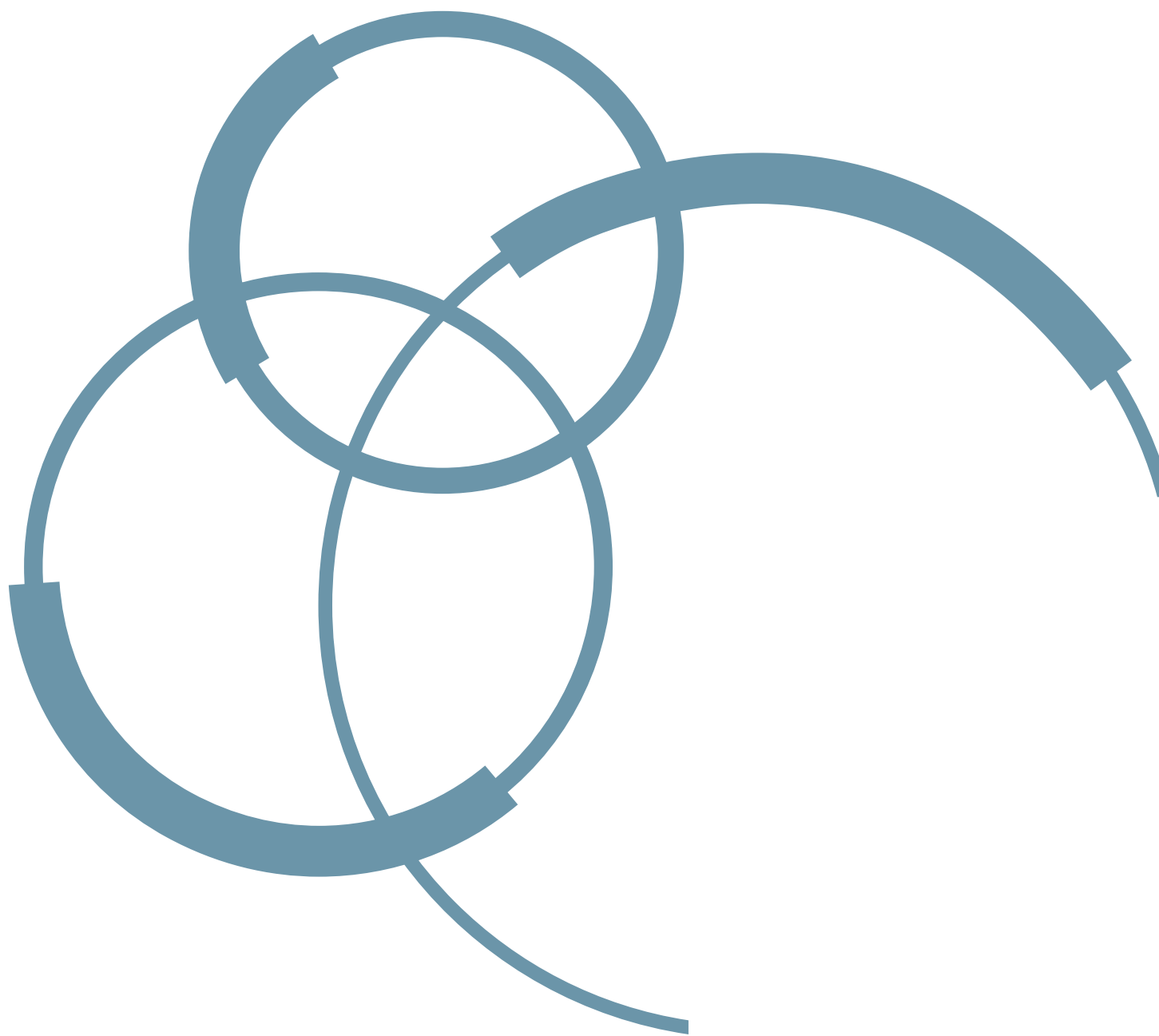
All lecture series are funded by the Luxembourg National Research Fund. The lecture series *Cancer Research, Infection and Immunity and Translational bioinformatics and systems biomedicine* benefit from RESCOM grants for scientific events, and the lecture series *Biomedical Research - from discovery to patients* is supported by a KITS grant.

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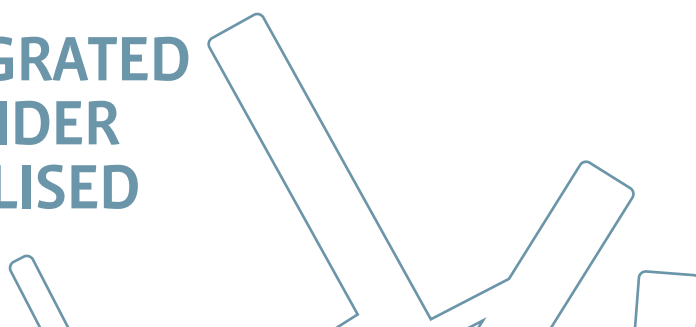
# Key role of IBBL in biomedical research

IBBL - Integrated BioBank of Luxembourg is an autonomous institute within LIH, providing researchers with the biological samples, data and technologies they need for their research projects. The close collaboration of IBBL with healthcare facilities and LIH's research departments is essential to advance biomedical research with a focus on personalised medicine.





**IBBL - AN INTEGRATED  
SERVICE PROVIDER  
FOR PERSONALISED  
MEDICINE**











As a truly “integrated” biobank, organised within LIH, IBBL - Integrated Biobank of Luxembourg provides more than just traditional sample collection and storage activities, offering instead a full range of biospecimen-related services to research institutions in Luxembourg and the European Union. In 2017, IBBL saw the move to its permanent facilities in Dudelange, contributed to the international standardisation of biobanking practices, supported the discovery of a new colorectal cancer biomarker and developed an assay to assess sample quality and fitness-for-purpose.

### A move for the better

The year 2017 marked the beginning of a new corporate identity for IBBL. As anticipated, the biobank relocated its entire staff and operations from Luxembourg City to a permanent location in Dudelange. The newly built facilities, connected to the “Laboratoire national de santé” (LNS) main building, boast a 2,000 m<sup>2</sup> floor area and a storage capacity of about five million samples. The tenfold increase in storage capacity and the doubling in floor area compared to the previous building are allowing IBBL to expand its service offerings and benefit from a wealth of new opportunities.

The premises also provide additional space for new equipment and have enabled IBBL to separate its laboratories according to different activities, such as DNA and RNA isolation, to prevent sample contamination. The seamless transition, which saw no significant service interruptions and no damage to any of IBBL’s samples or equipment, was made possible by the rigorous management work and the active involvement of the entire staff.

### Standardising biobanking practices

The standardisation of biobanking practices is one of IBBL’s top priorities. Indeed, IBBL has been contributing to the development of international biobanking technical standards as part of its efforts to support the quality of biospecimens and reproducibility of research results. In 2017, the biobank saw the approval of the ISO/DIS 20387 biobanking standard draft by the international community and made important steps forward in the conception of the draft version of ISO/AWI 21899, a complementary norm establishing the general requirements for the validation and verification of processing methods for biological material in biobanks.

Moreover, and as a result of the increased space, IBBL started preparing to become an authorised GMP (Good Manufacturing Practices) storage infrastructure, which will allow the storage of human cells and tissues for therapeutic applications. To top it all off, the biobank also successfully passed the recertification audit for ISO 9001:2008.

### Advancing biospecimen science

IBBL prides itself on being a truly integrated biobank, putting its expertise in biospecimen research and cutting-edge infrastructure at the disposal of the research community, partners and clients. This year again, the Biorefinery Department took yet another step forward in ensuring the accuracy and reproducibility of downstream analytical results.

The team identified two cytokines to be used as markers to characterise the time elapsed prior to serum and plasma samples being processed, providing a robust and accurate quality control tool to diagnose their “preanalytical health”. The usefulness of this assay is particularly evident when determining whether the quality of samples with undocumented pre-analytics, such as historical collections, is good enough to allow their use in downstream research applications. The development of a related assay focusing specifically on the assessment of the quality of peripheral blood mononuclear cell samples is currently ongoing, with results being set to be published in 2018.

## BIOGLOSSARY

The idea behind **personalised medicine** is that healthcare can be customised to fit the unique characteristics of each person’s or group of individuals’ disease.

A **biobank** bridges science and medicine by collecting biological samples and their associated data from patients and healthy donors before processing, storing and distributing them to researchers.

A **biospecimen** is a sample of biological material, such as urine, blood, tissue, cells, DNA or protein, to be stored in a biobank for future research.

A **biomarker** is a biological characteristic that is objectively measured and evaluated as an indicator of physiological or pathological processes, or of a response to a therapeutic intervention.

