

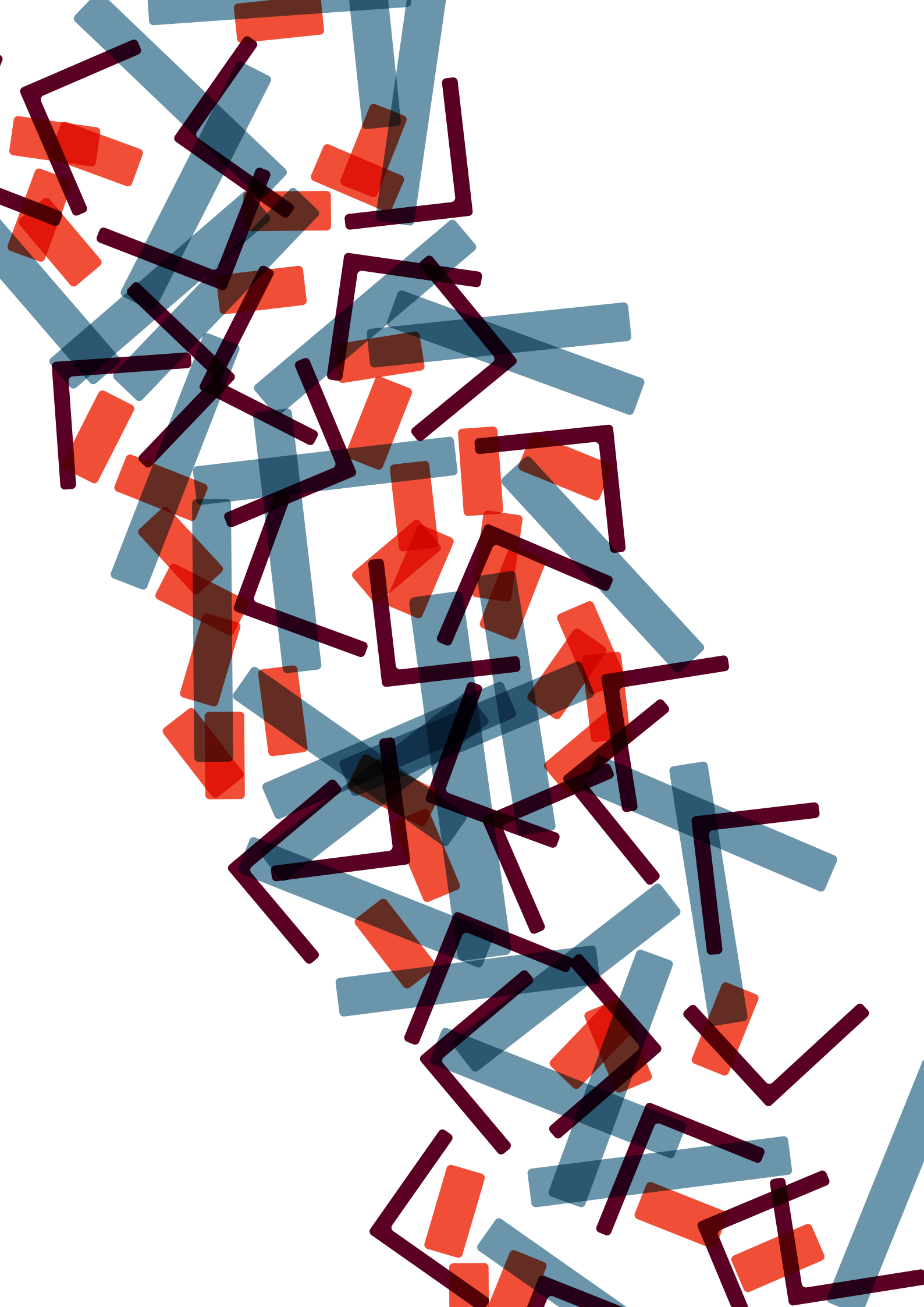
# LUXEMBOURG INSTITUTE OF HEALTH

RESEARCH DEDICATED TO LIFE

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ANNUAL REPORT 2016





# FOREWORD

## RESEARCH DEDICATED TO LIFE

*We are pleased to present you our annual report that looks back to an eventful year.*

The Luxembourg Institute of Health (LIH) encompasses three large thematic research departments reflecting its research priorities - Infection and Immunity, Oncology, Population Health, and a biobank IBBL, the Integrated BioBank of Luxembourg.

In 2016, LIH's research departments excelled in their scientific outcomes by authoring a total of 272 articles, including book chapters, public health reports and doctoral theses. This is a significant increase compared to 2015 when 253 articles were produced with roughly the same number of scientific staff. In 2016, 19 publications were of outstanding scientific quality and were published in international peer-reviewed journals with an impact factor higher than 10. With this, we surpassed our objective on scientific production defined in the performance contract that had been concluded with the Government from 2014 to 2017. In line with our valorisation objectives, LIH also filed five patent applications during the year, another overachievement.

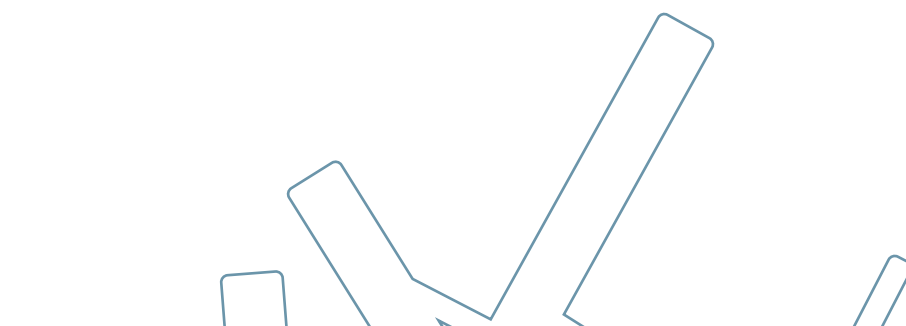
The institute's internal structure was profoundly reorganised during 2015, and its strategy was reshaped and refined. In 2016, the benefits of this reorganisation were already truly tangible. There had been an intensive work on

the branding of our corporate identity, for example with unifying business cards, presentations of our institution in- and outside Luxembourg, and the design of new flyers to broader advertise our activities. We also aimed to enhance corporate feeling within the institution and are proud of being ambassadors of LIH.

Each research department had its highlights in 2016.

One of the new research groups focussing on the gut microbiome, created in 2015 at the **Department of Infection and Immunity**, delivered a high-impact publication in the prestigious journal *Cell* about the influence of nutrition on our gut bacteria.

The **Department of Oncology** engaged in a strategic partnership with the German Cancer Research Centre DKFZ, a recognised leader in cancer research, to create a binational research unit that will be located partly within the department and partly at DKFZ. In 2017, the unit will implement new innovative treatment strategies, using oncolytic viruses to kill cancer cells. The department was also strengthened with the appointment of an expert in proteomics research to head the Proteome and Genome Research Unit as well as with a renowned researcher (PEARL chair) in neuropathology.



The **Department of Population Health** contributed for the first time within a large consortium to major worldwide public health studies about non-communicable diseases such as obesity, diabetes and hypertension, providing quality national data. Moreover, it surpassed the defined objectives for the inclusion of new participants for clinical and epidemiological studies. More than 1,000 new participants could be recruited in one year, many of them for the national Parkinson study NCER-PD, conducted jointly with the University of Luxembourg, “Centre Hospitalier de Luxembourg” and other national and international partners, and for the second wave of the ORISCAV-LUX study assessing national cardiovascular health.

LIH managed to maintain its ISO 9001:2008 certification and extended the scope to three new units. In 2016, the institute received substantial competitive funding to develop doctoral training with two out of three proposals for research and training programmes accepted for the grant scheme PRIDE of the Luxembourg National Research Fund. The two funded Doctoral Training Units, one in the field of immunology and one in oncology, will allow to train more than 30 PhD candidates over the next six years.

LIH has the mission to work towards improving health and healthcare. Together with our 350 co-workers we will endeavour to bring scientific progress straight to the patient. The current structure will allow us to head towards new opportunities when they arise.

Knowing where to move, LIH could efficiently contribute to the development of a position paper about Luxembourg’s research strategy for the next years until 2025. The institute was also involved in establishing the research strategy for the National Cancer Plan to optimise the country’s research efforts in oncology.

At LIH, nothing could progress without the continuous dedication of its collaborators. The overachievement of some of our objectives defined in the performance contract are due to the hard work of LIH’s staff, always striving for **excellence** while embodying **passion** and **integrity**.

We would like to thank them for the great job they did in 2016.



Dr Gregor Baertz  
President of LIH's Board of Directors



Dr Catherine Larue  
CEO ad interim of LIH

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excellence  
passion  
integrity

MISSION & VISION



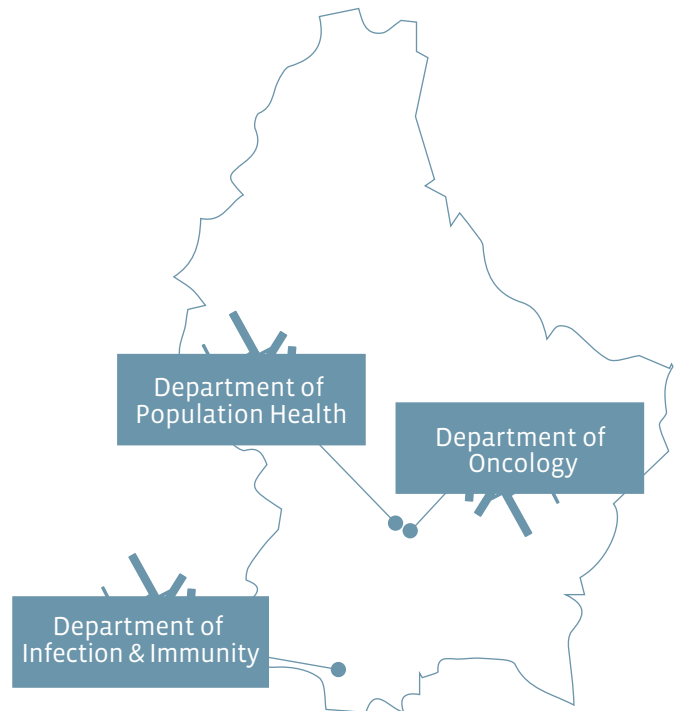




LH's **mission** is to generate and translate research knowledge into clinical applications with an impact on the future challenges of healthcare and personalised medicine.

Its **vision** is to put Luxembourg on the map of biomedical research and achieve leadership in focused areas.





## KEY FACTS

2016



# 3

RESEARCH  
DEPARTMENTS

# 1

BIOBANK



LUXEMBOURG  
INSTITUTE  
OF HEALTH  
RESEARCH DEDICATED TO LIFE

# 186

SCIENTISTS

# KEY FACTS\*

2016



**35**

GRANT PROPOSALS  
ACCEPTED



**192**

AGREEMENTS  
SIGNED



**10.9** €<sub>MIO</sub>

THIRD-PARTY  
INCOME



**351**

EMPLOYEES



**35**

NATIONALITIES

\*including IBBL





**13**

NEW PHD  
CANDIDATES



**292**

PUBLICATIONS



**43**

PUBLIC-PRIVATE  
PARTNERSHIPS



**270**

ONGOING PROJECTS





**SCIENTIFIC  
EXCELLENCE**







LUXEMBOURG  
INSTITUTE  
OF HEALTH  
RESPIRATORY MEDICINE

# EAT FIBRE OR BE EATEN!

High-fibre diet keeps gut microbes from degrading the colon's lining

How does a dietary fibre-deprived gut microbiota compensate the lack of nutrients, and what are the consequences for health? This is what a study, conducted by junior group leader Dr Mahesh Desai together with national and international teams, investigated.

## Diet affects microbiota

Human dietary habits used to include a large amount of fibres that have proven health benefits. Over the last few decades, this intake has fallen drastically, mainly due to the consumption of processed food and a change in lifestyles which has been connected to increased cases of intestinal diseases including colon cancer. However, the mechanisms behind these connections had remained poorly understood.

The researchers aimed to investigate the impact of a high-fibre and a fibre-deprived diet on the gut microbiota composition and physiology, and the resulting effects on the colonic mucus barrier. For this, they selected 14 representative, well-characterised bacterial species from the human gut to colonise the intestine of germ-free mice and observed that this synthetic microbiome was able to respond dynamically to variations in dietary fibre intake. Significantly more mucus-degrading bacteria were found in the absence of dietary fibre, leading to increased production of mucus-degrading bacterial enzymes.

## Starved microbes feed on gut mucus

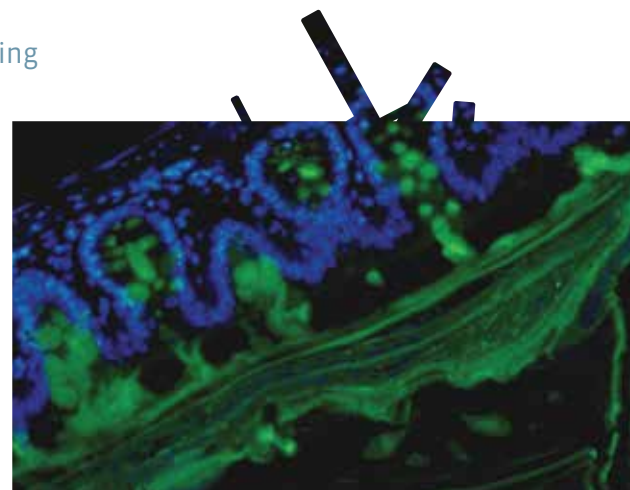
By analysing sections of the gut under the microscope, the scientists revealed that fibre deprivation leads the microbiota to degrade the colonic mucosal barrier to reduce its integrity. As the mucus lining of the gut is an important barrier to invasion of harmful microorganisms, this finding led to the hypothesis that fibre-deprived mice would be more susceptible to infection.

To test this, the researchers infected the thick and thin mucus layer of mice with an enteric pathogen. It managed to easily traverse the mucus layer to reach the outer layer of the gut and caused severe disease in mice fed with fibre-free diet. The “holes” created by the microbiota while eroding the mucus serve as wide open doors for pathogens to invade. In contrast, mice fed with fibre easily recovered from that same infection.

## Eat more fibre!

The findings of this study highlight the important role of fibre in nutrition and reveal a strong link between diet, gut microbiota and a healthy intestinal barrier.

The scientists also tried a diet excluding fruits and vegetables but integrating classical prebiotic supplementation. This diet resulted in a similar erosion of the mucus layer as observed in the lack of fibre. These results open up avenues for designing next-generation prebiotics using dietary therapeutics that would target human gut microbiome and might be useful in treating and preventing certain diseases of the intestinal tract.



Microscopy image of the mucus layer (in green) and mucus-producing goblet cells (in blue) in a mouse gut

“We found that low consumption of dietary fibre makes some of our friendly intestinal bacteria furious.”

Dr Mahesh Desai, principal investigator

## Publication:

The study was published in the November 2016 issue of the prestigious scientific journal *Cell* having an impact factor of 28.7. The publication, first-authored by Dr Mahesh Desai, is entitled “A dietary fibre-deprived gut microbiota degrades the colonic mucus barrier and enhances pathogen susceptibility”.

## Funding & Collaborations:

The study was primarily supported by the Luxembourg National Research Fund (INTER Mobility and CORE grants) as well as the National Institutes of Health (R01 grant).

The outcomes result from a collaboration under the lead of the Department of Infection and Immunity together with the Department of Oncology, the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg, the University of Michigan Medical School (Ann Arbor, United States), the Washington University School of Medicine (St-Louis, United States) and the Aix-Marseille University (Marseille, France).

## BIOGLOSSARY

**Dietary fibre** is an indigestible part of plant-derived food, made of carbohydrate.  
**Microbiota** is the entire collection of microorganisms in a specific niche, such as the gut.  
The **microbiome** comprises all of the genetic material within a microbiota.  
The **mucosal barrier** is said to be the body's second skin. It runs from the mouth to the anus, and serves as the first line of defence against infectious agents.  
An **enteric pathogen** is a microorganism causing disease in the gut.  
**Prebiotics** are non-digestible fibre compounds that promote the growth of beneficial microorganisms in the gut.

# OBESITY INCREASE IN LUXEMBOURG AND WORLDWIDE

Contribution to a large-scale study on global obesity estimations

A major public health study, led by a large international consortium involving LIH's Department of Population Health, aimed at estimating the worldwide trends in obesity. Conclusion? This condition continues to increase in almost every country: an alarming result.

## Data from all over the world

For this study, Body Mass Index (BMI) data was collected from almost 1,700 population-based measurement studies including a total of 19.2 million adult participants. The study's main investigators could pool and analyse reliable and comparable data from 200 countries and territories generated in the past 35 to 40 years. For Luxembourg, data coming from the ORISCAV-LUX study, conducted between 2007 and 2008 by Dr Ala'a Alkerwi and co-workers with more than 1,400 participants to assess national cardiovascular health, has been selected to assess the national obesity trends.

## Rising trends for obesity

The study revealed that the global age-standardised mean BMI increased significantly between 1975 and 2014. Within this period of time, it rose from 21.7 to 24.2 kg/m<sup>2</sup> in men, and from 22.1 to 24.4 kg/m<sup>2</sup> in women. China, USA, India, Mexico, Brazil and Russia were identified as the countries with the highest proportion of obese (BMI 30-35 kg/m<sup>2</sup>) and severely obese (BMI ≥ 35 kg/m<sup>2</sup>) people. BMI trends for Luxembourg steadily increased over the monitored time period and were above the global trends for both men and women.

Whereas obesity globally increased, underweight was found to be decreased, so that there are now more obese than underweight people on the planet.

## Global health targets unlikely to be met

For this report, an unprecedented amount of population-based data was collected to provide the lengthiest and most complete estimates of trends in obesity. The investigators utter that if those trends continue, the world will not be able to meet the global targets set at the 2011 United Nations high level meeting on non-communicable diseases. At this conference, it was defined that the rise of obesity and diabetes should be stopped by 2025, which, given the findings, seems virtually impossible.

“LIH's public health data serves not only on a national level but also for important global studies.”

Dr Ala'a Alkerwi, principal investigator

## Publication:

This study was published in April 2016 in open access in *The Lancet*, one of the best-known and high-ranked medical journals having an impact factor of 44.0. It is authored by a large consortium, the Non-Communicable Diseases Risk Factor Collaboration (NCD-RisC) coordinated by the WHO Collaborating Centre on NCD Surveillance and Epidemiology at Imperial College London (London, United Kingdom). The report is entitled “Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1,698 population-based measurement studies with 19.2 million participants”.

In addition to the publication, dynamic world maps and individual country data on obesity and other parameters can be viewed on the NCD-RisC website [www.ncdrisc.org](http://www.ncdrisc.org).

## Funding & Collaborations:

The research, coordinated by Imperial College London was supported by the Wellcome Trust and Grand Challenges Canada.

Dr Ala'a Alkerwi contributed to this study as a one of the more than 750 members of NCD-RisC.

## BIOCABULARY

The **Body Mass Index (BMI)** is a measure of body fat based on weight and height (kg/m<sup>2</sup>). It allows to classify into the categories “underweight”, “normal weight”, “overweight” “obese” and “severely obese”.

# NOVEL INSIGHTS INTO HEART REGENERATION

Grasping the regenerative capacity of the zebrafish heart at a systems level

The zebrafish is a key model system for vertebrate tissue regeneration after injury. A team of researcher from LIH's Department of Oncology, together with other cross-disciplinary partners, have reported a systems biology study that offers novel insights into heart regeneration in the zebrafish.

## A popular fish in science

In mammals, the heart has a limited potential for regeneration after injury. The ability of organ and limb regeneration in lower vertebrate species is a fascinating research topic, essentially because the comprehension of the underlying molecular mechanisms could lead to the development of strategies to stimulate human organ regeneration. Since the 1970's, the zebrafish has been a widely used genetic model organism to study how tissue regeneration occurs. These animals are capable of regenerating amputated fins and certain injured organs such as the brain, the spinal cord or the heart within weeks after damage.

## A complex network of gene expression

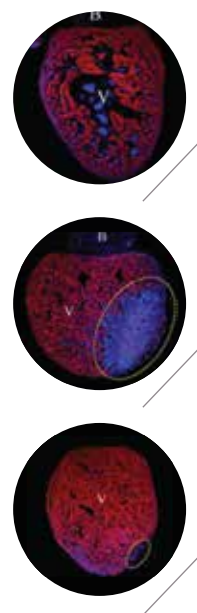
To get systematic insights into the phenomenon, the researchers performed genomic analysis of injured and control zebrafish hearts at different time-points after injury. Dr Sophie Rodius and Dr Francisco Azuaje from the NorLux Neuro-Oncology Laboratory identified important time-specific changes in gene expression

during heart generation and generated a dynamic co-expression network displaying genes that are expressed in a similar manner.

The analysis of this network uncovered modules of highly interconnected genes, which are specialised in biological processes essential to heart regeneration. Furthermore, they identified hundreds of network hubs with control roles in heart regeneration. Interestingly, most of these hubs are genes that can also be found in humans.

## From fish to human

This study is the first in-depth characterisation of the gene expression network of heart regeneration in the zebrafish. A further major outcome is a web-based resource that allows the interactive analysis of relevant data and models reported in this study. This resource will be valuable to the international scientific community and will greatly facilitate the understanding of zebrafish heart regeneration contributing to potential translation of this knowledge into new treatments for patients who suffered heart attacks.



Microscopy images of zebrafish heart sections before injury (top), one day after injury (middle) and two weeks after injury (bottom). Healthy myocardial tissue is shown in red and areas in a reparative process in blue. The injured area is indicated by a dotted circle

“Our study highlights the value of systematic unbiased approaches to unravelling novel biological knowledge.”

Dr Francisco Azuaje, principal investigator

## BIOCABULARY

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

**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).

A **gene co-expression network** is a graphic representation with nodes showing genes that are expressed similarly. In this undirected graph, each node corresponds to a gene.

A pair of nodes is connected with an edge if there is a significant co-expression relationship between them.

A **gene module** is a set of co-expressed genes in a gene co-expression network.

**Network hubs** are highly connected nodes in a gene co-expression network.

## Publication:

The findings were published in open access in the journal *Scientific Reports* (impact factor 5.2) of the Nature Publishing Group in May 2016. The article is titled “Analysis of the dynamic co-expression network of heart regeneration in the zebrafish” and is first-authored by Dr Sophie Rodius.

The generated genomic data can be visualised at <http://infused.vital-it.ch>.

## Funding & Collaborations:

The research was funded by the Luxembourg National Research Fund and the Swiss National Research Foundation, as part of the INFUSED project.

It involved researchers from the NorLux Neuro-Oncology Laboratory and the Proteome and Genome Research Unit at LIH, the Swiss Institute of Bioinformatics (Lausanne, Switzerland), the Centro Nacional de Investigaciones Cardiovasculares Carlos III (Madrid, Spain) and other institutions in Europe and the USA.



# PREDICTING THE OUTCOME AFTER A HEART ATTACK WITH A SIMPLE BLOOD TEST

## Circular RNAs as biomarkers

How can we better anticipate patient outcome after a heart attack? Researchers from the Cardiovascular Research Unit at LIH's Department of Population Health discovered, along with international collaborators, a circular ribonucleic acid (RNA) that can be measured in the blood and could serve as a biomarker to prevent heart failure.

### Consequences of a heart attack

Medicine has greatly improved survival of patients suffering a heart attack, but it still has not been able to decrease the subsequent damage to the heart muscle. About 15 to 20% of the patients develop a life threatening condition a few months after the infarction, a so-called left ventricular dysfunction. If the heart's left ventricle is damaged, the patients can develop heart failure, as the heart is not able anymore to pump blood adequately to meet the body's needs. About 60% of those patients die within five years after the heart attack.

### Focus on circular RNAs

Existing tools to detect patients at risk of developing left ventricular dysfunction have serious limitations, making the discovery of novel prognostic biomarkers essential. It is in that context that LIH's Cardiovascular Research Unit has been focusing on finding non-coding RNA molecules. Their use as biomarkers for various diseases is an active topic of investigation. Indeed, in the last few years different studies have demonstrated the importance of non-coding RNAs for cardiac development and cell differentiation, and several non-coding RNAs have been implicated in cardiovascular disease.

The researchers unveiled a novel circular RNA, called MICRA (Myocardial Infarction-associated Circular RNA), as predictor of left ventricular dysfunction after heart attack. They used blood samples from 409 patients of the national registry of patients with

myocardial infarction. Patients with low levels of MICRA in their blood were found to be at high risk to develop the life threatening dysfunction.

The discovery was validated in an independent group of 233 heart attack patients from the German LIFE-Leipzig study by collaborators from the Faculty of Medicine at the Leipzig University, Germany. In addition, the Institute of Cardiology in Warsaw, Poland, verified that the levels of MICRA in the left ventricle of patients with end-stage heart failure indicate whether this circular RNA plays a role in development of left ventricular dysfunction.

### MICRA has potential for clinical application

This study is the first showing that circular RNAs can be used as biomarkers for cardiac disorders. Although further studies are necessary to confirm the use of MICRA as biomarker in a prognostic test, these findings are highly relevant in the context of personalised medicine, helping physicians tailor diagnosis and treatment to the individual patient.



“MICRA is a very promising biomarker candidate due to its stability in the blood allowing a quantification in blood samples.”

Dr Yvan Devaux, Head of the Cardiovascular Research Unit

### Publication:

This study was published in September 2016 in the number one cardiology journal, the *Journal of the American College of Cardiology* (impact factor 17.8). It is titled “Myocardial infarction-associated circular RNA predicting left ventricular dysfunction” and first-authored by research engineer Mélanie Vausort.

### Funding & Collaborations:

This project was supported by intramural funding.

The study benefitted from a close collaboration with the Faculty of Medicine at the Leipzig University, Germany, and the Institute of Cardiology in Warsaw, Poland. The research groups involved in the study are part of a larger network named Cardiolinc™ ([www.cardiolinc.org](http://www.cardiolinc.org)), initiated a few years ago by Dr Yvan Devaux. Cardiolinc™ serves as an important exchange platform on the role of non-coding RNAs in cardiovascular disease. The network is currently composed of more than 50 international partners.

## BIOCABULARY

**Circular ribonucleic acids (RNAs)** are a type of non-coding RNAs. 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 **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 **left ventricle** is the heart's main pumping chamber.

A **prognostic** biomarker provides information on the likely outcome of a disease without treatment.

# COULD CHOCOLATE PREVENT CARDIOVASCULAR DISEASE AND TYPE 2 DIABETES?

Results from the ORISCAV-LUX study

There is the saying “a little of what you fancy does you good”. The results of a new study reveal the potential benefits of chocolate on health: the daily consumption of moderate amounts of chocolate may help to prevent cardiovascular disease and type 2 diabetes.

## Chocolate is healthy in moderated amounts

In this study, led by principal investigator Dr Ala'a Alkerwi and collaborators, it was found that people with higher consumption of chocolate had lower insulin levels, a well-known risk factor for cardiovascular disease, as well as improved liver enzyme levels. Over 80% of participants reported consuming an average of 24.8 grams of chocolate per day.

This newly gained knowledge could have an impact on recommendations by healthcare professionals to encourage individuals to consume a wide range of phytochemical-rich foods, which can include chocolate in moderate amounts. Nevertheless, it is important to differentiate between the natural product cocoa and the processed product chocolate, which is an energy-dense food. Therefore, physical activity, diet and other lifestyle factors must be carefully balanced to avoid detrimental weight gain over time.

Another interesting result of the study is that people who claimed to eat chocolate were younger, more physically active and had higher levels of education than those who claimed not to eat chocolate on a daily basis. It is possible that chocolate consumption may represent an overall marker for a cluster of favourable socio-demographic profiles, healthier lifestyle behaviours and better health status.

The results may be consolidated with randomised controlled trials in which a direct comparison is made between a chocolate-consuming and a control group.

## Observational data from Luxembourg

The findings were generated with data from more than 1,100 people aged 18 to 69 and living in Luxembourg, who were part of the ORISCAV-LUX study conducted between 2007 and 2008 to assess cardiovascular health and disease risks. To interpret the data, the researchers took into account the lifestyle of the participants as well as dietary factors, such as the simultaneous consumption of tea and coffee, two polyphenol-rich beverages potentially favouring the cardiometabolic effects of chocolate.

“Cocoa-based products may represent an additional dietary recommendation to improve cardiometabolic health.”

*Dr Ala'a Alkerwi, principal investigator*

## Publication:

The results of this study were published in the *British Journal of Nutrition* (impact factor 3.3) in March 2016. The article, first-authored by Dr Alkerwi, is titled “Daily chocolate consumption is inversely associated with insulin resistance and liver enzymes in the Observation of Cardiovascular Risk Factors in Luxembourg study”.

## Funding & Collaborations:

The study received financial support from the Luxembourg National Research Fund in the framework of the DIQUA-LUX project.

Research was conducted in close collaboration with the University of Warwick Medical School (United Kingdom), the University of South Australia (Australia) and the University of Maine (United States).

## BIOCABULARY

**Phytochemicals** are non-nutritive plant chemicals that have protective or disease preventive properties (e.g. polyphenols).

A **randomised controlled trial** is a scientific experiment that aims to reduce bias when testing a new treatment or feature. People participating in the trial are randomly allocated to a test or control group.



# CONTRIBUTION TO A BETTER GLOBAL ALLERGY CARE

Edition of the very first Molecular Allergology User's Guide

LIH's Department of Infection and Immunity substantially contributed to the publication of the world's first exhaustive handbook on molecular allergology. The book of more than 300 pages aims at improving global allergy care by promoting better patients treatments and facilitating experts' training. Named Molecular Allergology User's Guide, it was edited by the European Academy of Allergy and Clinical Immunology (EAACI).

## A collaborative achievement

The book covers all types of allergies, for example food allergy, hay fever, asthma, eczema, occupational allergies and insect venom hypersensitivity. It is composed of three main parts. The first is a comprehensive introduction presenting general concepts in allergology and allergy diagnosis. The second is about the traditional, clinically-driven top-down approach of allergy diagnosis and treatment, whereas the third presents the modern bottom-up approach which uses molecular fingerprinting of the patient's allergic response.

Creating the *Molecular Allergology User's Guide* was a tremendous effort: a task force on molecular allergology chaired by five experts was working on the project. It coordinated the contribution by 65 authors from 20 countries. One of the task force chairs was Prof Markus Ollert, Director of LIH's Department of Infection and Immunity. He also acted as an editor and an author in the project. He and two research group leaders from the department, Dr Christiane Hilger and Dr Annette Kuehn, edited eight of the 37 chapters of the handbook: a major input. Dr Martine Morisset, allergologist at the "Centre Hospitalier de Luxembourg", was also involved in the writing process.

## A handbook for the future specialists

According to the task force, there is a huge gap between new technologies emerging from allergy research and what is applied in patient care. The guide which explains in detail how to apply molecular testing in allergy diagnosis shall eventually fill this gap. The authors hope that it will serve to improve global allergy care and will be essential for the training of future specialists in allergology. The book shall also be of help for medical specialists working in other domains, paediatricians or dermatologists for instance, who want to acquire further knowledge for optimising and personalising allergy treatment.

The handbook was published and officially presented by the EAACI at an annual congress which took place in June 2016 in Vienna. In the future, it shall evolve to a web-based repository that can be updated on a regular basis with the latest advances in the field of allergology.



Interview with Prof Markus Ollert about the Molecular Allergology User's Guide

## Publication:

The Molecular Allergology User's Guide was published on the EAACI website [www.eaaci.org](http://www.eaaci.org) and also as a supplement in the journal *Pediatric Allergy and Immunology* (impact factor 3.9) in May 2016.

## BIOCABULARY

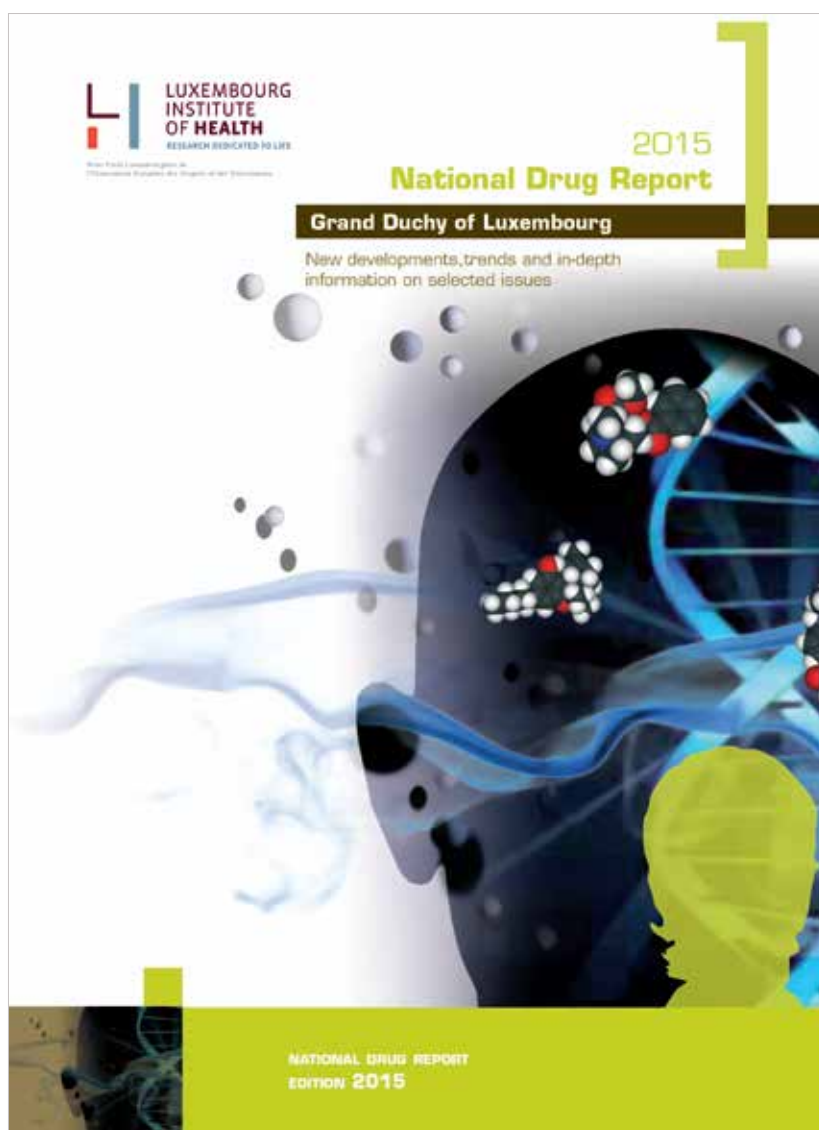
**Molecular fingerprinting** attempts to identify patterns of proteins in the blood or tissues to detect diseases.

# DELIVERING RELEVANT NATIONAL PUBLIC HEALTH INFORMATION

Three LIH reports published by the Ministry of Health

LIH has the role of first supplier of public health information in Luxembourg, enabling public authorities to make decisions based on scientific data and to communicate validated data to international institutions. This mission is reflected by the generation of three important reports by the Department of Population Health which have been published by the Ministry of Health in 2016.

## Zoom on the three reports:



### *2015 National Drug Report: Grand Duchy of Luxembourg*

This national report, published in French and English language in April, describes the framework in which drug use and drug trafficking evolve at the national level by providing a comprehensive overview of historical developments and recent trends. It reports on new developments and gives in-depth information on selected issues.

It was edited by the Luxembourg focal point of the European Monitoring Centre for Drugs and Drug Addiction, a centre that provides the European Union and its member states with a factual overview of European drug problems and a solid evidence base to support the drugs debate.

## BIOCABULARY

**Perinatal** relates to the time immediately before and after birth.



### *“Surveillance de la santé périnatale 2011-2013”*

In Luxembourg, a report on national perinatal health is regularly published providing an overview on the state of health of mothers and babies in Luxembourg. Based on exhaustive data collected from all maternities and independent midwives, the 2011-2013 report, published in May, highlights that Luxembourg provides quality healthcare to pregnant women, mothers and babies, and reveals relevant evolutions for variables such as birth rate, foetal and neonatal mortality and risk factors related to life style.

One of the findings is that the number of births registered in Luxembourg is steadily rising. Whereas there were slightly more than 6,200 deliveries in 2011, there were almost 6,700 in 2013. A slight increase was also recorded for the average age at which women give birth. It had remained stable for around ten years, but in 2012, it went for the first time above 31.



### *“Carte Sanitaire 2015”* (Health Card)

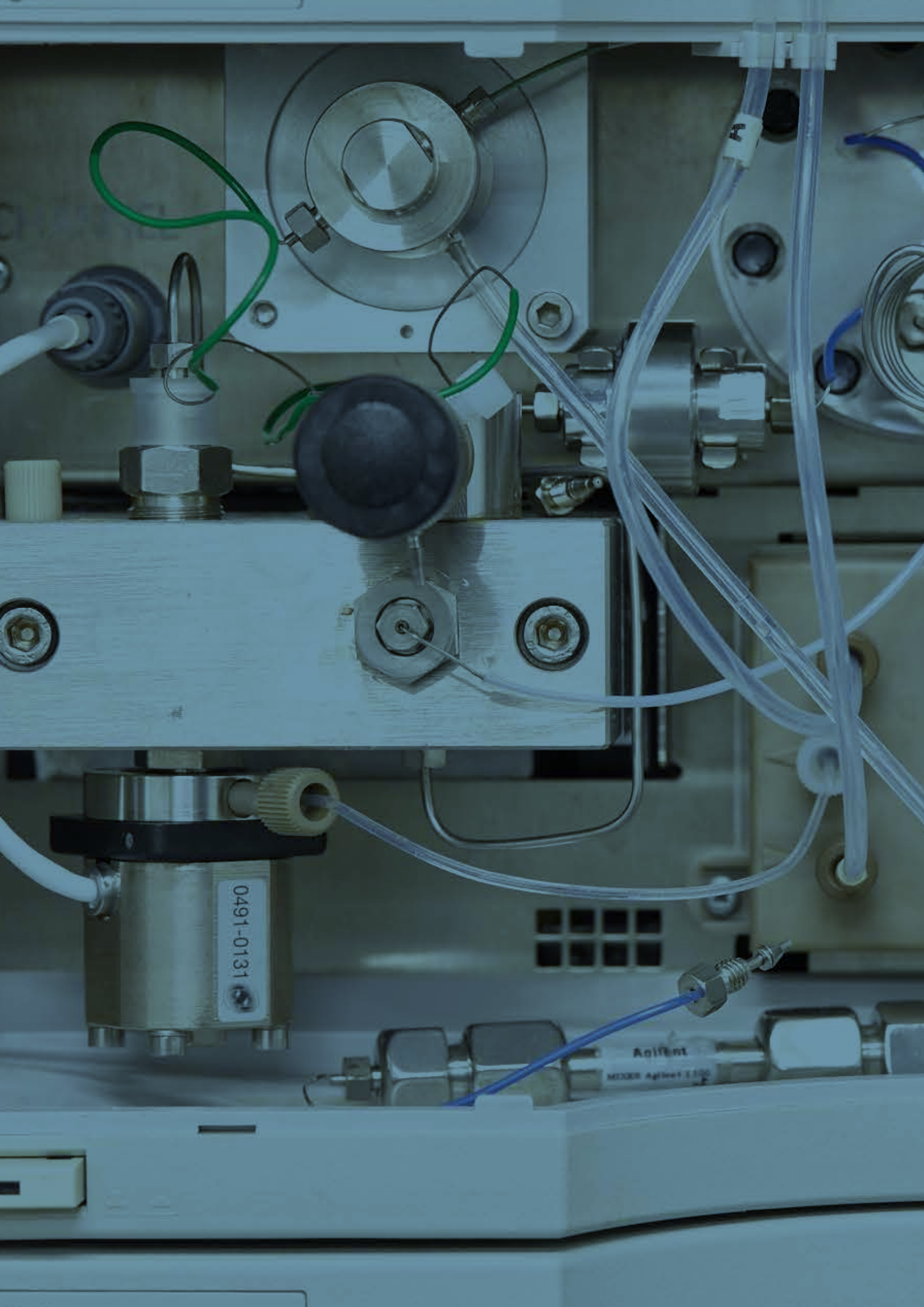
This report, which is an updated and concise version of the “*Carte Sanitaire 2012*” provides a thorough overview of the national hospital sector that enabled the Ministry of Health to carry out an up-to-date assessment of national health needs in terms of number of hospitals, beds and services. The report is also an informative document for hospital directors as well as for the broad public.

The detailed hospital inventory including services, resources, equipment and bed occupancy served as a basis for the ministry to present a new bill on hospital planning in September. The report pointed out that the rapid growing of Luxembourg's population needs to be considered for optimal hospital planning. One observation is that the hospital stays increased by 2.3% per year between 2002 and 2013, with more and more people using day hospitalisation.