**Cytokines** are small proteins released by cells that trigger cell signalling and affect the behaviour of surrounding cells.

**Peripheral blood mononuclear cells** are blood cells containing a round nucleus.



## Supporting national research

In line with one of its two strategic objectives, IBBL has been partnering with all major Luxembourgish research players in the biomedical field, lending its expertise to support advances in a variety of areas, from Parkinson's disease to personalised medicine and cancer. In 2017, the SOCS project - a partnership between IBBL, the Life Sciences Research Unit and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg as well as LIH and LNS - saw the discovery of MYO5B, a new prognostic biomarker for colorectal cancer. Its identification relied on an independent cohort of colorectal cancer patients, set up through the close cooperation between IBBL and the other partners. The collection will also be used for the future validation of the novel MYO5B biomarker, for which the research team is currently applying for funding.

## The EU External Quality Assessment programme provider

IBBL has been cultivating numerous relationships with key international players, being a valued partner in the consortia of several EU-funded projects. One such instance is SPIDIA4P, an EU-funded initiative seeking to bring about the standardisation of the pre-analytical workflows applied to

personalised medicine. Under the project, IBBL is leading the development and implementation of External Quality Assessment (EQA) schemes that will accompany the pre-analytical procedures. The EQAs will assess the efficiency of sample preparation methods in terms of the quality of the resulting samples, to be used for downstream diagnostic or research purposes. The inclusion in the SPIDIA4P Consortium stems from the international recognition of IBBL's expertise as the sole provider of Proficiency Testing programmes entirely dedicated to biospecimens.

## Keeping its promises

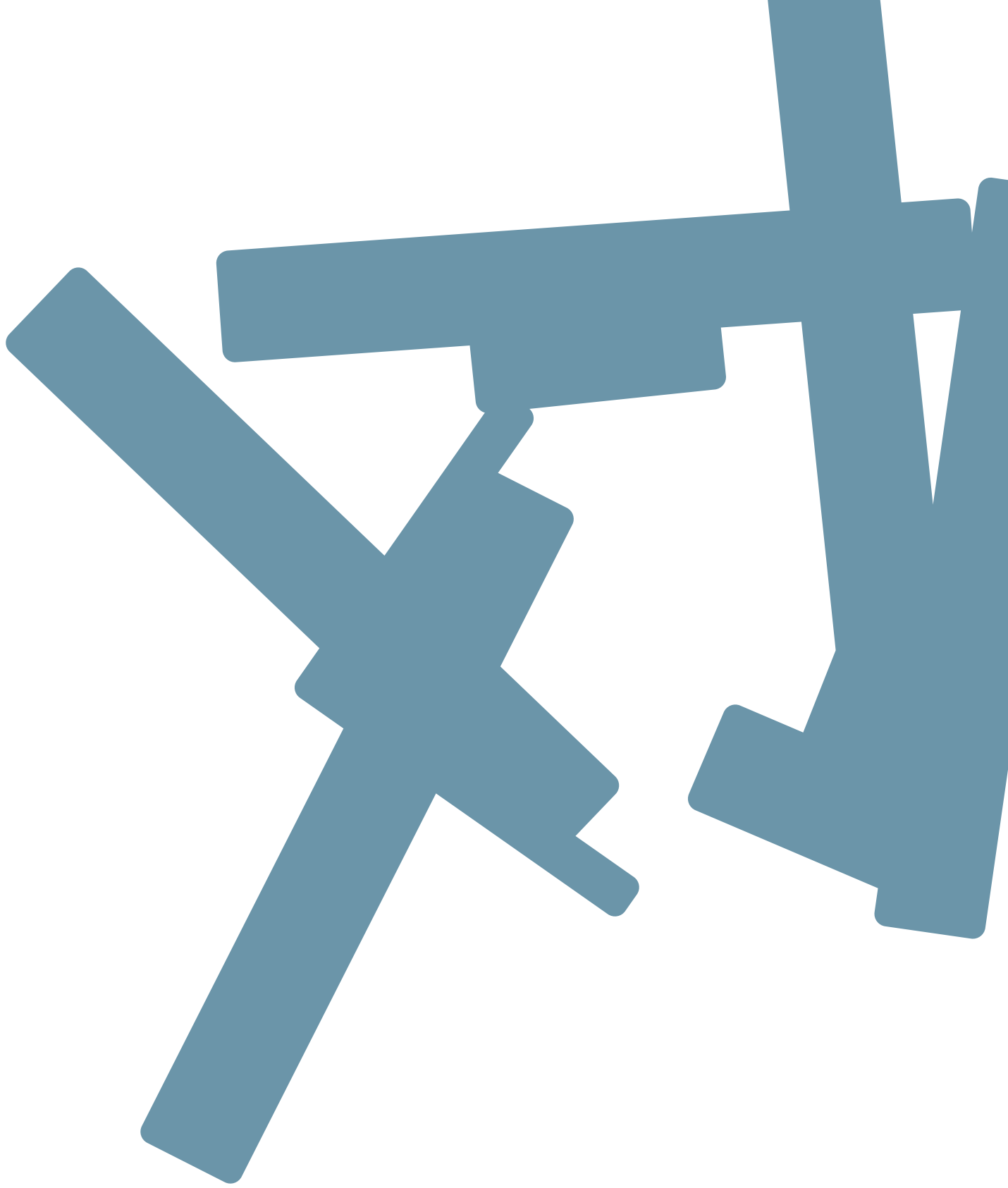
As a well-established research infrastructure active both nationally and internationally, IBBL has increasingly ambitious plans for the future. In 2018, the samples currently hosted in various partner organisations will be relocated to IBBL, owing to the additional space. Moreover, the activities to strengthen its European presence through collaborations and participation in European consortia will continue, in parallel with

the efforts to keep honouring contracts with existing partners and clients. Finally, IBBL will be pursuing its accreditation and certification operations to maintain its position as a quality-driven biobank.

Looking forward, the growing number of biospecimens securely stored at IBBL will enable researchers to decipher disease mechanisms. IBBL will keep ensuring that such valuable human samples, kindly donated by patients or study participants, are used to support the development of efficient treatments, whilst always respecting the wishes of the original donor.







## HIGHLIGHTS 2017









News, Events,  
Nominations & Awards

# HIGHLIGHTS 2017

JAN

## LIH becomes a member of EuroSafe

Since 1<sup>st</sup> January, LIH is a member of EuroSafe, the European Association for Injury Prevention and Safety Promotion. EuroSafe's mission is to prevent home and leisure accidents by working in partnership with industry, governments, research institutes and health and safety practitioners. It ensures the exchange of injury data and successful practices, and raises awareness on injury prevention at a European level. The institute is represented by Dritan Bejko, epidemiologist at the Epidemiology and Public Health Research Unit in the Department of Population Health, who is also a member of the advisory board of the European Injury Data Base - Network.



*Dritan Bejko, Luxembourg representative for EuroSafe*

## First training on animal experimentation and welfare in Luxembourg

Animal experimentation provides essential information to model and understand disease mechanisms. Appropriate training for every person engaged in the use of live vertebrate animals for scientific purposes is required by both the Council of Europe and the European Union. Starting in January, LIH and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg organised for the first time two training sessions on animal experimentation and welfare for scientists, enabling them to get adequately trained for the design of *in vivo* experiments in compliance with ethical and regulatory principles and respecting animal welfare. The new training comprised theoretical courses and practical workshops as well as E-learning modules.

FEB

## LIH cooperates with IBLA Luxembourg

LIH and "Institut fir Biologësch Landwirtschaft a Agrarkultur Luxembourg a.s.b.l." (IBLA), a Luxembourgish institute specialised in research, communication and agricultural extension services in organic agriculture, signed a "Memorandum of Understanding" on 21<sup>st</sup> February to formalise their cooperation in the field of agriculture, food production, nutrition and population health. This alliance is beneficial to work towards a more sustainable agriculture in Luxembourg. At LIH, Dr Torsten Bohn, Principal Investigator at the Epidemiology and Public Health Research Unit in the Department of Population Health and expert in nutrition and food science, is the driver of the cooperation. The collaborators will develop projects in the field of nutrition, namely on the topic of using protein-rich vegetables as a sustainable food source.

MAR

## LIH nominated WHO Collaborating Centre for Reference and Research on Measles Infections for the fifth time

The World Health Organisation (WHO) EURO Regional Office in Copenhagen nominated for the fifth consecutive time the WHO Collaborating Centre for Reference and Research on Measles Infections in Luxembourg located at LIH's Department of Infection and Immunity. This WHO Centre is led by Prof Claude Muller and Dr Judith Hübschen as Head and Deputy Head, respectively. The re-nomination is valid from March 2017 to March 2021, the first designation having been in February 1998. WHO expects policy and technical support provided to Member States in order to enhance their capacity to carry out surveillance and monitoring of measles infections.