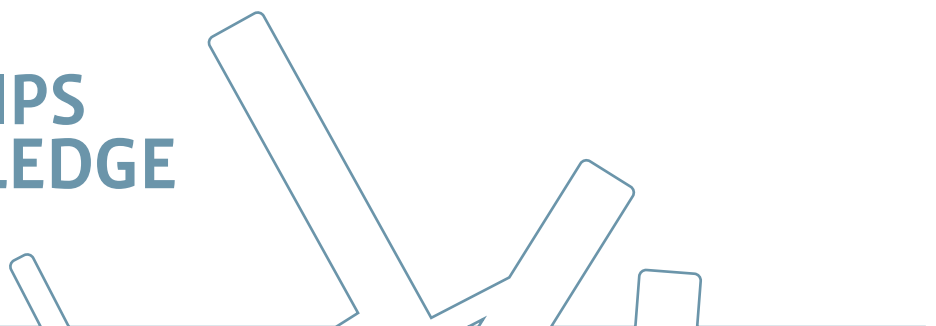
#### Publication:

All three reports are available for download on the Health Portal [www.sante.lu](http://www.sante.lu)

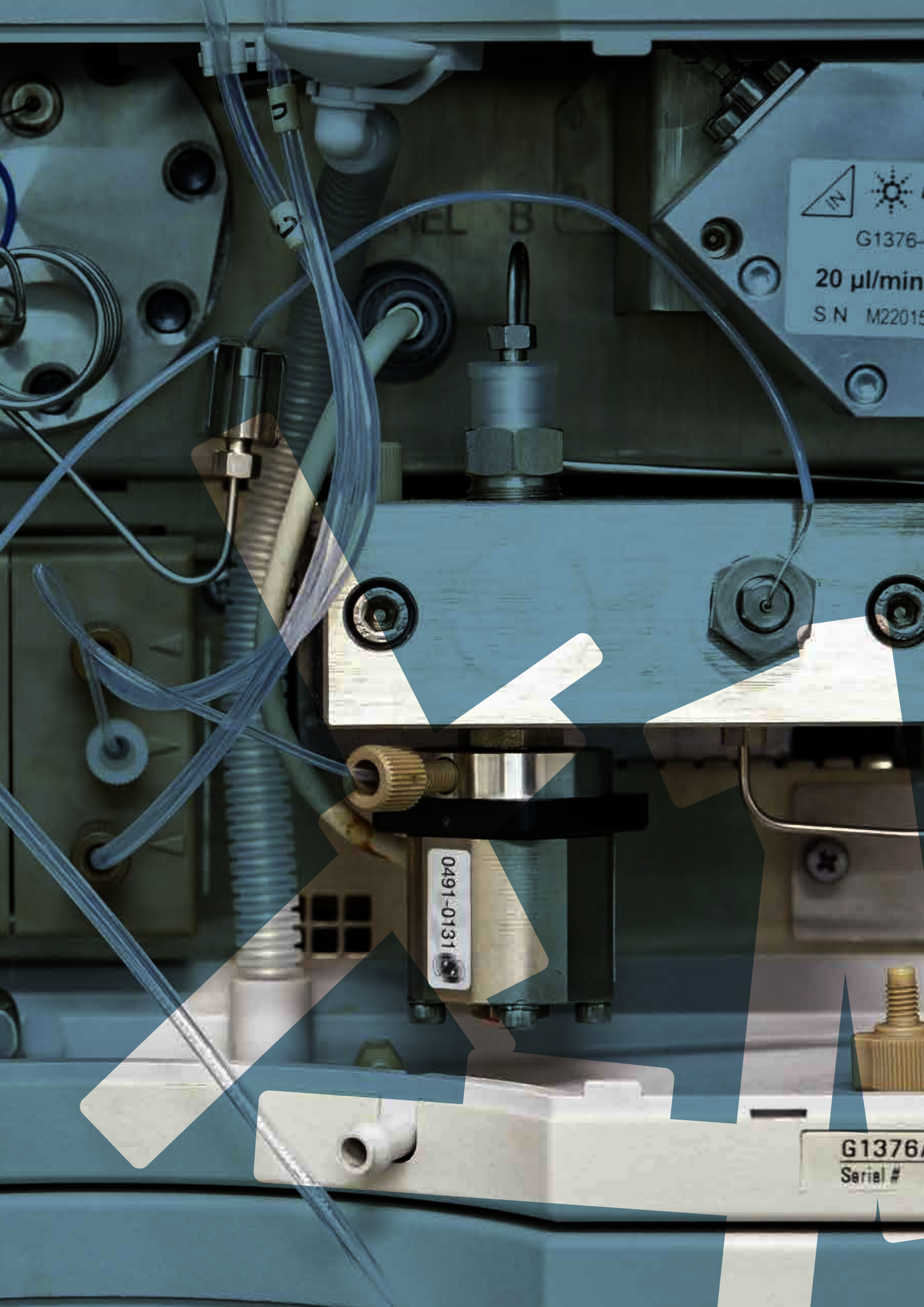




## **PARTNERSHIPS AND KNOWLEDGE TRANSFER**







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Serial #



# A NEW RESEARCH GROUP TO DEVELOP INNOVATIVE CANCER VIROTHERAPIES

Bilateral agreement signed with the DKFZ

LIH and the renowned German Cancer Research Centre “Deutsches Krebsforschungszentrum” (DKFZ) signed an agreement in December 2016 for the creation of a bi-national research team that will have an affiliation with both institutions.

The research group named LOVIT, standing for “Laboratory of Oncolytic Virus Immuno-Therapeutics”, will focus - as the name suggests - on the development of innovative therapeutics for cancer patients based on the use of oncolytic viruses. It will be led by Dr Antonio Marchini, an expert in cancer virotherapy, and use laboratory space at both LIH’s Department of Oncology and DKFZ starting from 2017 to host seven to eight team members.

## Viruses to treat cancer

Oncolytic viruses are promising anti-cancer agents because they selectively infect and kill cancer cells, and elicit robust anti-cancer immune responses. With the recent approval of the first oncolytic virus for treatment of metastatic skin cancer by the Food and Drug Administration in the United States, oncolytic virotherapy is gaining momentum quickly, with a number of oncolytic viruses being tested in various clinical trials for the treatment of different tumours.

LOVIT aims to combine two oncolytic viruses and investigate the therapeutic potential of adenovirus-parvovirus (Ad-PV) chimeras to provide preclinical evidence of their superior anti-cancer activity. One oncolytic parvovirus, the rat parvovirus H-1PV, has been recently evaluated in a first clinical trial in patients with recurrent glioblastoma, an aggressive brain tumour, proving its safety and showing first signs of efficacy.

## Improve the prototype

To enhance parvovirus efficacy, a prototype of Ad-PV chimeras has been developed at DKFZ by inserting an engineered version of the H-1PV genome into the adenovirus Ad5 genome. In a proof-of-concept study, the chimeras efficiently infected cancer cells and produced fully infectious viral particles. These particles can infect neighbouring cancer cells, kill them and induce secondary rounds of infection, thus amplifying the cell killing effect.

The Ad-PV chimera combines the advantages and circumvents the limitations of two distinct oncolytic viruses. It offers a large number of research opportunities to further improve anti-cancer potential. Therapeutic transgenes may be inserted into the chimeric genome. LOVIT will also look into combination strategies between the chimeras and other anti-cancer treatments. The goal will be to develop a second generation of Ad-PV chimeras as well as combination treatments, and test promising therapies in clinical trials. The first focus will be brain and pancreatic cancer.



Dr Antonio Marchini  
Head of the Laboratory of Oncolytic Virus  
Immuno-Therapeutics

## Funding & Collaborations:

The research group’s projects will be co-financed by LIH and DKFZ as well as by a grant from “Fondation Cancer”, the Luxembourg Cancer Foundation.

At LIH, LOVIT will collaborate with the other teams of the Department of Oncology, in particular with the NorLux Neuro-Oncology Laboratory working on brain tumours, and establish further collaborations in- and outside Luxembourg.

## BIOGLOSSARY

**Virotherapy** is a treatment using biotechnology to convert viruses into therapeutic agents. **Oncolytic** refers to the ability to kill cancer cells.

A **chimera** is a hybrid virus created by joining genetic fragments from two or more different viruses, including the genes essential for multiplication.

A **proof-of-concept** study is a study that demonstrates the feasibility of a method or verifies that a concept or theory has application potential.

A **transgene** is a gene that is transferred naturally or by genetic engineering techniques from one organism to another.



“*My team and I will work hard and to our best with the hope to provide new therapeutic options for cancer patients.*”

*Dr Antonio Marchini*



# TRAINING AND CAPACITY BUILDING FOR LABORATORIES IN THE BALKAN STATES

Activities of the WHO European Regional and National Reference Laboratory for Measles and Rubella

LIH's Department of Infection and Immunity hosts the World Health Organisation (WHO) European Regional and National Reference Laboratory for Measles and Rubella, led by Prof Claude Muller and Dr Judith Hübschen. It is one of only three Regional Reference Laboratories in the WHO European Region, holding the responsibility over 23 countries.

On a national level, it is in charge of diagnosis of national cases of measles and rubella viral infection and of disease surveillance. As a European Regional Laboratory, it confirms regional cases and outbreaks, performs virus characterisation and ensures quality control of laboratory testing. In addition, it is highly involved in training and capacity building missions in the National Reference Laboratories.

## On-site in Serbia...

In April 2016 for instance, a capacity building mission was conducted at the WHO National Reference Laboratory for Measles and Rubella in Belgrade, Serbia. An on-site accreditation visit in this laboratory earlier in 2016 revealed that there was a need to implement laboratory operating procedures and work practices to make molecular biology techniques fully compliant with WHO Measles and Rubella Laboratory standards.

During this mission, guidance was provided concerning laboratory standard operating procedures, the preparation and use of controls, transportation and shipment of clinical samples as well as laboratory biosafety issues.

## ...and at LIH

A few months later in October, LIH hosted three trainees from the National Reference Laboratories for Measles and Rubella in the Federation of Bosnia and Herzegovina, the Republika Srpska in Bosnia and Herzegovina, and Serbia.

The aim was to improve current laboratory procedures as well as to implement new methods, especially concerning virus characterisation and the use of WHO-supported sequence databases thanks to a hands-on laboratory training. A special focus was on WHO-compliant standard operating procedures, preparation of protocols, use and monitoring of controls for the different steps of each experiment and result analysis and documentation.



From left to right: Aurélie Sausy (LIH technician in charge of the laboratory training), Željka Šumić (laboratory technician at the National Reference Laboratory for Measles and Rubella in the Republika Srpska in Bosnia and Herzegovina), Dr Maja Bančević (Head of the National Reference Laboratory for Measles and Rubella in Serbia) and Dr Irma Salimović-Bešić (Assistant Professor at the National Reference Laboratory for Measles and Rubella in the Federation of Bosnia and Herzegovina).



*Our training is as much as possible adapted to the expectations and specific needs of the trainees.”*

*Dr Judith Hübschen, Deputy Head of the WHO European Regional and National Reference Laboratory for Measles and Rubella*

## Funding:

The WHO European Regional and National Reference Laboratory for Measles and Rubella is supported by the “Laboratoire national de santé”, the Luxembourg Ministry of Higher Education and Research, and the Ministry of Health.

For the three trainees coming to Luxembourg, the WHO Regional Office for Europe covered all costs related to travel, accommodation and living while the Reference Laboratory in Luxembourg, supported by a financial contribution of the Rotary Club Luxembourg-Vallées, paid the charges related to the practical training and will provide some laboratory material to the trainees' home laboratories to support local measles and rubella diagnostic capacities.

# SPORTS MEDICINE RESEARCH JOINTLY CONDUCTED WITH DECATHLON

## Decreased injury risk with motion control shoes

What is the impact of running shoe type and foot morphology on injury risk in recreational runners? A study conducted by LIH's Sports Medicine Research Laboratory at the Department of Population Health, in collaboration with the Movement Sciences Department at Decathlon, France, revealed interesting novel findings for both the scientific and the running community.

### 372 participants running

The study, a randomised controlled trial, was conducted with 372 leisure-time runners who reported their running activities and related injuries during a period of six months on the online platform [www.tipps.lu](http://www.tipps.lu). Participants of the study were given either standard running shoes or footwear with motion control features, designed to limit pronation movement, which is the inward roll of the foot during running.

### Foot posture matters

The study found that the use of motion control shoes was associated with an overall lower injury risk compared to standard shoes. In a secondary deeper analysis of the data, participants were divided into different categories according to their foot posture. It can be qualified either as neutral, as supinated, when the ankles lean outwards, or as pronated, when the ankles lean inwards.

When discriminating between those different postures, the researchers observed that the effect was true only for runners with pronated feet. Indeed, the rate at which the injuries occurred to runners with pronated feet was decreased by more than half in the motion control shoe group when compared to the standard shoe group.

This study tends to confirm the interest of shoes with motion control technology for runners with pronated feet: an interesting result to be considered by all running addicts! A next step could be to study further shoe models and to investigate the mechanisms involved in injuries during running.

“Our study is the very first to compare shoe models with and without motion control system in regular recreational runners.”

*Dr Laurent Malisoux, project leader*



#### Publication:

This study, first-authored by Dr Laurent Malisoux, was published in January 2016 in open access in the *British Journal of Sports Medicine* under the title “Injury risk in runners using standard or motion control shoes: a randomised controlled trial with participant and assessor blinding”. This journal is the highest-ranking in the field of sports medicine with an impact factor of 5.0.

#### Funding:

This project was co-funded by Decathlon, Movement Sciences Department, Villeneuve d'Ascq, France.

## BIOGLOSSARY

A **randomised controlled trial** is a scientific experiment that aims to reduce bias when testing a new treatment or feature. People participating in the trial are randomly allocated to a test or control group.

**Pronation** is the way the foot rolls inward when walking or running. It is part of the natural movement that helps the lower leg deal with shocks.

## Training and Workshops series

Acquiring new competences to increase career advancement and employability and adapting to the rapidly evolving technologies used in research is key for scientists. LIH's Training and Workshops series, specifically intended for early-stage researchers, supports the development of sound scientific and transferable skills, essential for the current and future career.

# 2016 | TRAINING & WORKSHOPS

**L** LUXEMBOURG  
INSTITUTE OF  
HEALTH  
RESEARCH ESTABLISHED IN 1998

FEB		29.02 9.30PM - 4.30PM	Genstat® appreciation course Prof Stephen Senn   Edison - Schumpeter   9h   12   Internal
MAR		31.03 & 01.04 9.30AM - 4.30PM	Intermediate statistics for life scientists Prof Stephen Senn   Edison - Schumpeter   24h   32   Internal / External
APR		11.04. & 19.04 2PM - 4PM	Principles of observational epidemiology Prof Severino Stranges   Edison - Sanger / Snow   4h   25   Internal / External
MAY		24.05. & 31.05 2PM - 4PM	Preventive medicine and public health Prof Severino Stranges   Edison - Sanger / Snow   4h   25   Internal / External
MAY		25.05 2PM - 4PM	Introduction to clinical research Dr Anna Chioia   Edison - Sanger / Snow   2h   30   Internal / External
JUN		06.06 9AM - 4PM	Project scheduling, planning and scoping Jo Schreiber   Edison - Sanger / Snow   6h   12   Internal
JUN		14.06 9AM - 12PM	Clinical research: Efficient start-up and planning to ensure a successful project Dr M. Gastonberg, Dr N. de Bruijn, M. Alexandre   Edison - Schumpeter   9h   22   Internal / External
JUN		20.06 & 22.06 1PM - 5PM / 9AM - 1PM	Epigenetics and DNA methylation Dr Jonathan Turner   House of BioHealth - Barré-Sinoussi   8h   16   Internal / External
SEP		14.09 10AM - 4PM	Writing a scientific publication Prof Claude Muller   House of BioHealth - Barré-Sinoussi   4h   12   Internal / External
SEP		16.09 1PM - 4PM	Introduction to translational research Dr Anna Chioia   Edison - Sanger / Snow   2h   30   Internal / External
SEP		20.09. & 21.09 9.30AM - 4.30PM	Basic statistics for life scientists Prof Stephen Senn   BAM - McClinch   14h   12   Internal / External
SEP		27.09 9AM - 12AM	Efficiently using MS PowerPoint: LHM templates, animations and smart arts Juliette Pertry, Sara Gubler   Edison - Sanger   2h   16   Internal
OCT		03.10. & 10.10 2PM - 4PM	Getting started with transcriptome analysis Dr Laurent Vallier   BAM - McClinch   6h   12   Internal / External
NOV		08.11 1.30PM - 4PM	Boosting your conference presentations Prof Dr Thamer, Dr B. Appenzeller   Edison - Schumpeter   9h (incl. 1h prep. time)   12   Internal / External
NOV		11.11 9.30AM - 12.30AM	Communication: Are you press fluent? Juliette Pertry   Edison - Sanger / Snow   4h   16   Internal
NOV		29.11. & 05.12 9.30AM - 4PM	Introduction to intellectual property management tools and rights Dr Fabienne Roussel   Edison - Schumpeter   9h   12   Internal

## Practical information

Courses are for free. Registration is required at the latest one week before course start.

LHM staff should register via e-training menu; register for an evening training and external participants from IL, LU and other by sending an email to [training@lhm.lu](mailto:training@lhm.lu). Please will be acknowledged as a Positive Insurance Recipient.

A certificate of attendance can be delivered after the courses. Please request it by sending an email to [training@lhm.lu](mailto:training@lhm.lu). More information on the course contents can be found at [www.lhm.training](http://www.lhm.training).

## Legend

- Location
- Real duration
- Max. participants
- Trainer
- Access
- Methodology
- Scientific skills
- Transferable skills
- Technology transfer

## Course Locations

**Edison Building**  
Schumpeter street ground floor, Sanger/Snow room (old floor)  
IL, rue Thomas Edison 1, level 1000  
**BAM (Barré-Sinoussi)**  
IL, rue Thomas Edison 1, level 1000  
**House of BioHealth**  
IL, rue Thomas Edison 1, level 1000  
**House of BioHealth**  
IL, rue Thomas Edison 1, level 1000

This series, held by dedicated members of LIH's staff, has been organised since 2013 with big success. All courses are held in English, are free of charge and are interactive by including exercises, case studies or hands-on training on technical equipment.

The 2016 series comprised 16 courses of the categories “scientific skills”, “transferable skills”, “methodology” and “intellectual property” given by 17 trainers. Most of the courses were open to externals from the University of Luxembourg or from the other publish research centres in Luxembourg. In total, 243 people attended of which 6% were externals.

Satisfaction surveys conducted at the end of each training revealed that the participants highly appreciated the course topics and content as well as the trainers' explanations and response to questions. Overall, 70% reported to be "very satisfied" and 29% indicated to be "satisfied". 97% reported that they acquired new knowledge and skills with the courses. The participants' feedback is used to continuously improve the course offer and practical organisation.



# SHARING BEST PRACTICES IN CLINICAL RESEARCH

## Special training for research nurses

The Clinical and Epidemiological Investigation Centre within the Department of Population Health coordinates clinical research activities at a national level. It supports local projects and helps scientists from the public and private sector to consolidate experimental findings through quality-assured clinical research involving patients and healthy individuals.

In this framework, and to share best practices acquired over the past few years, the centre is regularly organising training sessions promoting exchange with its experts.

In 2016, a training entitled “Pratique infirmière en recherche clinique”, was especially dedicated to nurses working in the clinical research field but welcoming as well any other medical staff members interested in implementing clinical trials from a nurse perspective.

Participants have been able to discuss subjects ranging from regulatory aspects in clinical research, over design, implementation and follow-up of clinical trials, to the mechanisms of drug delivery in the human body with Jérôme Graas, study nurse at LIH’s Clinical and Epidemiological Investigation Centre since 2009. A special focus was given to anti-cancer treatments as the centre is involved in numerous clinical trials related to cancer therapy.

Given the success of the sessions, training for this target group will be developed further in the future.



# TRAINING ACTIVITIES IN METHODOLOGY AND STATISTICS

A core field of expertise in research

LIH's Competence Centre for Methodology and Statistics, headed by Prof Stephen Senn, provides methodological support in statistical planning of clinical, public health and laboratory studies as well as in data analysis and handling. It is also highly engaged in training activities.

## Participation in a capacity building programme

The centre is involved in a capacity building programme of the European and Developing Countries Clinical Trials Partnership (EDCTP) and the World Health Organisation (WHO). EDCTP is a partnership of 14 European Union member states, Norway, Switzerland, and developing countries, formed in 2003 to fund acceleration of new clinical trial interventions to fight diseases such as AIDS, malaria and tuberculosis in the sub-Saharan African region.

Throughout 2016, the Competence Centre for Methodology and Statistics hosted three fellows in this framework: Dr Moussa Djimdé, a physician from the Malaria Research and Training Centre of the University of Bamako in Mali, Benjamin Sombié, a data manager from the "Centre National de Recherche et de Formation sur le Paludisme" in Burkina Faso, and Erick Mgina, a scientist from the National Institute of Medical Research - Tukuyu Research Centre in Tanzania.

They followed an intensive training in data management on projects related to tropical diseases such as malaria and schistosomiasis which also included basic statistical analysis and scientific writing. Returning to their home institution, they will be able to pass on the knowledge acquired at LIH. A re-integration plan for the sustainability of the training was also proposed and validated by WHO, and will be supervised by Dr Michel Vaillant, Deputy Head of the Competence Centre for Methodology and Statistics.

## Courses in Luxembourg and abroad

Members of the Competence Centre for Methodology and Statistics were also invited to give a number of statistics courses during 2016. These included courses in Luxembourg as part of a Good Clinical Practice training, at "Institut de Formation des Soins Infirmiers" in Thionville, Metz and Verdun (France), at Bachelor level at the University of Lorraine (France), to the organisation "Statisticians in the Pharmaceutical Industry" in London (United Kingdom), and to the International Society for Clinical Biostatistics in Budapest (Hungary) and in Prague (Czech Republic).

Additionally, a two-day training about statistical issues in drug development intended mainly for the pharmaceutical industry was organised in Luxembourg in May.



From left to right: Amadou Seck, data manager of the National Tuberculosis Programme, Dakar, Senegal; Benjamin Sombié, data manager at "Centre National de Recherche et de Formation sur le Paludisme", Ouagadougou, Burkina Faso; Dr Moussa Djimdé, physician at the Malaria Research and Training Centre, University of Sciences, Techniques and Technologies of Bamako, Mali; Hamado Ouédraogo, Coordinator of the Schistosomiasis Control Programme, Burkina Faso

## BIOGLOSSARY

**Schistosomiasis**, also known as snail fever, is a disease caused by parasitic flatworms called schistosomes, infecting the urinary tract or gut.

# SECONDMENT TO THE EUROPEAN MEDICINES AGENCY

Interview with Dr Olivier Collignon

Dr Olivier Collignon is a biostatistician at LIH's Competence Centre for Methodology and Statistics. Since October 2014, he is seconded to the European Medicines Agency (EMA) in London, United Kingdom.

## Focus on this secondment in an interview:

*Could you tell us about the mission of EMA?*

EMA is a decentralised agency of the European Union. The agency is responsible for the scientific evaluation, supervision and safety monitoring of medicines that are developed by pharmaceutical companies for use in the EU. To achieve these missions, EMA works with several scientific committees and working parties composed of thousands of European experts who evaluate medicines from early development to marketing authorisation and safety monitoring.

*What is your role at EMA?*

I am involved in very different and interesting types of activities. My main mission is to help the committees, working parties and EMA colleagues by providing high-quality scientific support with regard to medical products. More precisely, I give input on challenging methodological and statistical questions raised during the evaluation of clinical trials by the Committee for Medicinal Products for Human Use.

I also intervene during the Scientific Advice procedure, which in general occurs before a clinical trial is conducted, and in which companies prospectively ask regulators about the suitability of some critical aspects of their drug development programme, as for example the study design, the patient population in which the effect of the drug is to be investigated or the choice of the comparator to use as a control in the trial. This activity is especially rewarding because you can really have a positive impact on the drug development programme.

I conduct as well numerous research activities in regulatory science, often in collaboration with academia.

For example, I currently work on a follow-up project that consists in reviewing the outcome of clinical trials planned with an adaptive design. These trials, when properly planned, allow modifying some characteristics of the study while its data are being collected, as its sample size or the number of treatment arms. They have gained growing popularity over the past years, and for regulators it is important to have a deeper hindsight about their practical use by the pharmaceutical industry, like for example the type of adaptation performed, the indications in which they are more frequently used, or their impact on the trial success.

Another project that I am currently working on jointly with Prof Stephen Senn, Head of the Competence Centre for Methodology and Statistics, is about finding adequate ways of integrating historical controls in clinical trials. Indeed, instead of including a concurrent control arm - a placebo or a standard of care for example - it is currently thought one can benefit from the information brought by previous controls arms from similar clinical trials. This is however not so straightforward and there are some methodological caveats that we are currently investigating.

There are a lot of other interesting activities in which I am involved, like giving statistical input to medical or methodological European guidelines, providing statistical training, etc.

*Which expertise is required to fulfil your functions?*

My expertise in methodology and statistics in the field of clinical trials is essential for my functions. However, I had to get myself acquainted with the European drug development regulation, which is fundamental to fully understand the life cycle of medical products. On top of this, an extra effort



Dr Olivier Collignon

Biostatistician, seconded to the European Medicines Agency

is also necessary to gain medical knowledge on the current standard of care of a great variety of diseases. Overall, it is very important to have an overarching perspective of the processes and activities of EMA in order to help the system at best and to take initiatives.

*How is your work at EMA related to LIH and how could it be beneficial for the institute?*

There are different aspects. I have so far published several papers with EMA - and others are to follow - that I have also signed with my LIH affiliation. Therefore, I still contribute to the scientific production of LIH. Moreover, working at EMA allows me to represent LIH and Luxembourg through my activities on a European level and sometimes beyond, for example when attending international meetings. As such, I have recently been invited to give a keynote presentation at a conference in China about the use of single-arm trials in oncology. This was very exciting.

In addition, at LIH, our competence centre is involved in consulting activities for the pharmaceutical industry. With my expertise gained at EMA, I hope to be able on my return to help the institute to further develop our client portfolio and our business activities by taking advantage of my expertise of regulation in drug approval. I am sure this knowledge could also be beneficial for LIH's Clinical and Epidemiological Investigation Centre.

## BIOCABULARY

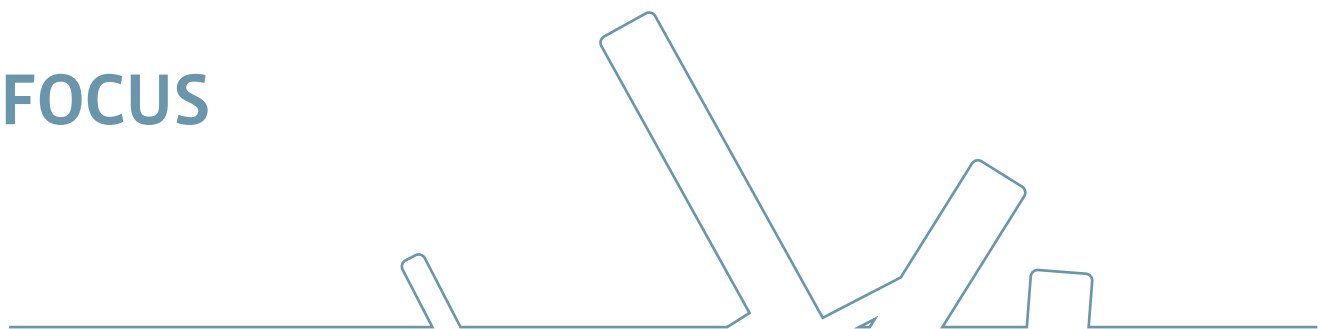
An **arm** of a clinical trial is a group of patients receiving a specific treatment (or no treatment).

**Regulatory science** consists in developing new tools, standards and approaches to assess the safety, efficacy and quality of medicines.





# FOCUS







# PROMOTING A TECHNOLOGICAL PLATFORM

Interview with Dr Gunnar Dittmar

New Head of LIH's Proteome and Genome Research Unit

On 1<sup>st</sup> October 2016, Dr Gunnar Dittmar was appointed as Head of the Proteome and Genome Research Unit in the Department of Oncology. He is the successor of Prof Bruno Domon, who had set up and headed the Proteomics research group for over five years.

In an interview, Dr Dittmar tells about his plans for the future development of the technological platform for genomics and proteomics research at LIH.

*Could you tell us a bit about your background? Where did you work before joining LIH?*

I have a strong background in chemistry and biochemistry from my university studies. I did my PhD at the DKFZ - the German Cancer Research Centre - in Heidelberg in 1997 working on a cell biology project, before crossing the Atlantic to work for six years, first as a postdoctoral fellow and later as an instructor of cell biology at the Harvard Medical School in Boston in the United States. Back to Germany, I was recruited as an independent group leader at the Max Delbrück Centre for Molecular Medicine, shortly MDC, in Berlin in 2003.

In 2007, I set up the MDC's Proteomics Unit that I led until my appointment at LIH. In 2014, I also became the Head of the Proteomics Core Facility of the Berlin Institute of Health, an application-targeted research centre in which the MDC and the "Charité Universitätsmedizin Berlin" joined forces. There, I built up a proteomics unit with a clinical focus.

Additionally, I am a Visiting Professor at the Technion - Israel Institute of Technology in Haifa for a few years now.

*Why did you decide to come to Luxembourg and join our institute?*

I have heard about the departure of Prof Domon, and co-workers recommended the institute to me. I already had connections to Luxembourg through collaborations with the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg to which I had been also invited to give a presentation. So, I had been to the Grand Duchy before.

LIH is a relatively young institute. I feel that it is dynamic and currently expanding. When I was working at the MDC, I experienced a very rapid development: during my 12 years at the institute, the staff increased from 350 to 1500. I hope to find a similar, lively and research-focused atmosphere at LIH, as I know it from the MDC.

*The research focus of the Proteome and Genome Research Unit is not widely known yet. What do you plan to do to give more visibility to the unit and open it to other LIH departments and external partners?*

Very simple: I will talk to people (*smiling*). I want to promote our activities among the Luxembourgish research community first. I will though not advertise the unit as a simple service platform for genomics and proteomics analysis. I aim to establish true research collaborations in which all partners work on an equal level. We can get very fruitful outcomes if biologists, clinicians and biochemists collaborate on a high scientific level to solve biological questions.

## BIOGLOSSARY

**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).

**Proteomics** is the large-scale study of the proteome (the proteins produced from genetic information) in a biological sample.

**Mass spectrometry** is an analytical technique that allows to identify and quantify individual molecules (e.g. proteins) based on their mass.

## Dr Gunnar Dittmar

Head of the Proteome and Genome  
Research Unit



### *What is your strategic vision for the unit?*

With my team, I aim to dig down to molecular levels of diseases and contribute to further develop tools for personalised medicine. For the genomics part, we need to specialise in the newest genome sequencing techniques if we want to be at the forefront of biomedical research. This requires that we acquire state-of-the-art sequencing equipment.

Regarding proteomics, I aim to add a technique named deep shot-gun proteomics that allows to analyse complex biological samples. We have good equipment available but limited capacity. To analyse a few hundred samples, a mass spectrometry instrument must run for several weeks. More machines will be needed to allow conducting larger studies.

### *Which international collaborations do you plan to have?*

I plan to have plenty (*smiling*)! I will of course stay in touch with the research institutes I worked for before: the MDC, the Charité and the Technion. I also aim to collaborate for instance with the Universities of Rostock, Dresden, Reading and Bilbao, the DKFZ and the Helmholtzzentrum Munich. And I want the research unit to become part of multi-partner European consortia as well.

### *A final more personal question: what do you like to do in your leisure time?*

Spending time with my family! I am a very active person; I am always doing something on weekends. I like hanging out with my children and the dogs. My favourite hobby is kite land boarding. It works best on a beach. I need to find a good place in Luxembourg for flying the kite. I also like cycling. I cycle to work every day, as I do not live very far from the institute.

## MAJOR EVENTS

### › LECTURE AND WORKSHOP SERIES IN INFECTION AND IMMUNITY

In 2016, LIH's Department of Infection and Immunity organised for the third time the "Lecture and Workshop Series in Infection and Immunity", a series of lectures and associated workshops given by invited speakers from abroad, internationally recognised for their research. The programme, specifically aimed at fostering scientific exchange and networking to contribute to accelerating research, addressed current hot topics and the latest results in immunology research.

Each lecture was followed by a workshop during which a restricted group of early-stage researchers could informally exchange with the speakers about their research topic and their career path.

Eleven lectures were organised in 2016 and attended by more than 400 people. One of the highlights of the series was the visit of Prof Douglas Green, a renowned American immunologist, Chair of the Department of Immunology at St. Jude Children's Research Hospital in Memphis, United States. So far, he has published more than 500 scientific articles and is one of the world's most cited molecular biologists.



#### Funding:

The "Lecture and Workshop Series in Infection and Immunity" is supported by the Luxembourg National Research Fund through the RESCOM funding scheme.

### › MEDICAL RESEARCH DAY

The second edition of the Medical Research Day ("Journée de la Recherche Médicale") held on 26<sup>th</sup> October was a big success. This event intended to stimulate the exchange between researchers in biomedicine, clinicians, students and the broad public to make medical research more tangible.

The Medical Research Day was held at the "Centre Hospitalier de Luxembourg" and was jointly organised by the hospital and LIH as well as by the Faculty of Science, Technology and Communication and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg.

An audience of over 200 people, mainly pupils and students, participated to the various workshops, presentations and mini-conferences including some spectacular experiments demonstrated by Mr Science. Numerous members of LIH staff were among the speakers and workshop facilitators, presenting clinical research and its professions as well as research topics in the fields of sports medicine, cardiovascular disease, allergology and oncology.



*Mister Science animating the Medical Research Day*

#### Funding:

The Medical Research Day was supported by various sponsors from Luxembourg.



## › SPORTS MEDICINE COLLOQUIA

The Sports Medicine Colloquia, organised by the Luxembourgish Academy of Sports Medicine, Sports Physiotherapy and Sports Science, are gathering internationally recognised speakers to address recent topics around sports medicine, sport science and physical activity that are of interest for researchers, medical doctors, athletes and the broad public.

In 2016, six events were organised including SPORTMEDICA, a one-day congress with an international dimension. Focusing on the topic competition medicine, the congress featured six international speakers - well-known scientists in the field of nutrition, regeneration, injury surveillance and physiotherapy, an expert in legal aspects in sports and a high-level trainer of Tour de France cyclists. It gathered 150 participants and provided ample occasion to summarise existing knowledge and stimulate discussions between different stakeholders in the field.

The Luxembourgish Academy of Sports Medicine, Sports Physiotherapy and Sports Science is composed of the Sport Medicine Research Laboratory which is part of LIH's Department of Population Health, the Luxembourg Society of Sports Physiotherapy, the Luxembourgish Sports Medicine Society, the Luxembourg Society of Research in Orthopaedics and Sports Medicine and the Sports Clinic of "Centre Hospitalier de Luxembourg".



*SPORTMEDICA congress held at Coque in Kirchberg*

### **Funding:**

The activities of the academy are funded by the different partners and generously supported by a range of private sponsors.

## › NATIONAL PhD WELCOME DAY

On 7<sup>th</sup> December, the very first edition of the National PhD Welcome Day took place in Luxembourg City at the Neumünster Abbey. More than 100 doctoral candidates of all disciplines who started their PhD in 2016 in the country were invited. Coming from all over the world, these young researchers represent an undeniable force for the future of Luxembourg research.

This initiative was the occasion to present the national research landscape and to strengthen the links between the various Luxembourgish public research stakeholders. A cultural visit of the city centre opened the event and a walking dinner closed it, giving PhD candidates the opportunity to mingle and visit the stands of the different organisers.

The event was jointly organised by the Luxembourg Institute of Science and Technology, the Luxembourg Institute of Socio-Economic Research, LIH, as well as Euraxess Luxembourg - the national service centre assisting for the mobility of researchers, LuxDoc - the national young researchers' association, and the Luxembourg National Research Fund.



*Participants of the National PhD Welcome Day held at Neumünster Abbey in Luxembourg City*

## › BREAST CANCER AWARENESS MONTH - LIH IN PINK

One in eight women will be diagnosed with breast cancer in her lifetime. At LIH, researchers are taking part to the fight against cancer. One research group at the Department of Oncology, the group of Dr Clément Thomas is specifically working on novel strategies to inhibit metastasis in breast cancer. The team aims to block the evasion of cancer cells from the primary tumour by making them unable to remodel and move.

This year's Pink October was the occasion to make people aware about breast cancer research. LIH's staff took the chance and distributed pink roses to people passing by in the pedestrian area in the centre of Luxembourg City to raise awareness on the subject.

200 roses given away in no time - and as many friendly encounters between the researchers and the people they are working for every day.



*Roses for Pink October with a message about breast cancer research at LIH*

# VALUABLE THIRD-PARTY FUNDING

## > TWO LARGE PhD TRAINING PROGRAMMES INITIATED

Two large Doctoral Training Units, CANBIO, with a research and training programme in oncology led by the Department of Oncology, and NextImmune, centred on research and training in the field of classical and computational immunology, led by the Department of Infection and Immunity, have been initiated in 2016.

Both PhD programmes, funded by PRIDE grants from the Luxembourg National Research Fund, will run over a period of 6.5 years. In 2016, large recruitment events led to the filling of more than half of the allocated PhD positions. The first doctoral candidates started in October and November.

### **CANBIO - Cancer biology focused on tumour escape mechanism**

CANBIO will provide state-of-the-art training in cancer biology and address the increasingly important clinical problem of tumour progression and relapse. It will tackle the major challenges of drug resistance and tumour escape from the immune system with the aim to develop more effective anti-cancer strategies.

PhD candidates within CANBIO will be engaged in a collaborative and interdisciplinary endeavour to deliver novel insight into tumour escape mechanisms, disease monitoring and large-scale data analysis in highly malignant cancers.

The research programme, coordinated by Prof Simone Niclou, will address aspects of the complexity and genetic heterogeneity of tumours, how tumour cells misuse the immune system to their own advantage and how therapy-induced changes in the tumour microenvironment affect tumour cells and induce resistance. Research projects will be conducted in LIH's Department of Oncology, in the Life Sciences Research Unit of the University of Luxembourg and at the "Laboratoire national de santé". Several projects involve external academic collaborations.

### **NextImmune - Advanced concepts for deciphering acute and chronic Inflammation**

The Doctoral Training Unit NextImmune will address key research and innovation challenges associated with initiation, diagnosis and treatment of inflammatory diseases.

Inflammation is a protective response of the immune system to infection, tissue stress and injury. A deregulation of the immune system can lead to pathologic inflammatory responses. Otherwise harmless molecules are then identified as dangerous by the body. This is what happens for example in autoimmune diseases and in allergies.

NextImmune aims to bridge classical immunology and systems biology in a single doctoral training environment to understand the mechanisms of acute and chronic inflammation in inflammatory disorders.

The programme, coordinated by Prof Markus Ollert, hosts research groups working in systems biology, inflammation, infection and molecular immunology from LIH's Department of Infection and Immunity and the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg. It will be conducted in collaboration with the University of Southern Denmark and other partners.

## BIOCABULARY

**Tumour heterogeneity** describes differences between tumours of the same type in different patients, and between cancer cells within a tumour. Both can lead to different responses to therapy.

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

## > FUNDING OF THREE FNR CORE RESEARCH PROGRAMMES

The Luxembourg National Research Fund supports multi-annual thematic research programmes with its central funding instrument CORE. Three research projects submitted by LIH have been selected for this valued third-party funding by international expert committees.

**Zoom on the three projects:**



**The MetCOEPs project will investigate how epigenetic changes influence the activity of genes and the proteins they encode.**

It is well known that adverse experiences in early life have an effect on epigenetic changes in our genome and play a primordial role in determining whether we remain healthy or develop an increased risk for common diseases throughout our life. The project, led by the "Immune Endocrine and Epigenetics" research group, will allow to better understand how environmental factors influence our wellbeing, and how epigenetics can help identify people at risk for diseases.

*"This project could allow for suitable early interventions that reduce disease risk."*

*Dr Jonathan Turner, Head of the "Immune Endocrine and Epigenetics" research group, Department of Infection and Immunity*



**The CAROPROT project aims to improve the current knowledge on the uptake of carotenoids by the human body.**

Carotenoids are secondary plant compounds that are likely to have health benefits as their consumption has been associated with reduced incidence of several chronic diseases. They have though a relatively low water solubility, requiring emulsification prior to their potential absorption. Specifically, not much is known on the interaction between proteins and carotenoids during digestion and on the solubilisation of carotenoids. Hypothesising that proteins enhance the solubilisation and digestion of lipid droplets, Dr Bohn plans to conduct, in addition to laboratory experiments, a human trial to study the effect of added proteins on carotenoid uptake from a test food, for example spinach.

*"This project may have implications for dietary recommendations and for the production of functional foods or food supplements."*

*Dr Torsten Bohn, principal investigator at the Epidemiology and Public Health Research Unit, Department of Population Health*



**The METASTALIM project will study metastasis in breast cancer.**

Metastasis is the primary cause of death from cancer. An early and critical step for the onset of metastasis is the acquisition by tumour cells of the ability to migrate across tissue and pass tissue barriers. To move, tumour cells slightly remodel their cytoskeleton to develop membrane protrusions termed invadopodia, literally meaning "invasive feet", that secrete enzymes degrading the extracellular matrix. The project will explore the interaction between two proteins associated with the cytoskeleton that were shown to promote invadopodia formation and activity.

*"This project aims to demonstrate that targeting the formation of invadopodia represents a promising strategy to inhibit breast cancer metastasis."*

*Dr Clément Thomas, Head of the "Cytoskeleton and Cancer Progression" research group, Department of Oncology*

## BIOCABULARY

**Epigenetics** is the study of changes in organisms caused by modification of gene expression not involving changes to the underlying DNA sequence of genes.

**Emulsification** is the breakdown of fat globules into tiny droplets.

The **cytoskeleton**, made up of three kinds of protein filaments, gives the cell its shape, helps it to organise its parts and plays a role in cell movement and division.

The **extracellular matrix** is a collection of molecules secreted by cells that provides structural and biochemical support to the surrounding cells.

## > PUMP PRIMING TO LAUNCH COLLABORATIVE RESEARCH PROJECTS

The Personalised Medicine Consortium, composed of the national biomedical research institutions, aims to build new collaborations and foster synergies between clinicians and researchers from Luxembourg, specifically by funding projects with a collaborative dimension. In 2016, three new research projects led by LIH were announced as being selected for pump prime funding. All projects are application-targeted and will contribute to reinforce the links between the biomedical research entities in Luxembourg.