Members of the WHO Collaborating Centre for Reference and Research on Measles Infections located at the Department of Infection and Immunity  
From left to right: Emilie Charpentier (technician), Prof Claude Muller (Head), Dr Judith Hübschen (Deputy Head), Aurélie Sausy (technician)



Cheque presentation by the Rotary Club Junglinster and Syrdall to Marc Vandelaer, IBBL's CEO ad interim, in the presence of Dr Catherine Larue, LIH's CEO ad interim

## Gesture of solidarity for IBBL from the Rotary Club

On 23<sup>rd</sup> March, IBBL - Integrated BioBank of Luxembourg was handed a cheque of 1,500 Euros by the Rotary Club Junglinster and Syrdall as a sign of solidarity and recognition. On this occasion the Rotary members first took a tour of the biobank's facilities and familiarised with its activities. A visit of the laboratories and the storage area for the biological samples were also on the agenda. The kind support of the Rotary Club contributed to the attribution of new laboratory equipment for the processing of biological samples.

APR

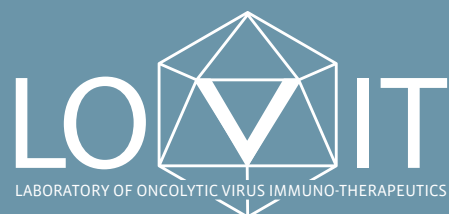
## Michael J. Fox Foundation visits Luxembourg

Since 2015, LIH is actively involved in the National Centre of Excellence in Research on Parkinson's Disease (NCER-PD) supported by the Luxembourg National Research Fund. On 21<sup>st</sup> and 22<sup>nd</sup> April, members of the Michael J. Fox Foundation for Parkinson's Research (MJFF) visited Luxembourg to discover the research programme on Parkinson's disease conducted in Luxembourg. They met Dr Catherine Larue, former CEO *ad interim* of LIH, and were able to learn more on the role of LIH and IBBL - Integrated BioBank of Luxembourg in the programme. The visit included a tour of the biobank, of the Parkinson Research Clinic at the "Centre Hospitalier de Luxembourg" and of the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg.

MAY

## LOVIT - Inauguration of a binational research unit

On 2<sup>nd</sup> May, LIH and the renowned German Cancer Research Centre (DKFZ) have inaugurated a new binational research unit named LOVIT - „Laboratory of Oncolytic Virus Immuno-Therapeutics". This unit, led by Dr Antonio Marchini, will develop new innovative strategies to fight cancer in the recently emerged field of oncolytic virotherapy, a treatment that uses viruses to destroy cancer cells. LOVIT is jointly funded by the two institutions and supported by a grant from the Luxembourg Cancer Foundation "Fondation Cancer".



dkfz

GERMAN  
CANCER RESEARCH CENTRE  
AT THE HEINRICH HEIMANNFondation  
CancerLUXEMBOURG  
INSTITUTE  
OF HEALTH



MAY



## Successful Luxembourg Microbiology Day

The Luxembourg Society for Microbiology (LSfM), founded in 2016, held its first national conference on 11<sup>th</sup> May at the "Laboratoire national de santé" in Dudelange. This "First Luxembourg Microbiology Day" was an occasion for its members, as well as prospective members, to meet, present and discuss their research and the impacts on science, health and economy. Dr Carole Devaux (Department of Infection and Immunity) and Dr Conny Mathay (IBBL - Integrated BioBank of Luxembourg) are members of the LSfM board.

## LuxCLIN conference on next-generation clinical research

The very first LuxCLIN conference was organised on 30<sup>th</sup> and 31<sup>st</sup> May at the "Centre Hospitalier de Luxembourg" by the Clinical and Epidemiological Investigation Centre of the Department of Population Health. The event, entitled "eClinical Research: getting virtual and personal - Innovative solutions for the use of electronic medical data to serve research purposes", gathered experts and opinion leaders to address the challenges and opportunities of next-generation clinical trials. It included an interactive and certified training for clinical investigators on "Good Clinical Practice" organised in collaboration with EF-GCP, the European Forum for Good Clinical Practice.



## World Hypertension Day: Learn to relax

On 15<sup>th</sup> May, date of the World Hypertension Day, LIH organised an open-air introduction to relaxation and meditation techniques in the Central Park - Luxembourg-Kirchberg. The lay public, mainly workers from the area, had the occasion to take part to Feldenkrais training, yoga, Pilates, sophrology and meditation sessions during their lunch break. They could test their blood pressure before and after these sessions to witness the effect of relaxation on blood pressure.



## LIH Science Quest: funding for a large outreach project

LIH aims to organise a large science-promoting event in February 2018, the first of its kind in Luxembourg, to present the institute's biomedical research activities to high school classes and the broad public in an unconventional and entertaining way. The concept of the "LIH Science Quest", inspired from adventure and escape games, was submitted for financial support to the Luxembourg National Research Fund. On 31<sup>st</sup> May, the funding agency officially announced its support for the project through the funding scheme "PSP - Promoting Science to the Public".





## Worldwide students to learn biobanking in Luxembourg

On 12<sup>th</sup> June, an international group of 13 students from Africa, Asia and Europe found their way back to “school”. Over a period of three weeks, they attended an intensive course on biobanking taught by an experienced team of lecturers from IBBL - Integrated Biobank of Luxembourg and other institutions at the University of Luxembourg. The participants working in biobanks or starting in the field gained experience in multiple aspects of biobanking, ranging from cryobiology, quality assurance and biospecimen science to logistical, regulatory and ethical issues. At the end of the programme, the students took an official written examination and eventually received a certificate delivered by the University of Luxembourg.



Participants of the biobanking training at the University of Luxembourg. The training was coordinated by Dr Fay Betsou, Chief Scientific Officer at IBBL (front)

JUNE



Dr Alexis Lion, project leader of “Sport-Santé”, awarded with the “Best Healthcare Educative Campaign of the Year Award” at the Luxembourg Healthcare Summit 2017

## Best Healthcare Educative Campaign of the Year Award for “Sport-Santé”

At the 4<sup>th</sup> edition of the Luxembourg Healthcare Summit on 15<sup>th</sup> June, the Sports Medicine Research Laboratory at the Department of Population Health was awarded with the “Best Healthcare Educative Campaign of the Year Award” for its project “Sport-Santé” that promotes therapeutic sport activities for patients. Led by Dr Alexis Lion since 2015, “Sport-Santé” aims to enlarge the course offer for patients and durably maintain it. The project goal is based on the evidence that therapeutic exercise is an important component in the treatment of diseases and improves the patients’ physical and mental well-being.

## Prize for best conference presentation

At the annual meeting of the Society of Hair Testing held from 12<sup>th</sup> to 14<sup>th</sup> June in Cardiff (United Kingdom), Emilie Hardy, research engineer at the Human Biomonitoring Research Unit in the Department of Population Health, was awarded the prize of the best oral presentation. She presented recent results on the evaluation of exposure of pregnant women to pesticides measured with hair samples. This project is of high relevance for public health, as several pesticides are suspected to have adverse health effects on the unborn child or to interfere with the hormone system of the mother.

## LUXCOR health event in Brussels

The first health event, organised by the Luxembourg Contact Office for Research and Innovation in Brussels (LUXCOR) jointly with LIH, was held in Brussels on 19<sup>th</sup> June. It gathered around 50 participants and was aimed at informing about Luxembourg’s efforts and developments in clinical and translational medicine, Big Data, eHealth and next-generation healthcare. LUXCOR is a joint venture between the six main Research, Development and Innovation stakeholder organisations in Luxembourg: LIH, the Luxembourg Institute of Socio-Economic Research (LISER), the Luxembourg Institute of Science and Technology (LIST), Luxinnovation, the Luxembourg National Research Fund and the University of Luxembourg.

## Award for sports medicine publication of high public interest

At the occasion of the annual congress of the German-Austrian-Swiss Society for Orthopaedic Sports Medicine GOTS held in Berlin (Germany) from 22<sup>nd</sup> to 24<sup>th</sup> June, Prof Daniel Theisen and his team, together with Dr Christian Nührenbörger and Prof Axel Urhausen, were awarded with the 2<sup>nd</sup> prize in the category “Paper of the highest public interest 2016” for a review published in the journal *Sports Orthopaedics and Traumatology*. The publication presents recent research findings on the relationship that exists between the risk of being injured during running, running biomechanics and footwear technology. Prof Daniel Theisen is Head of the Sports Medicine Research Laboratory at the Department of Population Health, Dr Christian Nührenbörger and Prof Axel Urhausen are sports medicine physicians from the “Centre Hospitalier de Luxembourg”.