### Zoom on the three projects:



#### Project Die-IBD - “Dietary fibre-deprived gut microbiome in inflammatory bowel disease”

Inflammatory bowel disease is a chronic inflammation of the digestive tract that is difficult to treat. The deficiency of dietary fibre disturbs the metabolism of the gut microbiome, which is thought to contribute to the development of the disease. The project team aims to set up experiments that could shed light on the role of diet in the pathogenesis of inflammatory bowel disease and may help to design dietary therapeutic strategies to combat the disease. Dr Mahesh Desai, Head of the Eco-Immunology and Microbiome” research group, Department of Infection and Immunity, will lead the project.

> In this project, the research group will interact with the biobank IBBL that will perform sequencing to characterise the microbial populations in faecal samples.

## BIOGLOSSARY

**Dietary fibre** is an indigestible part of plant-derived food, made of carbohydrate.

The **microbiome** comprises all of the genetic material within a microbiota, which is the entire collection of microorganisms in a specific niche, such as the gut.

**Epigenetics** is the study of changes in organisms caused by modification of gene expression not involving changes to the underlying DNA sequence of genes.

**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).

**Single-cell sequencing** examines the sequence information from individual cells, providing a higher resolution of cellular differences and a better understanding of the function of an individual cell in the context of its microenvironment.

**Tumour heterogeneity** describes differences between tumours of the same type in different patients, and between cancer cells within a tumour. Both can lead to different responses to therapy.



### **Project ESPOiRe - “Epigenetic stratification towards personalised care in rheumatoid arthritis”**

This research project will investigate the role for epigenetics in the development and pathogenesis of rheumatoid arthritis, a chronic disease affecting up to 1% of the population in developed countries. The project team hypothesises that characteristic epigenetic changes could allow the stratification of rheumatoid arthritis patients at their initial diagnosis. To test this, the epigenomes of 70 patients will be analysed.

The ESPOiRe project will be led by Dr Jonathan Turner, Head of the “Immune Endocrine and Epigenetics” research group, Department of Infection and Immunity.

➤ In this project, patient samples will be handled and stored by the biobank IBBL, and computational analysis of the epigenetic data will be performed at the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg.

### **Project SCellOmics - “A multi-omics based single-cell strategy to overcome therapy-driven resistance in glioblastoma: an entry-point for personalised treatment”**

Glioblastomas are malignant brain tumours that present a high genetic variation and rapidly develop resistance to anti-cancer treatment. Molecular characterisation of glioblastomas represents a first step towards understanding therapy resistance. The funded project aims to analyse patient tumour biopsies at the level of single cells with different omics techniques to better understand disease progression and therapy-related resistance. In addition, personalised treatment approaches that can overcome resistance associated with tumour heterogeneity will be tested in preclinical studies.

Prof Simone Niclou, Head of the NorLux Neuro-Oncology Laboratory, Department of Oncology, successfully submitted the project.

➤ This project is based on an ongoing collaboration with the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg where single cell-sequencing has been established. The biobank IBBL will develop optimal conditions for single cell storage.



*The accepted projects for pump priming were announced at the annual meeting of the Personalised Medicine Consortium held on 9<sup>th</sup> December at the “Laboratoire national de santé” in Dudelange*



## > FIVE RESEARCH PROJECTS FUNDED BY THE LUXEMBOURG CANCER FOUNDATION

For many years, “Fondation Cancer”, the Luxembourg Cancer Foundation, has been supporting projects in cancer research at LIH. In 2016, reiterating its trust in the institute’s research, five project applications were granted funding.



**Fondation  
Cancer**

Info · Aide · Recherche

### Improving data collection for the National Cancer Registry

A three year grant has been attributed to Michaël Schnell, bioinformatician at the Epidemiology and Public Health Research Unit in the Department of Population Health. His project entitled “Assistance based on rules and case” is part of the activities of the National Cancer Registry, managed by LIH and aimed at collecting data on cancer incidence and treatment in Luxembourg. This project allows Mr Schnell to carry out a PhD with the University of Lorraine. He will develop an informatics tool that can improve the quality of data collection for the registry and make data processing faster. Thus, the description of cancer incidence and treatment will be refined, epidemiological data on cancer will be available faster for interested parties, and eventually patient follow-up will be more efficient.

### Investigating brain tumour resistance to chemotherapy

A research project that aims to study a new chemotherapy resistance mechanism in glioblastoma, the most common and aggressive form of brain tumours, has been submitted to the foundation by Dr Sabina Fritah, scientist at the NorLux Neuro-Oncology Laboratory in the Department of Oncology. The project, which has been granted funding for three years, is based on preliminary work of the research unit which identified the involvement of long non-coding ribonucleic acids (lncRNAs) in the response of glioblastoma to drug treatment. Dr Fritah seeks to identify the biological function of two key lncRNAs in the brain and test whether they could be suitable for a combination treatment with chemotherapy.

### Efficiently combining radio- and immunotherapy

A two-year postgraduate fellowship has been granted to radiation oncologist Dr Jean-Philippe Nessler who will carry out research at the University of California, Los Angeles, United States, in collaboration with the NorLux Neuro-Oncology Laboratory at the Department of Oncology and the National Centre of Radiotherapy/Centre François Baclesse. This fellowship will allow the promising young researcher to investigate the effects of radiotherapy on the immune system. Radiotherapy is a good candidate for combinatorial immunotherapy strategies to fight cancer. The goal is to better understand the influence of radiation on immune cells, tumour response and inflammation of healthy tissue. Different radiotherapy protocols and combinations with immunotherapy will be tested to find the best strategy to block cells that have a suppressive effect in the immune system and obtain an optimal anti-tumour response. If successful, the project may continue at LIH afterwards with a specific focus on brain tumours.

## BIOCABULARY

**Long non-coding ribonucleic acids (lncRNAs)** are biomolecules encoded in the genome that are not translated into proteins as is the case for another more commonly known type of RNAs. They play a key role in modulating gene expression and thus regulate numerous cellular processes.

**Immunotherapy** is a treatment that uses the body’s own immune system to fight a disease. The **cytoskeleton**, made up of three kinds of protein filaments, gives the cell its shape, helps it to organise its parts and plays a role in cell movement and division.



### Testing innovative drug combinations against skin cancer

The Department of Oncology obtained another grant for a three-year research project on melanoma, the most aggressive type of skin cancer. The project, led by Dr Bassam Janji, Deputy Head of the Laboratory of Experimental Cancer Research, aims to investigate novel ways to improve current strategies in immunotherapy by using combinatorial drug approaches. The effectiveness of immunotherapeutic agents will be tested in combination with drugs blocking autophagy, the process of cell recycling which is activated under the low-oxygen conditions that exist in the tumour microenvironment and contributes to tumour resistance. The ultimate objective is to provide evidence that allows conducting clinical trials to test the combinatorial treatments on patients.

### Targeting tumour cell “feet” to block breast cancer metastasis

With the support of the Cancer Foundation, Dr Clément Thomas leading the “Cytoskeleton and Cancer Progression” research group at the Department of Oncology, aims to develop a novel strategy to inhibit metastasis in breast cancer. During the early stages of metastasis, tumour cells acquire invasive characteristics allowing them to leave the primary tumour. By remodeling their cytoskeleton, the cells form membrane protrusions, named invadopodia (literally “invasive feet”), with which they can progress through tissues. The goal of the three-year project is to study how invadopodia are formed and then target components, in particular proteins related to the cytoskeleton, involved in invadopodia formation to block cell movement. The clinical potential of these components to treat breast cancers associated with high metastatic risk will be assessed.



From left to right: Dr Carlo Bock, President of the Cancer Foundation; Dr Sabrina Fritah, scientist at LIH's Department of Oncology and leader of one of the financed projects; Dr Gregor Baertz, President of LIH's Board of Directors; Lucienne Thommes, Director of the Cancer Foundation

## > STRENGTHENED RESEARCH ACTIVITIES IN NEURO-ONCOLOGY AND NEURODEGENERATIVE DISEASES

Future creation of the “Luxembourg Centre of Neuropathology”

In 2016, Prof Michel Mittelbronn, a renowned neuropathologist from Germany, was recruited for a joint appointment starting from 1<sup>st</sup> January 2017 with the “Laboratoire national de santé” (LNS), LIH and the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg. Prof Mittelbronn will be the chair of a PEARL programme funded by the Luxembourg National Research Fund, PEARL being a funding scheme aimed at attracting top researchers in strategic research areas for Luxembourg.

Prof Mittelbronn previously headed the diagnostic neuropathology at the Edinger Institute - Institute of Neurology at the Goethe University Frankfurt/Main, the oldest brain research institute in Germany, which is among the largest neuropathological institutes in Europe.

Until now, neuropathology diagnostics were not covered by the LNS and despite a strong, internationally recognised research expertise in the “neuro” field at both LIH and LCSB, clinical neuropathology was missing from the agenda. Endowed with 2.6 million Euro from the PEARL programme, Prof Mittelbronn will set up, for the first time, a diagnostic neuropathology unit at the LNS and build a research team together with LIH and LCSB to strengthen their research activities in neuro-oncology and neurodegenerative diseases, respectively.

This “Luxembourg Centre of Neuropathology” primarily purposes to link the research-oriented neurosciences, which are excellently established in Luxembourg, with tissue-based clinically oriented research. Prof Mittelbronn’s arrival will finally allow LNS to provide services in the field of neuropathology, thus avoiding the transfer of specific analyses to foreign laboratories. This will shorten the time for clinicians to obtain diagnostic information.



PEARL Chair  
Prof Michel Mittelbronn

**“** I am looking forward to the upcoming task of establishing the Luxembourg Centre of Neuropathology, which aims to build a network of medical care, research and teaching between LNS, LIH and LCSB.”

Prof Michel Mittelbronn

# NEW AND ONGOING STUDIES

## › TOWARDS A PERSONALISED TREATMENT OF ALLERGIES

### Launch of the SYS-T-Act study

The allergy burden continues to grow worldwide. To counter allergies, which are excessive reactions of the immune system, immunotherapy can be used to "desensitise" patients. However, the effectiveness of the treatment varies from one patient to the next and cannot be predicted in advance.

In 2016, the Department of Infection and Immunity launched a new research project with the purpose to better predict the response of the immune system to immunotherapy against allergies and to adjust the treatment to the profile of each patient.

### Anticipate the response to treatment to specifically adapt it

In allergology, immunotherapy consists of progressive exposure to the allergen. In order to desensitise the body, the administered dose of allergen is gradually increased until the maintenance dose, allowing for long-term tolerance, is reached.

The project will investigate in particular the activation of T lymphocytes, a population of immune cells involved in allergic reactions. Advanced methods in computational biology will allow for the analysis and comparison of blood samples from patients allergic to pollen or insect venom, before and during immunotherapy.

The researchers expect to identify biomarkers in the patients' blood that can predict the immune response to anti-allergic treatment even before it is initiated. The treatment type, dose and duration could then be adapted beforehand to the patients' profiles.

### Involvement of the first patients

The physicians of the Immunology-Allergology Department at the "Centre Hospitalier de Luxembourg" have begun to include the first volunteer patients in the SYS-T-Act study. In a first phase, 15 patients with pollen allergy and 15 with a bee or wasp venom allergy expected to be treated with immunotherapy shall be recruited. Blood samples are taken at different times, before and during immunotherapy.

Later on, a follow-up project aims to include more than 100 patients to achieve more representative results. The study will also be extended to peanut and nut allergy.

### Joint effort of researchers and clinicians

The project will benefit from LIH's expertise in immunology and of the know-how in computational biology of the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg. The Immunology-Allergology Department at the "Centre Hospitalier de Luxembourg" regularly treats patients allergic to pollen and bee and wasp venom by immunotherapy. This service is therefore the ideal clinical partner to generate the biological samples. The biobank IBBL organises sample collection and adequately prepares the samples for subsequent analysis.

**“**Our project could have a significant impact on clinical practice. If successful, a simple blood test will enable physicians to specifically tailor the allergen immunotherapy to each patient.”

Prof Markus Ollert, Director of the Department of Infection and Immunity and project coordinator for SYS-T-Act

## BIOCABULARY

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

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

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

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.

### Funding:

The SYS-T-Act project is funded by a Pump Prime Fund of the Personalised Medicine Consortium.

## > EXPLORING THE NEUROPROTECTIVE BENEFIT OF MULTILINGUALISM

Launch of participant recruitment for the MemoLingua study

Dr Magali Perquin initiated the recruitment of participants for a new research project, named MemoLingua, to better understand how multilingualism can delay the onset of cognitive decline.

Alzheimer's disease, the most common form of dementia, results in a degeneration of cognitive, behavioural and functional capacities. The World Alzheimer Report 2016 states that 47 million people are living with dementia, and the worldwide estimates of its prevalence is projected to increase to more than 131 million by 2050.

### Multilingualism enhances cognitive reserve

The observed ability of delaying or minimising the clinical manifestation of Alzheimer's disease led to the concept of cognitive reserve. It is the capability of the brain to cope with its damages. Research evidence has demonstrated that cognitively stimulating life experiences as well as sustained mental activities (education, occupation, social and leisure activities) contribute to cognitive reserve.

Previous work from the MemoVie study conducted at LIH showed a strong association between actively-practiced multilingualism and cognitive protection, irrespective of other cognitively stimulating activities. This benefit on cognition might be related to the enhancement of cognitive and brain plasticity, thereby preserving brain functions from alterations during ageing. Culminating at three languages, this protection appeared even stronger with earlier and more rapid acquisition of multilingualism.

Based on these findings, the project MemoLingua was designed. With a novel neuroimaging approach developed in collaboration with the "Centre Hospitalier de Luxembourg" and the "Forschungszentrum Jülich" in Germany, Dr Perquin and co-workers aim to determine the functional areas of the brain that are linked to cognitive reserve mediated by multilingualism.

### Already more than 60 participants to the study

In a first phase of the project, participants aged over 65 are recruited in Luxembourg to collect extensive neuropsychological data and information on language abilities and habits, health history and lifestyle. The second phase, conducted at the "Forschungszentrum Jülich", consists in collecting and analysing neuroimaging acquired with functional magnetic resonance imaging (fMRI) and behavioural data.

During 2016, an fMRI experimental set-up to evaluate the extent, the intensity and the interrelationship of the brain areas engaged for memory processing was designed, tested and optimised. A pilot study was then conducted for the two phases of the project and the recruitment of participants has been initiated. Until end of the year, 65 participants could already be enrolled. They underwent more than 150 interviews, and 34 of them came to Jülich to perform the fMRI protocol. The recruitment of participants with different levels of cognitive and linguistic abilities will be continuing in 2017.

*“Through neuro-imaging, we will highlight the role and mechanisms of cognitive reserve in the context of multilingualism.”*

*Dr Magali Perquin, project leader of MemoLingua*



*Brain activity measured with fMRI during decision-making tasks*

### Funding & Collaborations:

This project is supported by intramural funding.

It has been developed by Dr Perquin in collaboration with Prof Gereon Fink, Head of the Department of Cognitive Neuroscience, Institute of Neuroscience and Medicine 3 at the "Forschungszentrum Jülich", Germany; Prof Juraj Kulolja leading the Cognitive Aging and Dementia group at the "Forschungszentrum Jülich"; Prof Nico Diederich, clinical neurologist at the Department of Neuroscience of the "Centre Hospitalier de Luxembourg"; and Dr Michel Vaillant, Deputy Head of the Competence Centre for Methodology and Statistics at LIH.

## BIOGLOSSARY

**Dementia** is a syndrome that involves severe loss of cognitive abilities as a result of disease or injury.

**Cognitive reserve** is a brain resource developed by lifelong challenging cognitive activities. It helps the brain to cope with cerebral damages.

**Functional magnetic resonance imaging (fMRI)** is a non-invasive technique for measuring and mapping brain activity. It detects changes associated with blood flow.

## > SUDDEN CARDIAC EVENTS IN SPORTS: REPORT THEM TO PREVENT THEM!

### Establishment of a national database

Much attention is drawn to cardiovascular health and associated risk factors in Luxembourg. The occurrence of sports-related sudden cardiac events, such as a strong chest pain or a heart attack during or shortly after sports practice, is however not well understood yet.

#### Identify who is at risk

To address the knowledge gap, the Sports Medicine Research Laboratory at the Department of Population Health, in collaboration with “Société pour la Recherche sur les Maladies Cardiovasculaires”, launched the first official Luxembourg database of sports-related sudden cardiac events (SCEs) in April 2015. The main purpose of this database, in line with national ethics and privacy regulations, is to improve the prevention of sports-related SCEs.

SCEs can affect both recreational and high-level sportsmen who have never experienced heart problems. They are not uncommon: in Luxembourg there is an estimated number of five cases per year. The database will allow to refine the estimation of the frequency of SCEs and to map the profiles of people at risk (sex, age, practiced sport and medical history). The research team aims to identify sports-related SCEs that took place between 2000 and 2016, and will continue monitoring until 2019.

To feed the database, the researchers rely on incidents reported by the media as well as testimonies of victims, their families or the ambulance service. An online form available at [www.cardiac-event-sport.lu](http://www.cardiac-event-sport.lu) allows entering data into the registry.

#### First outcomes

Preliminary results obtained during the first year of the project are already available: The identified SCE victims were predominantly male, aged between 14 and 80, and did not have previous heart problems. In most cases, SCEs occurred in training sessions or competitions, which indicates that the context of competition or high-intensity sport could increase the risk. Another risk factor appears to be the resumption of a too intense physical activity after a period of inactivity. The results do though not contradict the proven fact that regular physical activity promotes cardiovascular health and well-being in general.

The research project led by Eric Besenius, research assistant, and Prof Daniel Theisen, Head of the Sports Medicine Research Laboratory, can only have success if sufficient data is collected. Therefore, anyone who experienced or witnessed an SCE during or shortly following a sports activity in Luxembourg (or abroad for a resident or a person with a license for a Luxembourgish sports club) is encouraged to report the case on the website.

“The database will allow us to develop appropriate measures to prevent sport-related sudden cardiac events.”

Eric Besenius, project leader





## > LIH RECRUITS CONTROL PARTICIPANTS FOR THE PARKINSON STUDY NCER-PD

Interview with the 200<sup>th</sup> control participant

NCER-PD stands for “National Centre for Excellence in Research on Parkinson’s Disease”. It represents a joint effort between several partners in Luxembourg that unite their expertise in Parkinson’s disease: the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg, the “Centre Hospitalier de Luxembourg” and LIH, involving the Clinical and Epidemiological Investigation Centre, the Competence Centre for Methodology and Statistics and IBBL - Integrated BioBank of Luxembourg. The Luxembourg National Research Fund finances this large-scale project since spring 2015.

To answer the urgent questions regarding the occurrence of Parkinson’s disease and identify early diagnosis methods and improved treatments, researchers need to analyse clinical data and samples from hundreds of patients and healthy control persons. The active participation in the Luxembourgish Parkinson’s study is therefore an important prerequisite for the success of the NCER-PD research project.

The Clinical and Epidemiological Investigation Centre recruits the healthy control persons, not suffering from Parkinson’s disease. In 2016, the 200<sup>th</sup> control person visited the centre and was ready to give an interview.

Jean-Nicolas, 68 years,  
Luxembourger,  
from Pétange

*How did you hear about the NCER-PD study, and what motivated you in participating?*

I’m currently participating in one of your other projects, MemoLingua, which is taking place in the same building. I saw signs about the Parkinson study and asked for more information. The lady from the reception kindly informed me about the NCER-PD project and I immediately got interested in participating. I’m retired and have therefore quite some free time. I find it natural to dedicate some of this time to serve a useful cause and help improve research.

*How was your day here?*

I was asked a lot of questions, did some neuropsychological tests and analyses. Everything went very well, I was treated very well (*laugh*)! Nothing was painful - on the contrary - it was pretty pleasant! The team was very welcoming and friendly, especially the nurse who took care of me.

*What would you tell the people who are still hesitating in participating?*

I can only recommend other people to join this programme! It’s just a question of time, nothing else. Hurry up! It’s time to help!

*What would you tell the researchers and healthcare staff working on the project?*

I think they are doing a great job! I am pleased to bring my contribution and help them move forward! I would be pleased to participate to future projects! I can only support them!

*And to the Parkinson’s disease patients?*

They can count on the researchers! Those will find ways to help them and improve their lives!

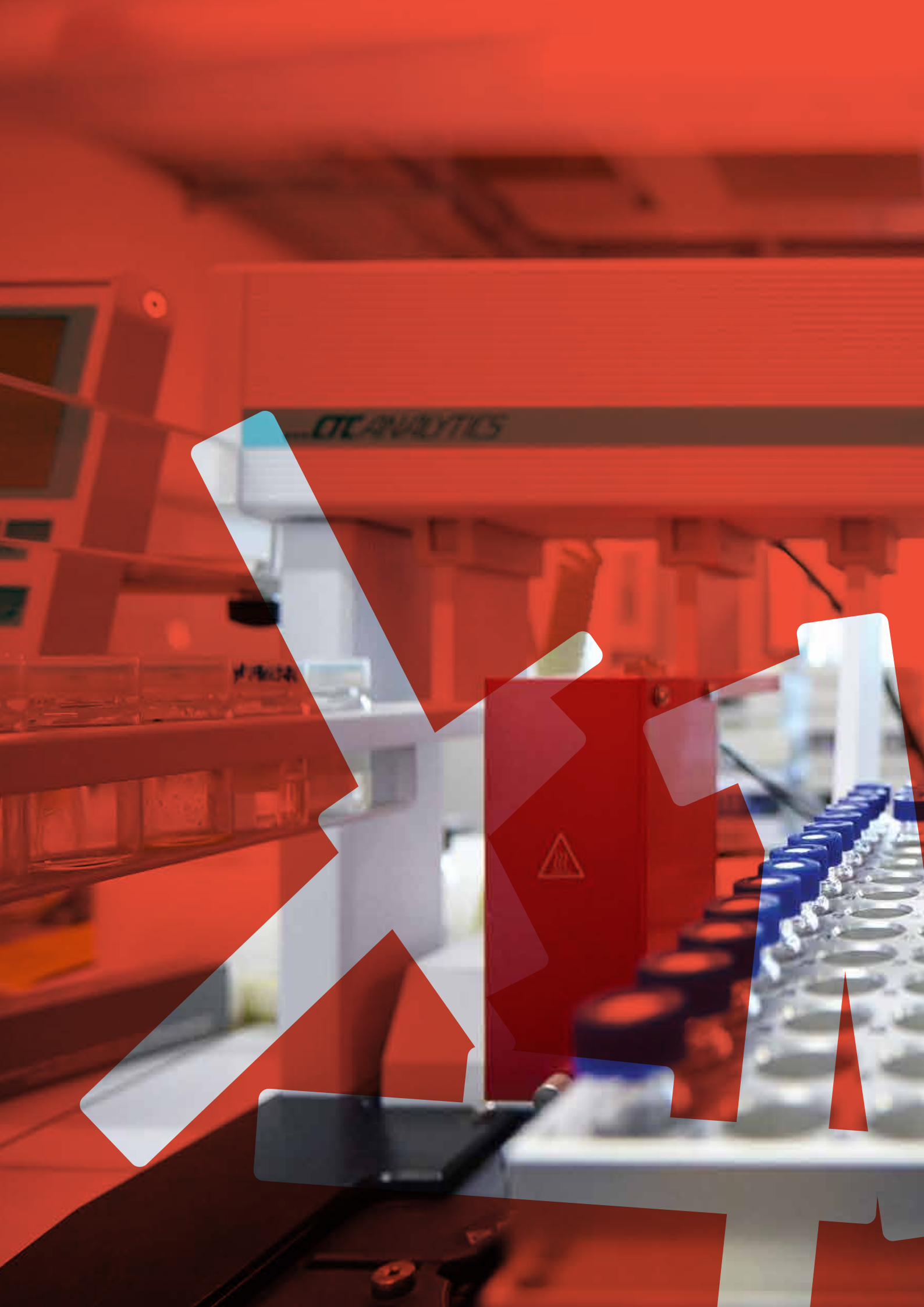


Jean-Nicolas, the 200<sup>th</sup> control person of the NCER-PD study, surrounded by healthcare personal and scientists of “Centre Hospitalier de Luxembourg” and LIH



**SUCCESSFUL PhD  
THESES: READY FOR  
THE FUTURE!**





# SUCCESSFUL PhD THESES: READY FOR THE FUTURE!

PhD candidates are the next generation of leading researchers and managers. In 2016, three doctoral candidates who conducted a PhD project at LIH successfully defended their thesis and took the next step for their career.



“One of the privileges I had as a PhD candidate at LIH were the numerous opportunities to participate in national and international conferences. These were all highly enriching experiences. The exchange with other more experienced scientists provided me with new ideas for my research and future career.”

Dr Martyna Szpakowska

## Dr Martyna Szpakowska

Department of Infection and Immunity > Infectious Diseases Research Unit > Molecular Signalling and Virus-Host Interactions Research Group

>Nationality: Polish

>Doctoral School/University: “Structure and function of biological macromolecules, bioinformatics and modelling” Doctoral School, University of Liège, Belgium

>Supervisors: Dr Andy Chevigné (LIH), Prof Jacques Piette (University of Liège)

>PhD defence: 20<sup>th</sup> April

>Thesis title: “Molecular insights into recognition, activation and function of the atypical chemokine receptor CXCR7/ACKR3”

>Funding: AFR PhD grant, Luxembourg National Research Fund

>Publications: Three research articles and three reviews, of which four as first author

>Major achievements during the PhD:

- > Detailed study of the chemokine receptor CXCR7/ACKR3
- > Identification of a new ligand for the receptor

>Other: PhD thesis rated as “outstanding” by the assessment committee

>Current position: Postdoctoral researcher at VIB-VUB Centre for Structural Biology in Brussels; ongoing collaboration with LIH



“Completing my PhD project at LIH allowed me to work with experts in my field and state-of-the-art techniques. Above all, I am grateful for having been part of a great team.”

Dr Adèle Bourmaud



*What I appreciated most during my PhD at LIH was the excellence of the researchers combined with that of the medical doctors associated with our research unit. This allowed for a complementary approach - both scientific and clinical - enabling to get a global view on the research question of my PhD project."*

*Dr Caroline Mouton*

## Dr Adèle Bourmaud

Department of Oncology > Proteome and Genome Research Unit

- >Nationality: French
- >Doctoral School/University: Doctoral School in Systems and Molecular Biomedicine, University of Luxembourg, Luxembourg
- >Supervisors: Prof Bruno Domon (LIH), Dr Sébastien Gallien (LIH)
- >PhD defence: 5<sup>th</sup> July
- >Thesis title: "Towards harmonisation of proteomics methods. Implication for high resolution / accurate mass targeted methods"
- >Funding: CORE project, Luxembourg National Research Fund
- >Publications: Four articles, of which three as first author, and one book chapter
- >Major achievements during the PhD:
  - > Development of a procedure to routinely assess the uniformity of proteomics analyses
  - > Evaluation of a method named "parallel reaction monitoring" for targeted proteomics
- >Other: Organiser of the Life Sciences PhD Days in 2014
- >Current position: Postdoctoral researcher at LIH's Proteome and Genome Research Unit

## Dr Caroline Mouton

Department of Population Health > Sports Medicine Research Laboratory

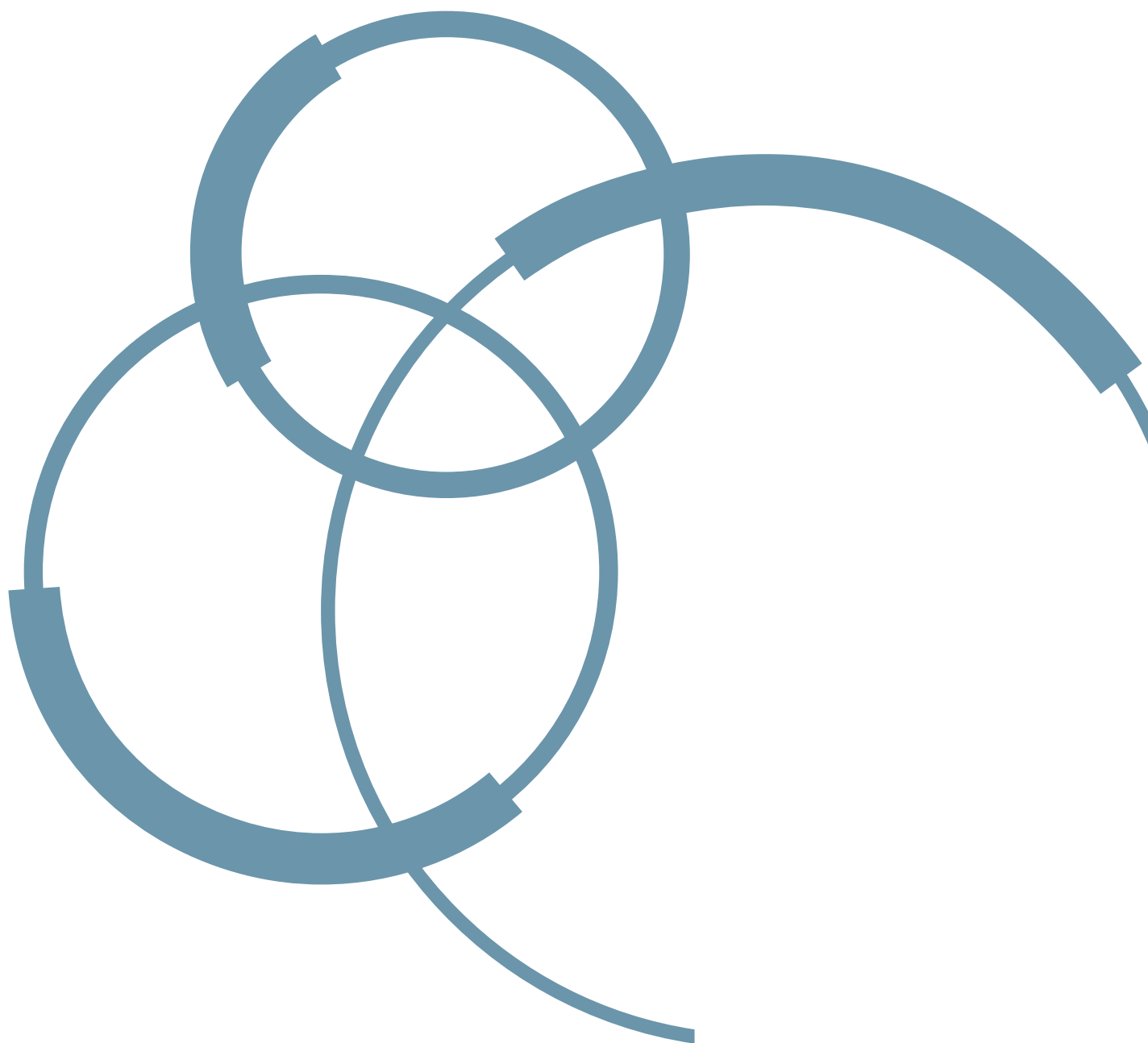
- >Nationality: French
- >Doctoral School/University: Saarland University, Germany
- >Supervisors: Prof Daniel Theisen (LIH), Prof Romain Seil (LIH), Prof Tim Meyer (Saarland University)
- >PhD defence: 14<sup>th</sup> July
- >Thesis title: "Towards an increased understanding of physiologic and pathologic multidirectional knee laxity measurements: a small step in the individualisation of care of anterior cruciate ligament injuries"
- >Funding: AFR-PPP PhD grant, Luxembourg National Research Fund, involving a public-private partnership with Genourob, Laval, France
- >Publications: Exceptional number of 13 research articles, of which seven as a first author, and three book chapters
- >Major achievements during the PhD:
  - > Analysis of a database of anterior cruciate ligament-injured patients visiting the "Centre Hospitalier de Luxembourg"
  - > Development of protocols to measure knee laxity with specialised devices
- >Other: Award for the best clinical communication at the Annual Congress of the French Society of Arthroscopy in 2014
- >Current position: Scientific collaborator at the "Centre Hospitalier de Luxembourg" in the "Cellule d'Enseignement Médical et de Recherche"; ongoing collaboration with LIH

## BIOGLOSSARY

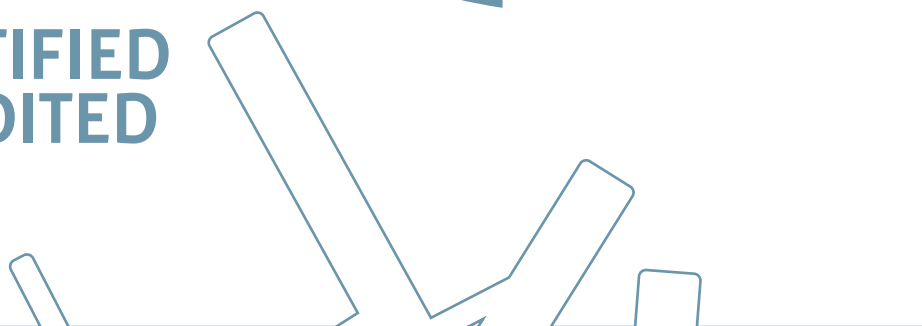
A **chemokine receptor** is a protein located on the cell surface that binds chemokines, small signalling molecules secreted by the cells.  
 A **ligand** is a molecule binding to a receptor (e.g. chemokines are ligands of the chemokine receptor). The binding produces a signal in the cell activating or inhibiting cellular processes.  
**Proteomics** is the large-scale study of the proteome (the proteins produced from genetic information) in a biological sample.  
**Targeted proteomics** is the analysis of a pre-selected group of proteins in a biological sample.  
**Knee laxity** is the elasticity or looseness of knee ligaments.  
 The **anterior cruciate ligament** is a ligament in the knee.







**IBBL - A CERTIFIED  
AND ACCREDITED  
BIOSERVICE  
PROVIDER**







Since 2015, IBBL - Integrated BioBank of Luxembourg, whose mission is to provide biospecimen-related services and a biobanking infrastructure for applied medical research, has been an autonomous institute organised within LIH. Over the last year, IBBL and LIH's research departments continued working hand in hand with national and international partners to advance research in areas such as cancer, diabetes, microbiome and Parkinson's disease. By extending the scope of its ISO accreditation\*, diversifying its collection of biological samples and refining its operations, IBBL concluded 2016 with great success.



## Quality first

Since the beginning, quality has been a key focus for IBBL. Its continuous efforts were again recognised as the end of 2016 came along with exciting news: not only did the biobank pass the follow-up audit for ISO 17025 (general requirements for the competence of testing and calibration laboratories), but it also extended the scope of its accreditation, most notably to a characterisation method that differentiates it from other biobanks worldwide in the eyes of the microbiome scientific community.

As good news always come in pairs, this major achievement was preceded by successful follow-up audits for ISO 9001 (general quality management) and NF S96-900 (quality of biological resource centres).

## Stronger together

At a national level, IBBL kept on driving partnerships on multiple projects. Within the "National Centre of Excellence in Research on Parkinson's Disease", shortly NCER-PD, IBBL collected biological samples, such as blood, urine and saliva from just over 580 patients and healthy donors. IBBL also set up quality control tests at each critical step of the sample handling to ensure that researchers receive fit-for-purpose samples of uniform quality and to maximise donors' contribution to research. Another milestone in 2016 was the launch of the Luxembourg Society for Microbiology. The decision to bundle and consolidate the activities of all local actors was made at a time when the field of microbiology was undergoing a true renaissance with a panoply of chronic diseases having been linked to changes in the microbial communities that inhabit for example the human gut. Speaking of which, a study led by researchers from several Luxembourgish institutes showed clear differences between healthy and diabetic individuals in the way bacteria function.

## BIOGLOSSARY

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.

The **human microbiome** consists of all the microorganisms that inhabit, for example, the human gut.

A **tumourbank** is a collection of frozen tumour tissues for future diagnostic or research purposes.

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

**Metabolomics** is the large-scale study of small molecules from our metabolism, commonly known as metabolites, within cells, biofluids, tissues or organisms.

\*The full accreditation scope is available on [www.ibbl.lu/about-ibbl/#quality](http://www.ibbl.lu/about-ibbl/#quality)

## Beyond borders

At the level of the Greater Region, IBBL teamed up with the Clinique Ambroise Paré and a private pathology laboratory from Thionville to establish the first France-Luxembourg cross-border collection of frozen tumour tissues, which can benefit both patients and cancer researchers. The project is a prime precedent for the tumourbank that IBBL is preparing together with Luxembourgish partners within the framework of the National Cancer Plan. Another large-scale success is the selection of IBBL as the preferred biobanking infrastructure and scientific partner for the precision medicine clinical research carried out by the European Organisation for the Research and Treatment of Cancer. One reason why the biobank has joined the organisation as a trusted and valued partner is the growing recognition of its biorefinery department.

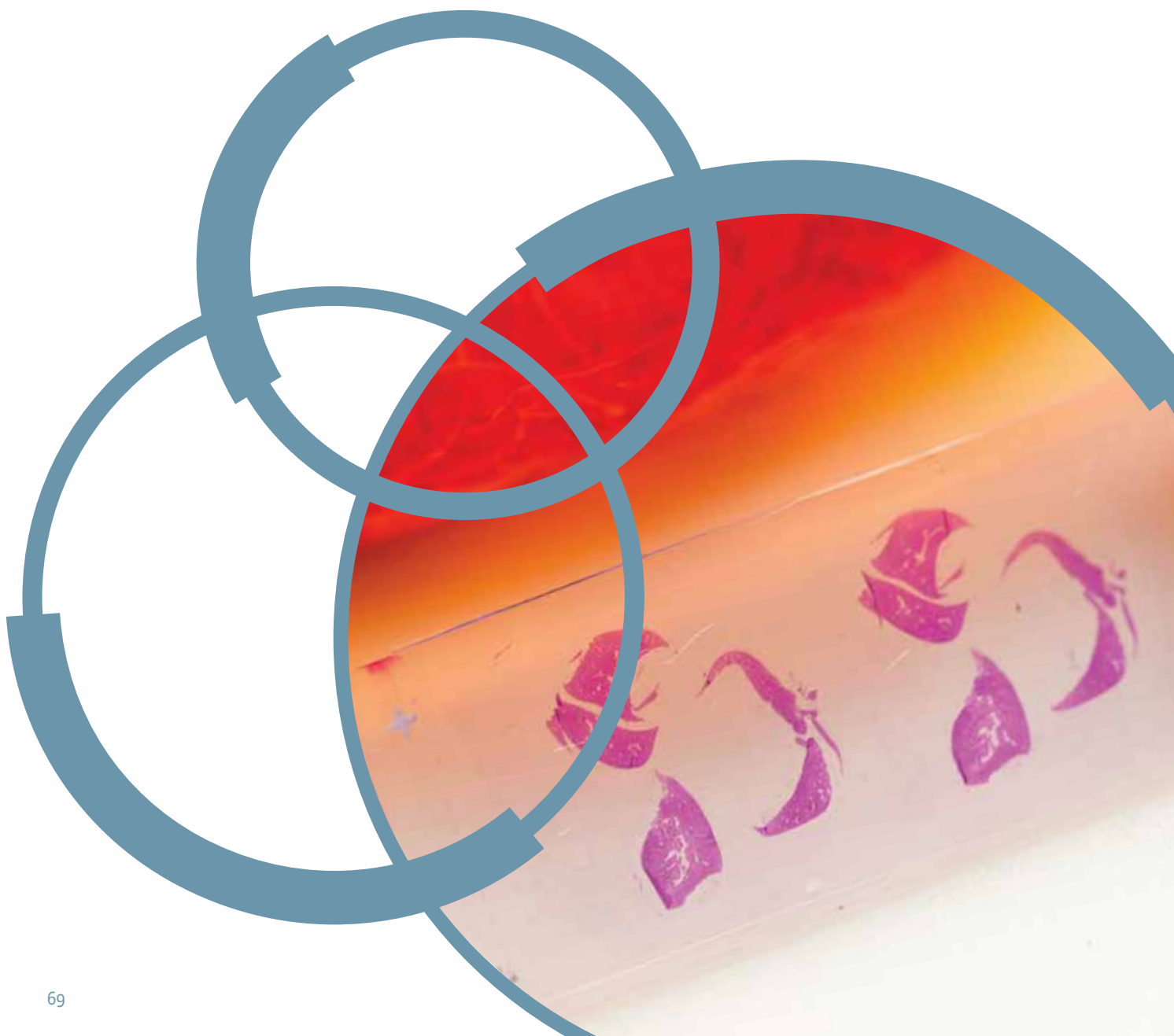
## More than a traditional biobank

Led by Dr Fay Betsou, IBBL's biorefinery department is deemed as one of the leading research groups focusing on the quality of biospecimens. In 2016, one of the projects explored the effect of 10 years of storage in  $-80^{\circ}\text{C}$  freezers on thyroid cancer tissues. Some others evaluated better ways to collect and handle biological samples, by comparing the impact of variations in temperature and delays during processing of blood samples on downstream metabolomics applications.