## Donation for brain research from the Rotary Club Luxembourg

For the fifth time, the Rotary Club Luxembourg collected donations for brain research with its initiative “Espoir en tête” by organising movie sessions in cinemas. 60,000 Euros were donated for two research projects, one of them to be carried out by LIH’s Department of Oncology in collaboration with the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg. A reception was held at Kinepolis Kirchberg on 30<sup>th</sup> June. The project, led by Dr Alessandro Michelucci, will investigate the molecular heterogeneity of microglia, resident immune cells in the brain involved in neuroinflammation associated with brain diseases such as neurodegenerative disorders and cancer.



*Ceremony organised by Rotary Club Luxembourg to hand over two cheques of a total of 60,000 Euros to support brain research in Luxembourg*

JULY



*Prof Romain Seil*

## Nomination to the Scientific Committee of the Rizzoli Orthopaedic Institute

Prof Romain Seil, orthopaedic surgeon at the “Centre Hospitalier de Luxembourg” and scientific consultant at the Sports Medicine Research Laboratory within LIH’s Department of Population Health, was nominated to the Scientific Committee of the Rizzoli Orthopaedic Institute in Bologna (Italy) for a period of four years. Founded in the 19<sup>th</sup> century by the famous surgeon Francesco Rizzoli, the Rizzoli Orthopaedic Institute is the oldest orthopaedic institute in the world.

AUG

## Mark of 1000 participants passed for ORISCAV-LUX2

ORISCAV-LUX2 is a health study that aims to assess the cardiovascular health of Luxembourg’s resident population and to identify the potentially modifiable risk factors in order to suggest efficient preventive health measures. The recruitment of participants for ORISCAV-LUX2 runs from January 2016 to January 2018. On 17<sup>th</sup> August, the 1000<sup>th</sup> and 1001<sup>st</sup> participants took part in the study and received a special welcome by the ORISCAV-LUX2 team. The first wave of ORISCAV-LUX was conducted between 2007 and 2008 with more than 1,400 participants. The second wave is expected to include a similar number of participants.



*From left to right: Daniela Valoura Esteves (research nurse), Marylène d'Incau (research nurse coordinator of ORISCAV-LUX2), Elizabeth (ORISCAV-LUX2 participant #1000), Gustavo (ORISCAV-LUX2 participant #1001), Aurélie Wiederkehr (research nurse) and Dr Ala'a Alkerwi (project leader of ORISCAV-LUX2 and Principal Investigator)*

SEPT

## Presidency of the Luxembourg AIDS Surveillance Committee

On 1<sup>st</sup> September, Dr Carole Devaux, Deputy Head of the Infectious Diseases Research Unit at the Department of Infection and Immunity, was nominated by the Ministry of Health as new president of the Luxembourg Surveillance Committee for AIDS, Hepatitis and Sexually Transmitted Diseases. The missions of the committee are to inform the general public, target groups and health professionals on all issues related to AIDS, hepatitis and sexually transmitted infections as well as to closely collaborate with national and international organisations to develop and implement disease control programmes.



From left to right: Dr Jean-Claude Schmit (Director of Health, Ministry of Health), Dr Carole Devaux (President of the Luxembourg Surveillance Committee for AIDS, Hepatitis and Sexually Transmitted Diseases, LIH), Lydia Mutsch (Minister of Health, Ministry of Health), Anne Calteux, (Senior Policy Advisor, Ministry of Health)



Speakers and organisers of the Handball Congress

## International Handball Congress organised in Luxembourg

On 16<sup>th</sup> September took place the Handball Congress "Medical and Training Aspects in Handball" at the International University of Health, Exercise and Sports LUNEX in Differdange (Luxembourg). The congress focussing on injury prevention in one of the most popular team sports was of high scientific quality and had an international dimension with around 150 participants coming from all over Europe. This event was organised by the Luxembourg Academy of Medicine, Physical Therapy and Science into Sports that includes the Sports Medicine Research Laboratory at LIH's Department of Population Health.

## Workshop on Health Economics

An interactive workshop on Health Economics in the National and European context was held on 19<sup>th</sup> September at the "Centre Hospitalier de Luxembourg". It was organised by the Health Economics and Evidence Synthesis Research Unit of the Department of Population Health. The event brought together international experts in health economics as well as national stakeholders operating in healthcare to discuss the opportunities that health economic research has to offer in informing national policy to improve health and healthcare in Luxembourg.



LIH booth at Place d'Armes in Luxembourg City

## World Heart Day: Spy your heart

At the occasion of the World Heart Day, LIH organised a booth in the centre of Luxembourg City on 30<sup>th</sup> September. Amongst other activities, the lay public was invited to take part in the detective game "Spy your heart", designed by the Cardiovascular Research Unit at the Department of Population Health, to learn about the importance of biomarker research for the diagnosis and prevention of cardiovascular disease which is the world's leading cause of death.







## Pink October: Think pink and...DANCE!

During the month of October, countless initiatives are organised worldwide to raise awareness on breast cancer. LIH and the Luxembourg Cancer Foundation "Fondation Cancer" co-organised a dance workshop in Luxembourg City on 1<sup>st</sup> October to show solidarity with cancer patients and inform the public about the benefits of sports and healthy life style in cancer prevention. The participants had the opportunity to sway their hips on colourful rhythms and learn some basics of Zumba, Capoeira and Salsa.

## Poster prize at an international symposium

Amy Parrish, first-year doctoral candidate at the Eco-Immunology and Microbiome Research Group in the Department of Infection and Immunity, had the opportunity to present her research project with a poster at the "New Frontiers Symposium of Microbiome", an international scientific meeting held on 12<sup>th</sup> and 13<sup>th</sup> October in Nijmegen (Netherlands). The symposium was attended by over 350 scientists, including several leaders in the research field from Europe and beyond. Amy Parrish's poster was selected out of more than 30 posters from early-stage researchers for a prize offered by one of the sponsors of the symposium.



Quiz with QR codes  
by Mister Science

## Intensive training on the optimisation of evidence from clinical trials

From 16<sup>th</sup> to 19<sup>th</sup> October, on the initiative of Prof Stephen Senn, Head of the Competence Centre for Methodology and Statistics, two training sessions were organised in Luxembourg City for the research community and pharmaceutical industry on how to optimise evidence from clinical trials. Both courses were targeted at statisticians, regulatory scientists, Clinical Research Associates, clinical epidemiologists, medical advisors and health economists, and gathered 30 and 23 participants, respectively.



## Medical Research Day for the young generation

On 18<sup>th</sup> October, the third edition of the Medical Research Day was held at the "Centre Hospitalier de Luxembourg" (CHL) to open the world of medical research to the young generation. In line with their research and education missions, CHL, LIH and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg co-organised this event that is gaining more success from year to year. More than 300 high school students were informed about the mechanisms and challenges of medical research by the presentation of current projects in the fields of sports medicine, oncology, allergology, infectious diseases, cardiovascular disorders and many others. The young people also had the opportunity to participate to a quiz moderated by Luxembourg's famous "Mister Science".

## Kick-off retreat for the Doctoral Training Unit CANBIO

The Department of Oncology is coordinating the doctoral research and training programme CANBIO in oncology, supported by the PRIDE funding scheme of the Luxembourg National Research Fund. CANBIO provides state-of-the-art training in cancer biology and addresses the increasingly important clinical problems of tumour progression and relapse, drug resistance and tumour escape from the immune system. On 19<sup>th</sup> and 20<sup>th</sup> October, all CANBIO PhD candidates, their supervisors and other invitees from the cancer research community in Luxembourg met for the first CANBIO retreat in Mondorf-les-Bains to exchange and officially kick off the programme.



## Pelican grants for PhD candidates to support training and mobility

Andrés Cano Galiano and Matthieu Gobin, both PhD candidates at the NorLux Neuro-Oncology Laboratory at the Department of Oncology, were two of the successful applicants of the Pelican Grant 2017 from the foundation “Fondation du Pélican de Mie et Pierre Hippert-Faber” that is under the aegis of the “Fondation de Luxembourg”. The foundation yearly awards a number of applying PhD candidates affiliated with the Doctoral Programme in Systems and Molecular Biomedicine of the Doctoral School in Science and Engineering at the University of Luxembourg with a grant to be used for training activities and professional development. On 24<sup>th</sup> October both PhD candidates were informed that they shall receive 10.000 Euros.