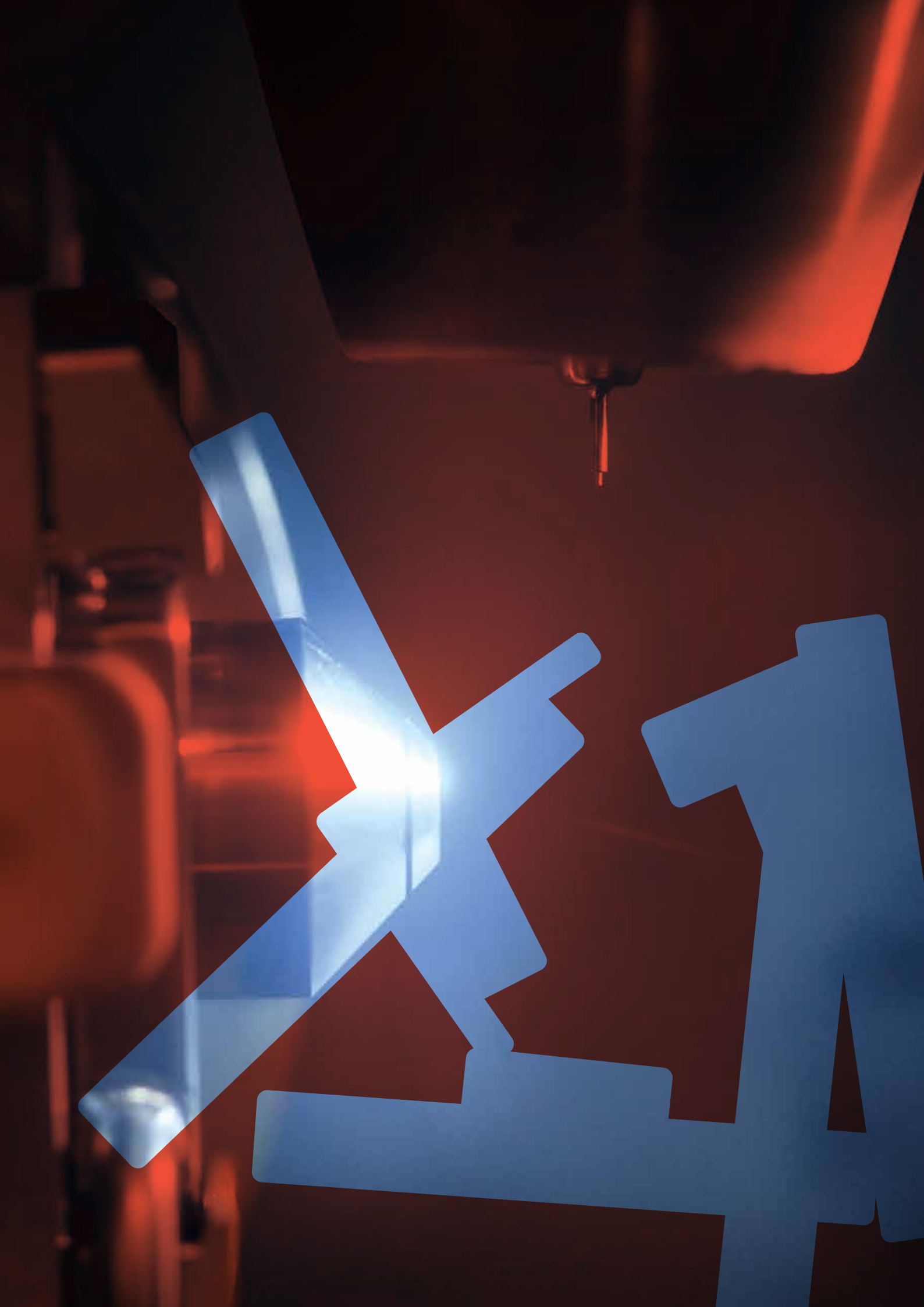
Overall, IBBL's various research projects led to 21 scientific publications. Moreover, in response to its clients' needs, IBBL also increased the number of testing and processing schemes in the Proficiency Testing (PT) programme, used by laboratories across the world to verify and benchmark their performance. This year, 94 laboratories from 26 different countries registered for a total of 354 PT schemes.

## Towards new horizons

2017 is bringing about new challenges and opportunities. Besides the move to Dudelange planned for the second semester, there is a handful of thrilling projects in the pipeline. The new facilities will more than double IBBL's floor area and will allow the biobank to increase further the size and diversity of its sample collection. Among the new projects, some will reinforce national cooperation in developing better healthcare solutions, while others will enhance Luxembourg's visibility in Europe and on the other side of the world.







## HIGHLIGHTS 2016





Discoveries, Events,  
Nominations, Awards & News

# HIGHLIGHTS 2016

JAN

## Dr Catherine Larue appointed as interim Chief Executive Officer of LIH

Dr Catherine Larue took over the general management of LIH as CEO *ad interim* on 1<sup>st</sup> January. She succeeded Dr Jean-Claude Schmit, who has been managing the institute for the last eight years and was appointed Director of Health at the Luxembourg Ministry of Health. Since 2012, Dr Catherine Larue has successfully held the position of CEO of IBBL, where she focused on business strategy and development of new personalised medicine initiatives. Before that, she worked for more than 20 years in research and development in the pharmaceutical industry.

## LIH becomes a member of EuroHealthNet

Since 1<sup>st</sup> January, LIH is part of EuroHealthNet. This network is a not-for-profit partnership of organisations, agencies and statutory bodies promoting health and health equity between and within European countries. First Prof Saverio Stranges, former Scientific Director of the Department of Population Health, then Dr Anna Chioti, Director *ad interim* of the Department of Population Health, were appointed as members of the Executive Committee. LIH's membership will allow to establish strong relationships with the main European stakeholders involved in disease prevention and health promotion, and to maximise collaborations that help to tackle well-known but also new health-related issues at both national and European level.

## Institution-wide implementation of a staff appraisal system

The constant changes of the research environment bring along new jobs, practices and technologies which are as many new opportunities for LIH's employees. It is in this context that the institute implemented, as stated in its performance contract, a staff appraisal system allowing to define the professional objectives of all its employees and evaluate their performance and evolution. This policy will enable the institute to make the most of its talents and help employees develop their careers while serving the organisation's priorities. It is applied institution-wide since 1<sup>st</sup> January.

## Dr Catherine Larue nominated to be part of an advisory group for Horizon 2020

Since 1<sup>st</sup> January, Dr Catherine Larue, CEO *ad interim* of LIH, is part of an advisory group for Horizon 2020, the European Research and Innovation programme. Horizon 2020 is the biggest European programme ever with nearly 80 billion Euro of funding available over seven years, from 2014 to 2020, aimed at securing Europe's global competitiveness.

## Launch of the Luxembourg Society for Microbiology

Microbiology is the study of microorganisms, which despite their notorious reputation as disease-causing agents, play essential roles in our daily lives and are integral to the maintenance of human health. Most research institutions in Luxembourg have ongoing research activities in the field of microbiology, which is currently undergoing a technology-driven revolution. The Luxembourg Society for Microbiology was founded to consolidate these research activities and bundle all expertise on the national level. A launch event was organised on 22<sup>nd</sup> January. Among the founding board members are Dr Fay Betsou from IBBL and Dr Carole Devaux from the Department of Infection and Immunity.



Dr Jos Even presenting the Luxembourg Society for Microbiology

FEB

## “Talking hands” for the World Cancer Day

At the occasion of the World Cancer Day on 4<sup>th</sup> February, LIH participated in a large Facebook campaign named “We can - I can” to raise awareness on cancer. Many members of LIH’s staff made their hands talk by writing supportive messages on them and posting photos on the wall of the institutional Facebook page. In parallel, LIH also informed on social media about the research conducted at the three research units of the Department of Oncology to prevent, diagnose and treat cancer.



*Facebook campaign for the World Cancer Day*



## Fun-filled quiz evening for the Rare Disease Day

For the second consecutive year, the association ALAN - Maladies Rares Luxembourg and LIH collaborated to raise awareness among Luxembourg's general public on rare diseases and research conducted in this field. On 27<sup>th</sup> February, at the occasion of the international Rare Disease Day, a quiz evening was organised in partnership with “Maison des Jeunes Mamer” and “Jong Fuerscher Lëtzebuerg”. Luxembourg’s famous Mister Science moderated the fully booked event.

MAR

## Science Club visits Department of Infection and Immunity

LIH aims to present its research activities to the broad public, in particular to the young generation. On 26<sup>th</sup> March, the Science Club of the National Museum of Natural History, a group of teenagers interested in science and technology, was invited to the Department of Infection and Immunity at the House of BioHealth in Esch-sur-Alzette. The young people could discover the research conducted in the field of allergology and could apply classical molecular biology techniques during a hands-on workshop.



*The Science Club members put themselves in the shoes of researchers during a hands-on workshop at the Department of Infection and Immunity*



APR

## World Health Day campaign to “beat diabetes”

The World Health Day 2016 on 7<sup>th</sup> April had the slogan “beat diabetes” and focused on the burden of diabetes through numerous initiatives organised all over the planet. Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. LIH designed two flyers to inform patients and the general public about diabetes. One flyer summarised recent results on the occurrence of diabetes in Luxembourg obtained with the ORISCAV-LUX study and the European Health Examination Survey (EHES) conducted at LIH. The other flyer was intended to raise awareness about gestational diabetes and was distributed specifically in maternities.



## Launch of EUROCAROTEN, a new COST Action on carotenoid research

On 18<sup>th</sup> April, European researchers and industrial representatives from 28 countries kicked off a new European COST (European Cooperation in Science and Technology) Action network in Brussels named EUROCAROTEN. Its goal is to enhance competitiveness of the European agro-food industry and promote health by coordinating research on carotenoids. Luxembourg is part of the network with the involvement of Dr Torsten Bohn, principal investigator at the Epidemiology and Public Health Research Unit within LIH's Department of Population Health. He is in charge of one of the working groups dedicated to carotenoids and health. In addition, his PhD candidate Joana Corte-Real is acting as a co-chair of the young researchers' representatives of EUROCAROTEN.

## Prof Romain Seil appointed president of ESSKA

On 7<sup>th</sup> May at the 17<sup>th</sup> congress of the European Society of Sports Traumatology, Knee Surgery and Arthroscopy (ESSKA) in Barcelona, more than 4,000 participants applauded the appointment of Prof Romain Seil as new president. The Luxembourgish who works as an orthopaedic surgeon at the “Centre Hospitalier de Luxembourg” and as a principal investigator at the Sports Medicine Research Laboratory within LIH's Department of Population Health, has previously held the positions of Secretary General and Vice President of the society. Prof Seil will chair ESSKA for a period of two years, an important professional commitment. The presidency represents a great showcase for Luxembourg and underlines its excellent positioning in the field of orthopaedic surgery and research.

## LIH hosts a COST PhD school on avian coronavirus research

From 25<sup>th</sup> to 27<sup>th</sup> April, Dr Chantal Snoeck, scientist at the Department of Infection and Immunity, organised a PhD school at the House of BioHealth in Esch-sur-Alzette in the framework of the COST (European Cooperation in Science and Technology) Action “Towards control of avian coronaviruses: strategies for diagnosis, surveillance and vaccination”, in which she is a workgroup leader. PhD candidates of the COST Action working in different European countries on research projects related to coronaviruses infecting birds attended the event together with foreign trainees and local young researchers.



Attendees of the COST PhD school held at LIH. Organiser Dr Chantal Snoeck is on the very right

MAY



Prof Romain Seil giving a speech at the ESSKA congress in Barcelona following his appointment as new president of the society

## Second edition of the Flow Cytometry User Meeting

The National Cytometry Platform within LIH's Department of Infection and Immunity and the company BD Biosciences invited to the second edition of the Flow Cytometry User Meeting on 10<sup>th</sup> May at the House of BioHealth in Esch-sur-Alzette. During this meeting open to LIH staff and external researchers, scientists routinely using flow cytometry, a technology to measure the characteristics of cells, shared their knowledge and experiences. Next to that, BD Biosciences application specialists gave workshops on instrument features and optimal experimental design.

## A quiz game to inform at the occasion of the World Hypertension Day

Every year, 17<sup>th</sup> May is dedicated to raise awareness on hypertension with the World Hypertension Day. A blood pressure of 14/8 or higher is considered as hypertension. LIH participated by inviting the broad public to take part in a quiz game on hypertension on Facebook. By trying to answer 12 questions people could learn about the principal causes of elevated blood pressure and how to prevent this major risk factor that can lead to severe cardiovascular disease.



LIH quiz game for Facebook on how to prevent hypertension

The Personalised Medicine Conference took place at the European Commission in Brussels



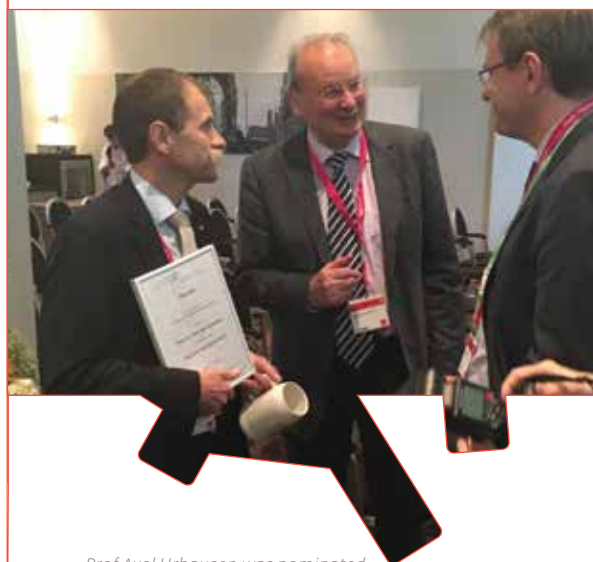
JUNE

## Prof Axel Urhausen awarded Sports Medicine Physician of the Year

The "Gesellschaft für Orthopädisch-Traumatologische Sportmedizin" (GOTS), which is the German-Austrian-Swiss Society for Orthopaedic Sports Medicine, has held its annual congress in Munich from 17<sup>th</sup> to 18<sup>th</sup> June. At this occasion, Prof Axel Urhausen, orthopaedic surgeon at the "Centre Hospitalier de Luxembourg" and principal investigator at the Sports Medicine Research Laboratory within LIH's Department of Population Health, was nominated as "Sports Medicine Physician of the Year". Prof Urhausen is the first Luxembourger to be given this prestigious award for his lifetime achievements in sports medicine.

## LIH joins the discussion on how to bring innovation to the market

Developing tools for personalised medicine, which is the concept of patient-tailored therapy, is one of LIH's key objectives. On 1<sup>st</sup> and 2<sup>nd</sup> June, the European Commission organised a Personalised Medicine Conference in Brussels followed by more than 1,000 participants. Dr Catherine Larue, CEO *ad interim* of LIH, was invited as a speaker to be part of a lively discussion on the challenges for implementing personalised medicine. With her long-standing experience in the pharmaceutical industry and her more recent immersion in the public research sector, she confidently dissected the different challenges that currently hinder an accelerated and efficient market entry of personalised therapies and diagnostics.



Prof Axel Urhausen was nominated as "Sports Medicine Physician of the Year" during the annual conference of the GOTS

## First ever PhD retreat organised in Luxembourg

The PhD retreat “Life after PhD”, organised on 21<sup>st</sup> June, aimed to give PhD candidates a glimpse into different career paths for PhD holders. The event was an initiative taken by Sean Sapcariu from the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg and Anne Dirkse from LIH, two PhD representatives of the University of Luxembourg’s Doctoral School in Systems and Molecular Biomedicine. The overwhelming participation and positive response from over 60 biomedical PhD candidates and nearly 30 guests, showed that career opportunities after a PhD are an important topic and that PhD candidates acquire an interesting set of skills during their doctoral studies, which they can valorise on the job market.



*PhD retreat held in the chapel of the Neumünster Abbey in Luxembourg City*

## Re-thinking European healthcare at the European Health Parliament

Europe must confront numerous healthcare problems that require new solutions. For almost seven months, Dr Xianqing Mao, postdoctoral researcher at the Laboratory of Experimental Cancer Research at the Department of Oncology, had been a delegate of the European Health Parliament and took part in a dynamic discussion about Europe’s major health challenges. More than 50 young professionals from different backgrounds were debating on important health and healthcare issues and published a final report end of June to share recommendations with policy makers and the healthcare community. Dr Mao has contributed to the part “digital skills for the medical profession”.



*Cover page of the European Health Parliament report giving recommendations on European healthcare*

JULY

## Jointly raising awareness on the World Hepatitis Day

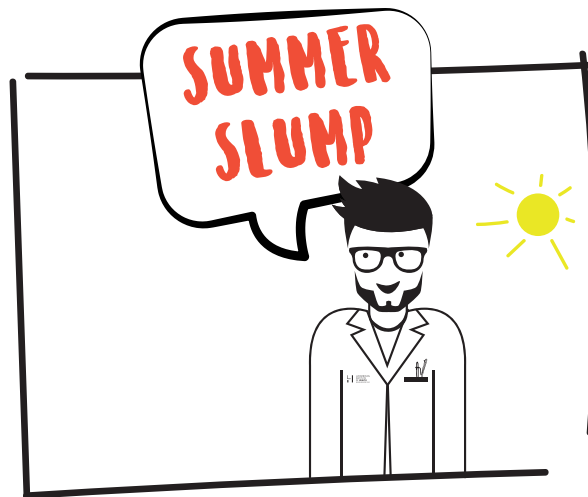
For the World Hepatitis Day on 28<sup>th</sup> July, LIH, together with the Ministry of Health and “HIV Berodung” of the Red-Cross Luxembourg informed about the transmission, prevention, diagnosis and treatment of hepatitis as well as research being done in Luxembourg. This disease of viral origin is characterised by an inflammation of the liver. A stand to distribute information material was set up in front of the Luxembourg train station. To catch attention, passing pedestrians were invited to participate to the completion of a big graffiti containing a message to raise awareness on the disease. People could also do a fast hepatitis-screening test in an equipped van (DIMPS project of the Red-Cross, the “Centre Hospitalier de Luxembourg” and the Ministry of Health).



*Team of the information booth for the World Hepatitis Day at the Luxembourg train station*



AUG



SEPT

## Promoting cardiovascular disease prevention at the World Heart Day

A large event organised by multiple national partners was held at the hospital "Hôpital Schuman - Kirchberg" on 29<sup>th</sup> September for the World Heart Day. Members of the Cardiovascular Research Unit, the Sports Medicine Research Laboratory and the Epidemiology and Public Health research unit of LIH's Department of Population Health engaged themselves to inform the public about cardiovascular disease prevention. With the help of a game suitable for both children and adults the Cardiovascular Research Unit explained its research activities on cardiovascular disease in a playful manner.



LIH stand on cardiovascular research for the World Heart Day at "Hôpital Schuman - Kirchberg"



Participants to one of the therapeutical fitness courses offered in Luxembourg and promoted by the "Sport-Santé" project

## LIH joins the HEPA Europe network

It is proven that physical activity has a therapeutic effect on certain diseases, such as cancer or cardiovascular disorders. To create awareness on the health benefit of sports, LIH launched the project "Sport-Santé" in 2015. One and a half year later, on 30<sup>th</sup> September, LIH became the first Luxembourg institution to join the European network for the promotion of Health-Enhancing Physical Activity (HEPA). This network shares innovative population-based approaches to promote therapeutic sports and disseminates strategies, programmes and best practices as well as the latest research findings in the field. Supported by the World Health Organisation, it currently includes 158 institutions and organisations from 36 European countries.

## Dr Anna Chioti nominated as a member of the IMI2-JU scientific committee

Dr Anna Chioti, Director *ad interim* of LIH's Department of Population Health, was designated among a list of candidates to become a member of the Scientific Committee of the Innovative Medicines Initiative 2 Joint Undertaking (IMI2-JU) for a period of two years starting from 1<sup>st</sup> October. IMI is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. IMI2-JU is the second programme of IMI, launched in 2014 for ten years and intending to develop next-generation vaccines, medicines and treatments, such as new antibiotics. Dr Chioti's appointment provides an opportunity for Luxembourg to be at the forefront of strategic research priorities for EU public-private partnerships.



*Dr Anna Chioti, Director ad interim of the Department of Population Health and newly elected member of the Scientific Committee of IMI2-JU*

## Dr Catherine Larue becomes "Chevalier de la Légion d'Honneur"

On 7<sup>th</sup> October, Dr Catherine Larue, CEO *ad interim* of LIH, received the grade of "Chevalier de la Légion d'Honneur" (Knight of the Legion of Honour) of the French Republic from His Excellency Ambassador Guy Yelda at the "Résidence de France" in Luxembourg. With this award the French Republic shows its recognition for an outstanding career path dedicated to science and healthcare, and illustrates the excellent level of cooperation between Luxembourg and France. The "Légion d'Honneur", founded in May 1802 by Napoléon Bonaparte, is the oldest and highest French distinction and one of the world's most famous.

OCT



*Project leader Dr Ala'a Alkerwi and her team of the ORISCAV-LUX study*

## ORISCAV-LUX study receives the Healthcare Research Award

Dr Ala'a Alkerwi, principal investigator and project leader of the ORISCAV-LUX study, and her team were awarded the Healthcare Research Award at the Luxembourg Healthcare Summit on 6<sup>th</sup> October. This award honours outstanding research conducted in Luxembourg that has an impact on the healthcare sector. Dr Alkerwi has been working for many years on the nationwide large-scale population-based study ORISCAV-LUX standing for "Observation des Risques et de la Santé Cardiovasculaire au Luxembourg". The study allowed establishing key baseline information on the occurrence of modifiable and preventable cardiovascular risk factors, including obesity, elevated blood pressure, diabetes, lipid disorders, smoking, physical activity and dietary habits among adults in Luxembourg.