## Well-attended National PhD Welcome Day

The second edition of the National PhD Welcome Day took place on 26<sup>th</sup> October, gathering more than 100 first-year PhD candidates based in Luxembourg from all disciplines at the Maison du Savoir on the Belval Campus in Esch-sur-Alzette. The event, organised by the University of Luxembourg together with all Luxembourgish public research stakeholders, aimed to give an insight on doctoral training in Luxembourg and inform about the increasingly important topic of Open Science. The event encompassed the National Open Science Conference, a conference accessible to all researchers, explaining the principles, benefits and challenges of open access, open research data and open source.

## FNR Award for “Outstanding Scientific Publication”

On 27<sup>th</sup> October, the Luxembourg National Research Fund (FNR) held the ninth edition of the FNR Awards in Esch-sur-Alzette, presenting seven awards for excellence in research, innovation and science communication. Dr Mahesh Desai, leading the Eco-Immunology and Microbiome Research Group at the Department of Infection and Immunity, received the FNR Award for “Outstanding Scientific Publication” for his first-authorship on a publication in the prestigious journal *Cell*, published in the November issue of 2016. The publication entitled “A dietary fibre-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility” presents a study on the influence of nutrition on gut microbes.



Dr Ulf Nehrbaas (CEO of LIH), Dr Mahesh Desai (FNR awardee) and Prof Markus Ollert (Director of the Department of Infection and Immunity)



NOV

## Inaugural Retreat of the Doctoral Training Unit NextImmune

LIH is the coordinating institution for NextImmune, the doctoral research and training programme in next-generation immunosciences supported by the PRIDE funding scheme of the Luxembourg National Research Fund. The first scientific retreat gathering all NextImmune PhD candidates and their supervisors as well as cooperation partners, external scientific advisors and special guests took place in Mondorf-les-Bains on 2<sup>nd</sup> and 3<sup>rd</sup> November. NextImmune aims to bridge classical immunology and systems biology to understand the mechanisms of acute and chronic inflammation in autoimmune, allergic and infectious diseases. The inaugural retreat was the first occasion for all members and stakeholders to meet and network.



*Prof Markus Ollert, NextImmune coordinator and Director of the Department of Infection and Immunity, welcoming the attendees of the NextImmune retreat*

## Cardiolinc™ becomes a non-profit organisation

Cardiolinc™, an international research network focusing on next-generation technologies to personalise diagnostics and treatment for cardiovascular disease, was formally launched as a non-profit organisation on 6<sup>th</sup> November. The network was founded by Dr Yvan Devaux, Head of the Cardiovascular Research Unit at the Department of Population Health, postdoctoral fellow Dr Clarissa Pedrosa da Costa Gomes, and collaborators from the Universities of Bristol, Leicester and Maastricht. Cardiolinc™ helps connect researchers from multiple disciplines, clinicians and private companies to fight the world's main cause of death. Created in 2014, it currently has more than 70 members.



## Career support for postdoctoral researchers

The third edition of the Cross-border Postdoctorales, a four-day career orientation workshop organised by "Association Bernard Grégory" and the Franco-German University in partnership with Luxembourg's public research institutions, was held in Luxembourg City from 6<sup>th</sup> to 9<sup>th</sup> November. Two postdoctoral fellows from LIH were selected to participate. The workshop allowed the attendees to reflect on a professional reorientation to the private sector and efficiently prepare this next career step. Participants were also informed about the job market in the Greater Region and met PhD holders and recruiters working in areas outside of academia.

## LIH in touch with the public at the Science Festival

Attracting over 10,000 visitors every two years, the Science Festival is Luxembourg's largest public event to promote science and research. From 9<sup>th</sup> to 12<sup>th</sup> November, the National Museum of Natural History and the Luxembourg National Research Fund hosted the 11<sup>th</sup> edition of the Luxembourg Science Festival in Luxembourg City. LIH was present with three interactive workshops that allowed participants to assess their physical fitness and mental performance, and get knowledge about their body composition. The workshops aimed to inform the public about some of the institute's activities in the field of population health. IBBL - Integrated BioBank of Luxembourg had a workshop on cancer titled "When our cells go crazy".



## Nomination of a Focal Point for injury prevention in Luxembourg

Dritan Bejko, epidemiologist at the Epidemiology and Public Health Research Unit in the Department of Population Health, has been designated on 20<sup>th</sup> November by Lydia Mutsch, Minister of Health, to act as Focal Point for injury prevention in Luxembourg for the World Health Organisation. Dr Bejko is project leader for the programme RETRACE collecting information on injuries and accidents in the emergency departments of the hospitals in Luxembourg each year.

Dritan Bejko



Aurélie Fischer,  
nominated Operational  
Contact Point for HIV  
epidemiology



© CHL/Paul Fougere

## Designation of an Operational Contact Point for HIV epidemiology

The Ministry of Health appointed Aurélie Fischer, Clinical Research Coordinator at the Clinical and Epidemiological Investigation Centre in the Department of Population Health, as Operational Contact Point for HIV epidemiology for the European Centre for Diseases Control (ECDC) and the Joint United Nations Programme on HIV/AIDS (UNAIDS). LIH is involved in infectious disease monitoring at the national level. In this context, the institute regularly provides specific figures for Luxembourg related to HIV and hepatitis infection to the Ministry of Health and to European and international bodies such as ECDC, UNAIDS, UNICEF and the World Health Organisation. Since 2016, Aurélie Fischer is responsible for collecting data for these organisations.

DEC



©CHL

## World AIDS Day

The World AIDS Day is the annual occasion to show solidarity with HIV-positive people and inform about preventive measures. Different national actors in HIV prevention including LIH invited to an awareness and solidarity event on 1<sup>st</sup> December for high school classes. The event was followed by an exhibition and prize ceremony for the art contest « Preventive Art - Demystify Condoms » in the presence of Lydia Mutsch, the Minister of Health. Moreover, red ribbons and condoms were distributed at the main train station in Luxembourg City.

## Award for two doctoral candidates at the PhD Days 2017

Two doctoral candidates from LIH were awarded with the "Excellent Presentation Award" for their oral presentations given at the PhD Days of the Doctoral School in Science and Engineering, held on 7<sup>th</sup> and 8<sup>th</sup> December on the Belval campus in Esch-sur-Alzette. Antoun Al Absi, PhD candidate at the Laboratory of Experimental Cancer Research in the Department of Oncology, received the first prize by presenting his work on the evasion of breast cancer cells to the immune response. The second prize was handed to Torkia Lalem, PhD candidate at the Cardiovascular Research Unit in the Department of Population Health, reporting on a new biomarker for cardiac function after heart attack that could be specifically used in females.



©PhD Days

PhD candidate Antoun Al Absi, winner of the first prize of the "Excellent Presentation Award", with Prof Serge Haan, Director of the Doctoral School in Systems and Molecular Biomedicine



019

LPVALOP

021

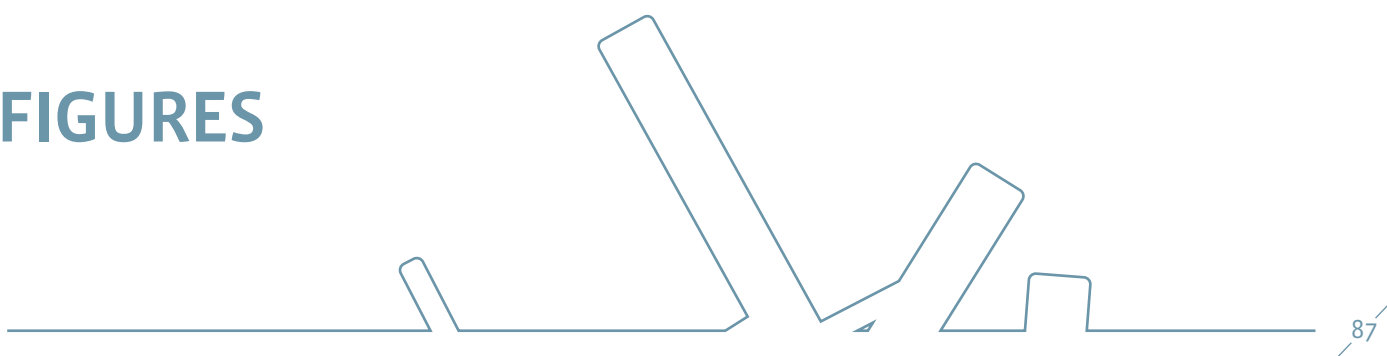
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## FIGURES







J232



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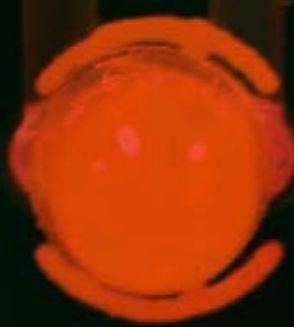
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± TRAYMO ±

017

030



The **Board of Directors** is nominated by the Government and is composed of nine external members of different professional backgrounds. Its mission is to oversee the activities at LIH. It is responsible for the general organisation, for defining internal rules, for budget control, for framework contracts with partner organisations and for approving new strategies.

The **Executive Committee**, composed of the Chief Executive Officer, the Chief Financial and Administrative Officer and the directors of the three research departments, is responsible for the implementation of the strategy approved by the Board of Directors and for day-to-day management of the institution. It guarantees the compliance with ethical principles, conventions and national laws.

The **Coordinating Council** is a consultative body composed of internal representatives of the researchers, the personal delegation and the research and innovation support personnel. It issues advisory opinions to the Board of Directors regarding research policy, development and innovation and can advise on the content of the pluriennial performance contract to be concluded with the Government.

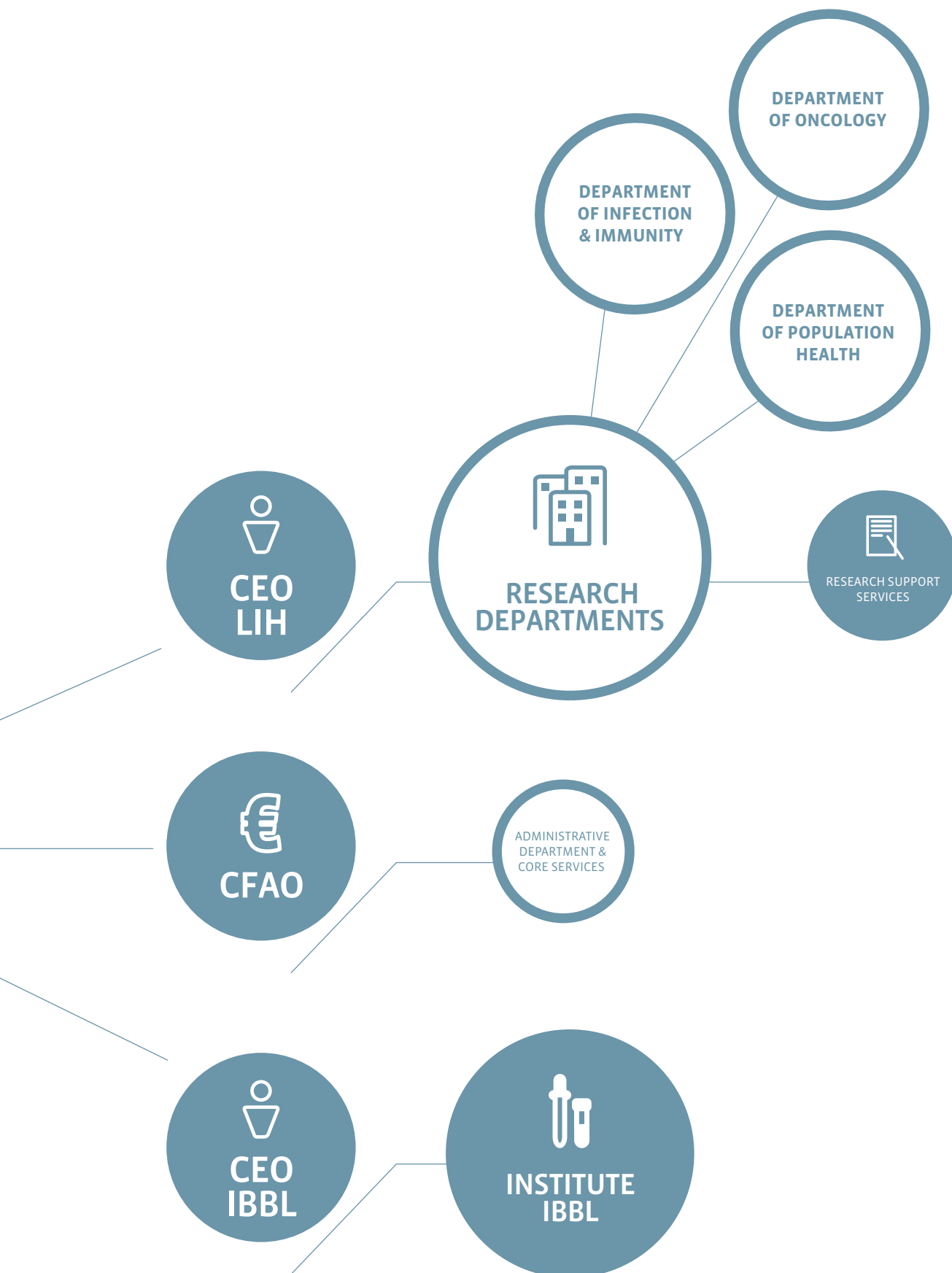
Each research department has a **Scientific Advisory Board**. These boards are consultative bodies to the Board of Directors and comprise high-ranking external scientists. Their composition reflects the scientific area in which the departments are active. Their main tasks are to advise on the strategic and scientific orientations of the departments and to provide a scientific evaluation of the research units.



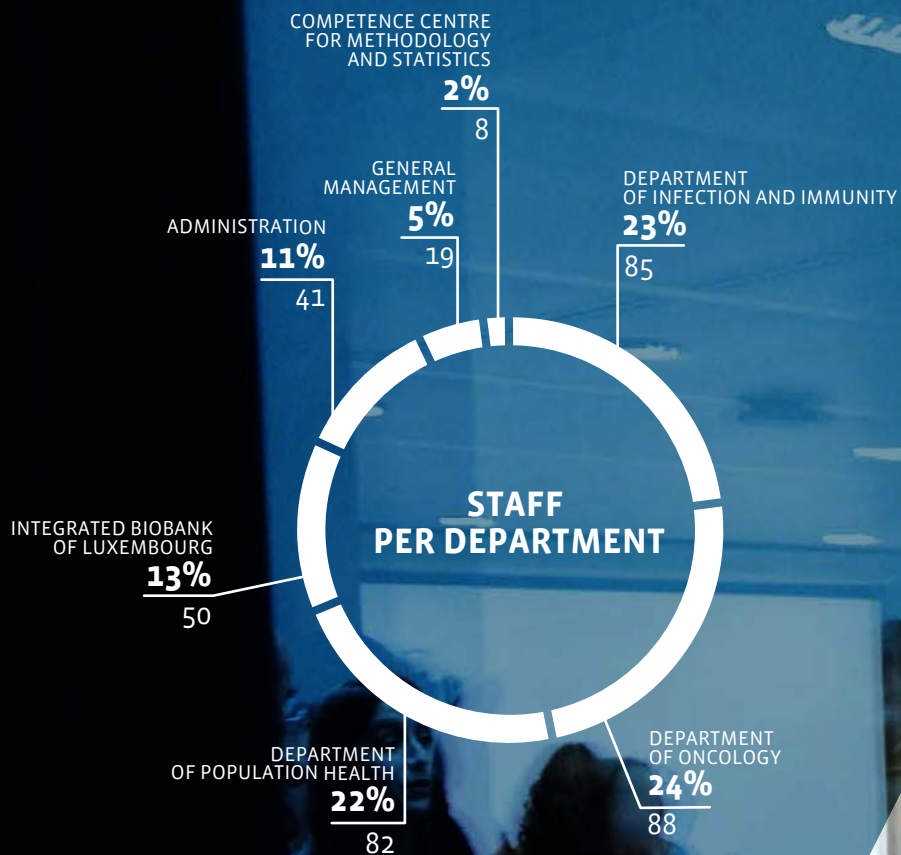
*Board of Directors (from left to right): Xavier Poos (Commissaire de Gouvernement), Dr Viviane Bremer, Stéphanie Damgé, Patrizia Luchetta, Dr Gregor Baertz (president), Dr Nadine C. Martin (vice-president), Dr Hugues Malonne and Dr Robert Müller. Absent: Pierrot Schiltz, Prof Evelyn Schroeck.*



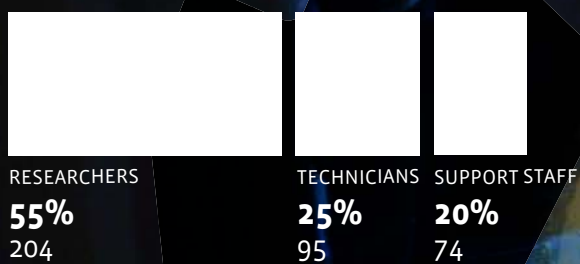
## GOVERNANCE





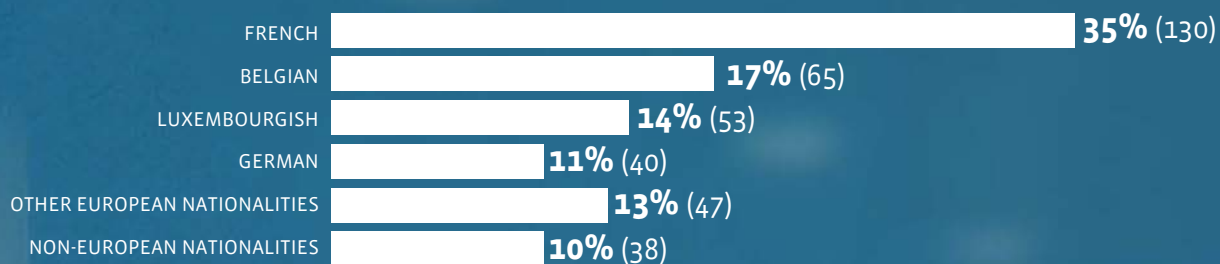


## STAFF BY FUNCTION

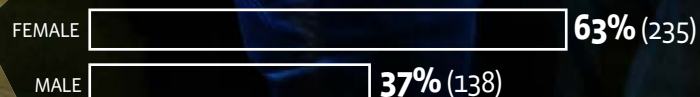


## HUMAN RESOURCES

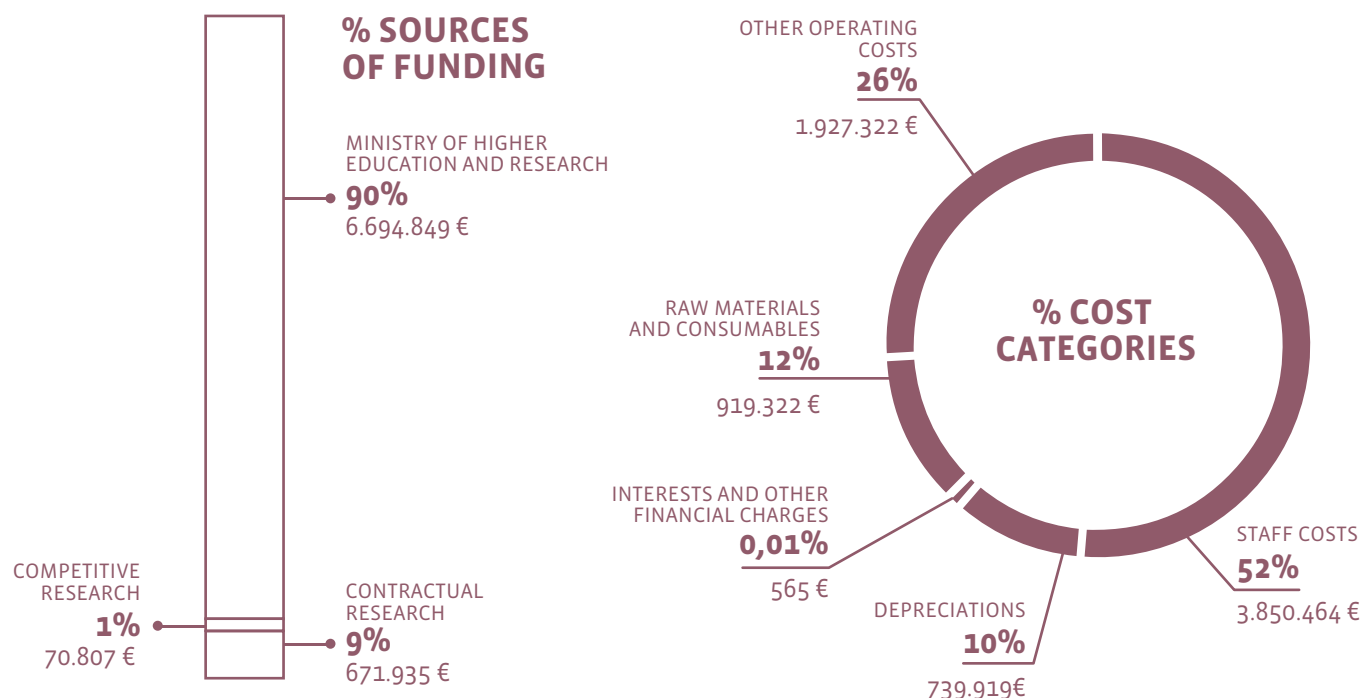
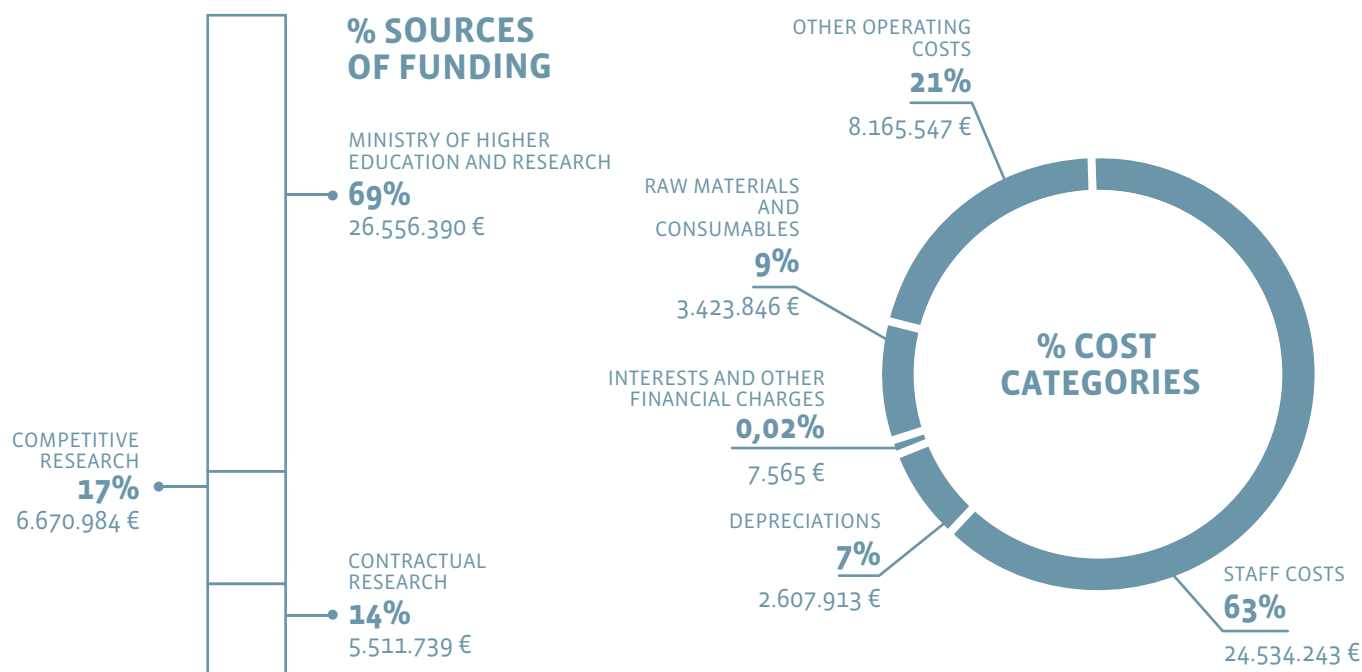
## STAFF BY NATIONALITIES



## STAFF BY GENDER







## FINANCES

### STATUTORY EXPENSES

**PROFIT AND LOSS ACCOUNT (EUR)**

	<b>2017</b> 01.01 - 31.12.17	<b>2016</b> 01.01 - 31.12.16
<b>A. CHARGES</b>		
1. Use of merchandise, raw materials and consumable materials	4.343.168	3.983.822
2. Other expenses	10.103.869	8.418.262
3. Staff costs	28.384.706	26.030.254
4. Value adjustment on intangible and tangible fixed assets	3.336.832	3.418.292
5. Interests and other financial charges	8.131	5.844
6. Profit for the financial year	0	0
<b>TOTAL CHARGES</b>	<b>46.176.706</b>	<b>41.856.474</b>
<b>B. INCOME</b>		
1. Net turnover	1.757.498	1.539.165
2. Subsidies	43.868.440	40.133.531
3. Other income	78.568	130.945
4. Interests and other financial income	29.622	52.833
5. Loss for the financial year	442.578	0
<b>TOTAL INCOME</b>	<b>46.176.706</b>	<b>41.856.474</b>

# FINANCES

## PROFIT AND LOSS ACCOUNT

(31<sup>st</sup> December 2017, incl. IBBL)

**ASSETS (EUR)****2017**  
01.01 - 31.12.17**2016**  
01.01 - 31.12.16**FIXED ASSETS**

Intangible fixed assets	829.365	695.070
Tangible fixed assets	8.122.938	9.110.073
Financial fixed assets	425.585	424.555
<b>TOTAL FIXED ASSETS</b>	<b>9.377.888</b>	<b>10.229.698</b>

**CURRENT ASSETS****Debtors**

<b>1. Trade debtors</b>	<b>1.077.438</b>	<b>1.080.984</b>
a. Becoming due and payable within one year	1.058.894	1.062.440
b. Becoming due and payable after more than one year	18.544	18.544
<b>2. Other debtors</b>	<b>6.976.361</b>	<b>3.936.571</b>
a. Becoming due and payable within one year	6.976.361	3.936.571
Cash at bank and in hand	<b>24.760.483</b>	<b>21.804.458</b>

**TOTAL CURRENT ASSETS****32.814.282**      **26.822.013****Prepayments**

<b>TOTAL ASSETS</b>	<b>42.849.027</b>	<b>37.575.571</b>
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# FINANCES

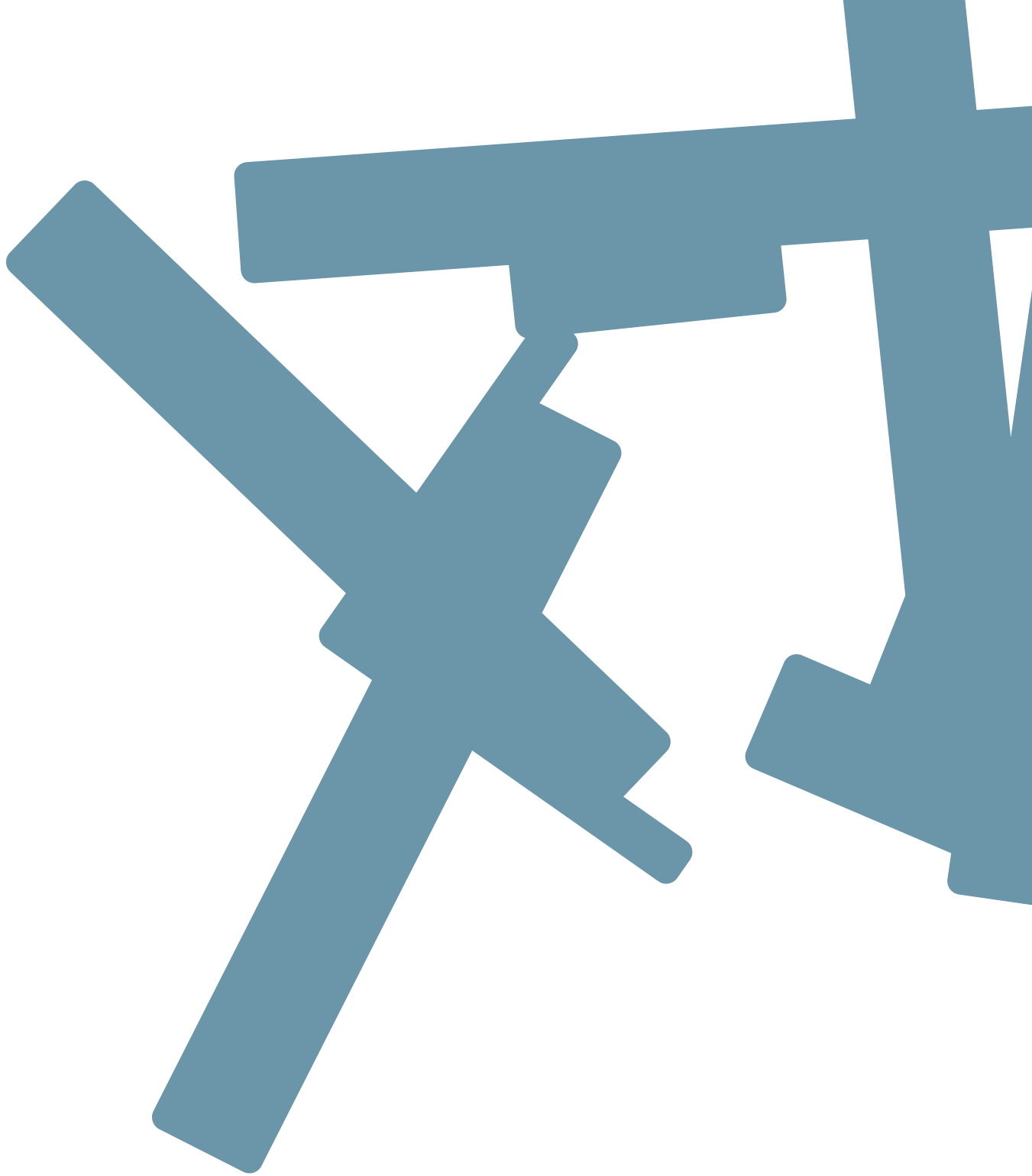
## BALANCE SHEET

(31st December 2017, incl. IBBL)

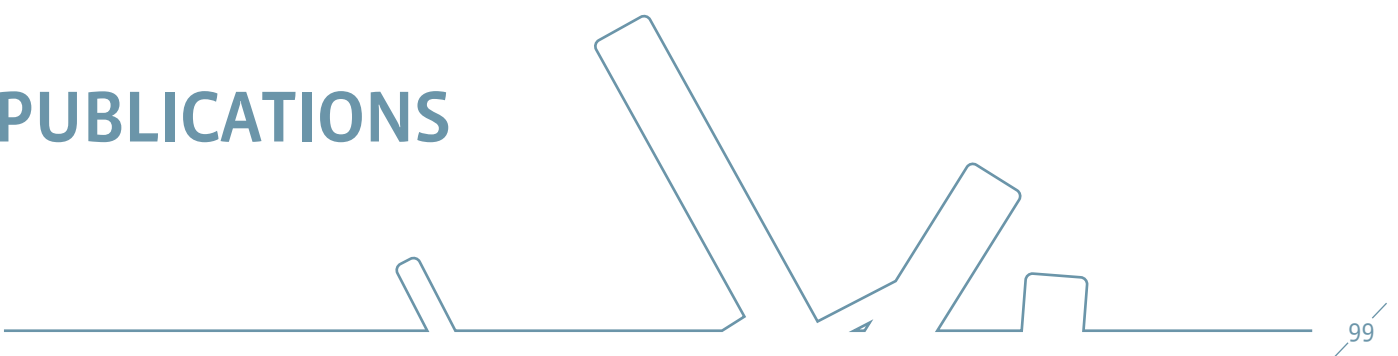
<b>LIABILITIES (EUR)</b>	<b>2017</b> 01.01 - 31.12.17	<b>2016</b> 01.01 - 31.12.16
<b>CAPITAL AND RESERVES</b>		
Financial wealth	4.099.157	4.099.157
Reserves	1.486.881	1.486.881
Profit or loss brought forward	8.494.366	8.494.366
Profit or loss for the financial year	-442.578	0
Capital investment subsidies	9.886.546	9.490.224
<b>TOTAL CAPITAL AND RESERVES</b>	<b>23.524.372</b>	<b>23.570.628</b>
<b>Available reserve for projects</b>	<b>14.260.441</b>	<b>9.150.822</b>
<b>Provisions</b>	<b>1.661.304</b>	<b>1.441.957</b>
<b>NON-SUBORDINATED DEBTS</b>		
<b>1. Trade creditors</b>	<b>2.406.668</b>	<b>2.478.806</b>
a. Becoming due and payable within one year	2.385.707	2.457.845
b. Becoming due and payable after more than one year	20.961	20.961
<b>2. Tax and social security debts</b>	<b>945.406</b>	<b>895.219</b>
a. Tax debts	4.837	12.384
b. Social security debts	940.569	882.835
<b>3. Other creditors</b>	<b>45.875</b>	<b>37.990</b>
a. Becoming due and payable within one year	45.875	37.990
<b>TOTAL AVAILABLE RESERVE FOR PROJECTS, PROVISIONS AND CREDITORS</b>	<b>19.319.694</b>	<b>14.004.794</b>
<b>Deferred income</b>	<b>4.961</b>	<b>149</b>
<b>TOTAL CAPITAL, RESERVES AND LIABILITIES</b>	<b>42.849.027</b>	<b>37.575.571</b>







## PUBLICATIONS









# COMPETENCE CENTRE FOR METHODOLOGY AND STATISTICS

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Gamble C, Krishan A, Stocken D, Lewis S, Juszcak E, Dore C, Williamson PR, Altman DG, Montgomery A, Lim P, Berlin J, Senn S, Day S, Barbachano Y, Loder E. **Guidelines for the content of statistical analysis plans in clinical trials.** *JAMA*. 2017; 318(23): 2337-2343. *IF: 44.405 (2016)*

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**Note:** *The Competence Centre for Methodology and Statistics also contributed significantly to several studies published by the different research departments (listed in the following sections).*

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