*Dr Catherine Larue receiving the distinction "Chevalier de la Légion d'Honneur" by His Excellency Ambassador Guy Yelda*

## Cancer researchers receive the FNR Award for Outstanding Scientific Publication

On 14<sup>th</sup> October, the Luxembourg National Research Fund held the 8<sup>th</sup> edition of the FNR Awards, presenting four awards for excellence in science and research communication. Dr Jérôme Paggetti and Dr Etienne Moussay from the Laboratory of Experimental Cancer Research in LIH's Department of Oncology were awarded for an outstanding scientific publication on novel findings in cancer research that appeared in the acclaimed medical journal *Blood*. The publication Paggetti *et al.*, 2015 reports a study showing how cancer cells in chronic lymphatic leukaemia manipulate surrounding cells to their advantage to ensure their survival and proliferation.



Photo: © Charles Garatini

FNR awardees Dr Jérôme Paggetti (left) and Dr Etienne Moussay (right)

## ISO 9001:2008 re-certification and scope extension

On 20<sup>th</sup> and 21<sup>st</sup> October took place the external audit for LIH's quality management system applied to its administrative and research-support services and certain activities of the research departments. The institute was able to renew its ISO 9001:2008 certification and could even extend it to the new Risk and Compliance Management Unit, the Human Biomonitoring Research Unit and the new animal facility. The biobank IBBL also successfully passed the follow-up audits of its ISO 9001:2008 and NF S96-900 certifications as well as its ISO17025:2005 accreditation, for which the scope could be extended.



From left to right: Dr Catherine Larue (CEO ad interim of LIH), Dr Marie-Paule Kiény (Assistant Director General for Health Systems and Innovation at the World Health Organisation), Prof Markus Ollert (Director of LIH's Department of Infection and Immunity) and Dr Jean-Claude Schmit (Director of Health, Ministry of Health) at the Ministry of Health in the Villa Louvigny, Luxembourg City

## Stimulating seminar on Ebola research and development

LIH invited Dr Marie-Paule Kiény, Assistant Director General for Health Systems and Innovation at the World Health Organisation, to give a seminar on "Lessons learned from Ebola R&D during a public health emergency" on 18<sup>th</sup> October. The seminar, supported by the Ministry of Health and held within its premises at the Villa Louvigny in Luxembourg City, provided an insight on how the global health community managed to cope with the Ebola outbreak that hit West Africa in 2014. She highlighted the elaboration of a global strategy and preparedness plan ensuring that targeted R&D can strengthen the emergency response by bringing medical technologies to patients during epidemics.

## Inaugural lecture at the University of Sheffield by Honorary Professor Stephen Senn

Prof Stephen Senn, Head of LIH's Competence Centre for Methodology and Statistics and Honorary Professor of Medical Statistics at the University of Sheffield since end of 2015, was invited to give an inaugural lecture for the University's School of Health and Related Research on 26<sup>th</sup> October. The School's inaugural lecture series provides an opportunity to celebrate the recent professorship appointments with each lecture representing a significant milestone in an academic's career. The subject of Prof Senn's lecture was "Numbers needed to mislead, meta-analysis and muddled thinking".



## Cancer researchers rewarded for Translational Medical Research at the Medical Research Day

At the closing of the second edition of the Medical Research Day ("Journée de la Recherche Médicale") held on 26<sup>th</sup> October, Dr Jérôme Paggetti and Dr Etienne Moussay from the Laboratory of Experimental Cancer Research in LIH's Department of Oncology received the Award for Translational Medical Research for their outstanding collaborative research work on blood cancer. They have made an important contribution to research on chronic lymphatic leukaemia that led to a better understanding of how the tumour microenvironment is manipulated. The findings may pave the way for the development of new cancer treatment strategies.

## European project IDeAl receives a 6-month funding extension

IDeAl, standing for "Integrated Design and Analysis on small population group trials" is a multiparty three-year project funded by the 7<sup>th</sup> Framework Programme for Research and Technological Development of the European Commission. It aims at establishing new statistical methods specifically adapted to clinical trials on treatments for rare diseases typically involving small sample population groups. At LIH, members of the Competence Centre for Methodology and Statistics are leading one of the work packages of the project. Thanks to the high quality of the scientific output of this project, the funding by the European Commission could be extended for a period of six months as announced during a wrap-up meeting on 31<sup>st</sup> October.



Organisers and awardees of the Medical Research Day 2016. Dr Etienne Moussay (9<sup>th</sup> person from the left) holding a certificate for the Translational Medical Research Award that he shares with Dr Jérôme Paggetti

NOV

## Career workshop for postdoctoral researchers at the Cross-border Postdoctoriales

The second edition of the Cross-border Postdoctoriales, 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 7<sup>th</sup> to 10<sup>th</sup> November. Three postdoctoral researchers 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 different companies.



Participants and part of the invited speakers of the second edition of the Cross-border Postdoctoriales held in Luxembourg

## LIH submits a proposal to the Horizon 2020 Teaming programme

The Teaming action under Horizon 2020, the European Research and Innovation programme, supports the creation of new centres of excellence. A consortium composed of the Luxembourg National Research Fund, LIH and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg, submitted a proposal on 15<sup>th</sup> November to team up with the “Center for Innovative Medicinsk Teknologi” (Denmark) and the “Nationales Centrum für Tumorerkrankungen” (Germany) to establish a Centre of Excellence in Digital Health and Personalised Medicine. The centre shall address future medical and societal needs by ensuring that innovation from the bench will reach patient care. The project is focused on cancer and neuro-degenerative diseases, two areas in which there is both existing excellence in pre-clinical research and an important clinical unmet need.

## Politics Meets Research: participation to a pairing scheme

The Luxembourg National Research Fund organised an initiative to get members of the parliament (MP) in touch with researchers through a pairing scheme. To enable the worlds of research and politics to get to know each other better, every MP and researcher pair visited each other's respective work environments. At LIH, Dr Christiane Hilger from the Department of Infection and Immunity paired with MP Mrs Sylvie Andrich-Duval. On 14<sup>th</sup> November, Mrs Andrich-Duval was invited to visit LIH's premises at the House of BioHealth in Esch-sur-Alzette. She highly appreciated the guided visit and interesting talks organised for her as well as the openness of the researchers she encountered.



Visit of MP Mrs Sylvie Andrich-Duval at LIH. From left to right: Dr Christiane Hilger, principal investigator at the Department of Infection and Immunity, MP Mrs Sylvie Andrich-Duval, and Prof Markus Ollert, Director of the Department of Infection and Immunity

DEC

## Researchers' Days to get in touch with the public

The Researchers' Days 2016, organised by the Luxembourg National Research Fund on 2<sup>nd</sup> and 3<sup>rd</sup> December allowed school classes and the lay public to discover more than 20 interactive science workshops and join “science cafés” to discuss science directly with the researchers. LIH was well represented at the event with five different activities conceived by its staff. Among these was a workshop on microbes, “the little bugs that affect our lives”, organised by Dr Chantal Snoeck and other members of the Infectious Diseases Research Unit at the Department of Infection and Immunity. This workshop provided knowledge about omnipresence, detection and transmission ways of microbes and explained how to prevent and manage disease outbreaks in a playful manner, much appreciated by the youngest!



LIH workshop on “the little bugs that affect our lives” at the Researchers' Days 2016



*Erasmus+ Award ceremony at the annual conference of Anefore. Dr Laurence Fond-Harmant is the third awardee from the left holding a trophy*

## Multinational LIH-coordinated project rewarded with Erasmus+ Award

On 19<sup>th</sup> December, Dr Laurence Fond-Harmant, scientist at the Epidemiology and Public Health Research Unit in LIH's Department of Population Health, was awarded an "Erasmus+ Strategic Project" trophy. She coordinates a European project aiming at developing networks of professionals for mental health of elderly patients with psychic disorders. Among the project goals are an analysis of the management and current practices of mental healthcare networks for the elderly, the set-up of a European exchange platform to establish and follow-up networking, and the publication of a recommendation guide. The award was handed over during the annual conference of Anefore, the national agency in charge of the promotion and implementation of European programmes for education and lifelong learning.

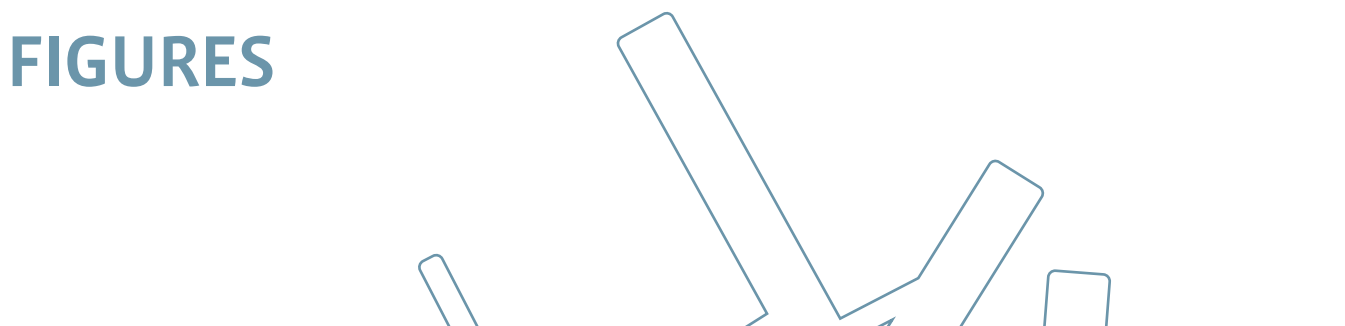
## Recruitment action for the Parkinson study NCER-PD

For NCER-PD, the National Centre for Excellence in Research on Parkinson's disease, LIH is in charge of recruiting a total of 800 healthy control persons whose clinical data and samples will be compared to those of Parkinson patients. On 15<sup>th</sup> December, LIH had the opportunity to conduct an information and recruitment action for the study at the Christmas market of the banking and financial service company Société Générale in Luxembourg. The strong support of the Société Générale's management allowed LIH's teams to have constructive exchanges with the employees, who showed a marked interest for participation in the study.

## Dr Torsten Bohn receives an Adjunct Associate Professorship from the University of Luxembourg

On 22<sup>nd</sup> December, Dr Torsten Bohn, principal investigator at the Epidemiology and Public Health Research Unit in LIH's Department of Population Health, was conferred the title of Adjunct Associate Professor of the University of Luxembourg by a committee of specialists established by the Rector on proposal of the University Council. Dr Bohn has been an external lecturer at the University of Luxembourg since 2011. He holds practical courses in biochemistry and lectures on "nutrition and metabolism" for undergraduate students, corresponding to about 60 teaching hours per year.

## FIGURES











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.

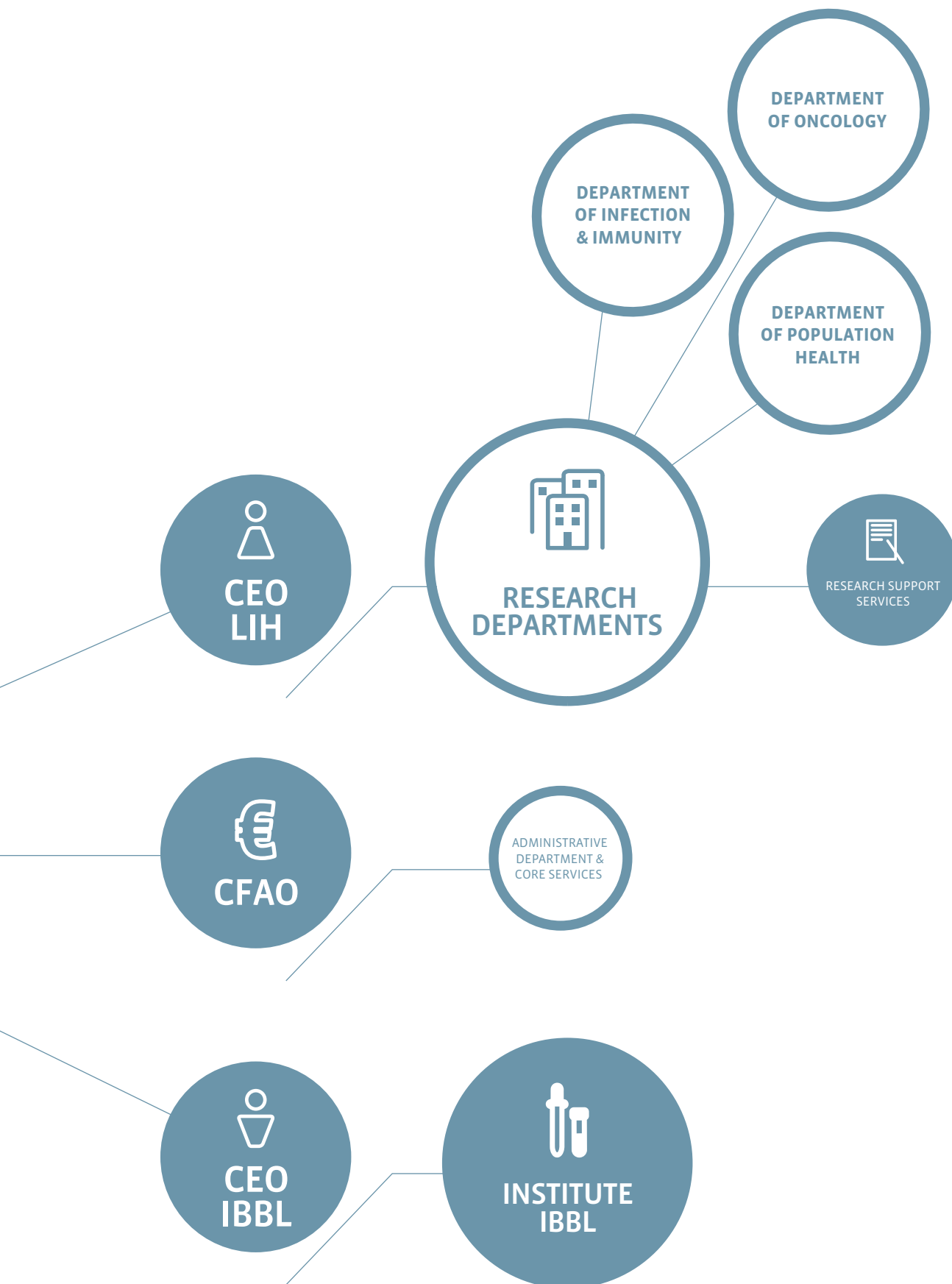
The **Coordinating Council** is a consultative body composed of internal representatives of the researchers, the personal delegation and the research and innovation support personnel. It issues advisory opinions to the Board of Directors regarding research policy, development and innovation. It will also advise on the content of the next 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.



## GOVERNANCE





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› UNIVERSITY OF SOUTH AUSTRALIA

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› FEDERAL UNIVERSITY OF SÃO PAULO  
› FEDERAL UNIVERSITY OF MINAS GERAIS

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› PEKING UNIVERSITY  
› CHINESE ACADEMY OF SCIENCES  
› KAILUAN GENERAL HOSPITAL  
› NATIONAL CENTRE OF CARDIOVASCULAR DISEASES

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› UNIVERSITY OF CYPRUS

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› NATIONAL INSTITUTE OF PUBLIC HEALTH

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› COPENHAGEN UNIVERSITY HOSPITAL

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› UNIVERSITY HOSPITAL OF TAMPERE  
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› UNIVERSITY OF LORRAINE  
› UNIVERSITY HOSPITAL NANCY  
› UNIVERSITY OF STRASBOURG  
› CNRS CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE  
› FEDERAL UNIVERSITY IN TOULOUSE  
› UNIVERSITY OF LILLE  
› INSTITUT PASTEUR LILLE  
› PARIS DIDEROT UNIVERSITY  
› CENTRE HOSPITALIER REGIONAL UNIVERSITAIRE DE LILLE  
› PARIS DESCARTES UNIVERSITY  
› AIX-MARSEILLE UNIVERSITY

## GERMANY

› TECHNICAL UNIVERSITY OF MUNICH  
› ROBERT KOCH INSTITUT  
› UNIVERSITY HEIDELBERG  
› GERMAN CANCER RESEARCH CENTRE  
› UNIVERSITY OF BONN  
› UNIVERSITY HOSPITAL HEIDELBERG  
› UNIVERSITY HOSPITAL ULM  
› HELMHOLTZ CENTRE MUNICH  
› LUDWIG MAXIMILIANS UNIVERSITY OF MUNICH  
› UNIVERSITY OF MUNSTER  
› UNIVERSITY OF ULM  
› UNIVERSITY OF TRIER  
› UNIVERSITY OF DUISBURG-ESSEN  
› UNIVERSITY OF COLOGNE  
› LEIPZIG UNIVERSITY

## GREECE

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› UNIVERSITY OF CRETE

## GREENLAND

› UNIVERSITY OF GREENLAND

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› CHINESE UNIVERSITY OF HONG KONG

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› CHIRAYU MEDICAL COLLEGE & HOSPITAL

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› RESEARCH INSTITUTE FOR PRIMORDIAL PREVENTION OF NON-COMMUNICABLE DISEASE

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## ISRAEL

› HADASSAH MEDICAL CENTRE

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› UNIVERSITY OF PADUA  
› UNIVERSITY OF INSUBRIA  
› UNIVERSITY OF FLORENCE  
› ISTITUTO SUPERIORE DI SANITÀ  
› UNIVERSITY OF TURIN  
› UNIVERSITY OF BRESCIA  
› UNIVERSITY OF PALERMO  
› NATIONAL RESEARCH COUNCIL  
› UNIVERSITY OF BARI  
› ASSOCIAZIONE CALABRESE DI EPATOLOGIA  
› IRCCS NEUROMED – ISTITUTO NEUROLOGICO MEDITERRANEO

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› KYOTO UNIVERSITY  
› KYUSHU UNIVERSITY  
› NIIGATA UNIVERSITY  
› UNIVERSITY OF TOKYO

## JORDAN

› EASTERN MEDITERRANEAN PUBLIC HEALTH NETWORK

## KENYA

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## LUXEMBOURG

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› UNIVERSITY OF LUXEMBOURG  
› LUXEMBOURG INSTITUTE OF SCIENCE AND TECHNOLOGY

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## NORWAY

› UNIVERSITY OF BERGEN  
› UNIVERSITY OF OSLO  
› NORWEGIAN UNIVERSITY OF SCIENCE AND TECHNOLOGY  
› NORWEGIAN SCHOOL OF SPORT SCIENCES

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› MEDICAL UNIVERSITY OF SILESIA  
› THE CARDINAL WYSZYNSKI INSTITUTE OF CARDIOLOGY

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## SERBIA

› UNIVERSITY OF BELGRADE

## SINGAPORE

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› SINGAPORE EYE RESEARCH INSTITUTE  
› DUKE-NUS MEDICAL SCHOOL

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› UNIVERSITEIT STELLENBOSCH  
› UNIVERSITY OF WITWATERSRAND  
› SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

# PARTNERS\*



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- > NATIONAL CANCER CENTRE

## **SPAIN**

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- > UNIVERSITY OF ZARAGOZA
- > AUTONOMOUS UNIVERSITY OF MADRID
- > UNIVERSITY OF SANTIAGO DE COMPOSTELA
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- > CENTRO NACIONAL DE INVESTIGACIONES CARDIOVASCULARES CARLOS III

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- > LUND UNIVERSITY
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## **SWITZERLAND**

- > GENEVA UNIVERSITY HOSPITAL
- > UNIVERSITY OF LAUSANNE
- > UNIVERSITY OF ZURICH
- > LAUSANNE UNIVERSITY HOSPITAL
- > SWISS INSTITUTE OF BIOINFORMATICS

## **TAIWAN**

- > NATIONAL TAIWAN UNIVERSITY
- > ACADEMIA SINICA

## **THAILAND**

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## **THE NETHERLANDS**

- > ERASMUS UNIVERSITY MEDICAL CENTRE
- > UNIVERSITY MEDICAL CENTRE UTRECHT
- > ACADEMIC MEDICAL CENTRE
- > MEDICAL CENTRE LEEUWARDEN

## **UNITED KINGDOM**

- > WARWICK MEDICAL SCHOOL
- > UNIVERSITY OF NORTHUMBRIA
- > UNIVERSITY OF OXFORD
- > UNIVERSITY COLLEGE DUBLIN
- > IMPERIAL COLLEGE LONDON
- > UNIVERSITY OF MANCHESTER
- > UNIVERSITY OF OXFORD
- > LIVERPOOL SCHOOL OF TROPICAL MEDICINE
- > UNIVERSITY COLLEGE LONDON
- > UNIVERSITY OF EDINBURGH
- > UNIVERSITY OF CAMBRIDGE
- > KING'S COLLEGE LONDON
- > UNIVERSITY OF SOUTHAMPTON
- > MRC LIFECOURSE EPIDEMIOLOGY UNIT

## **UNITED STATES**

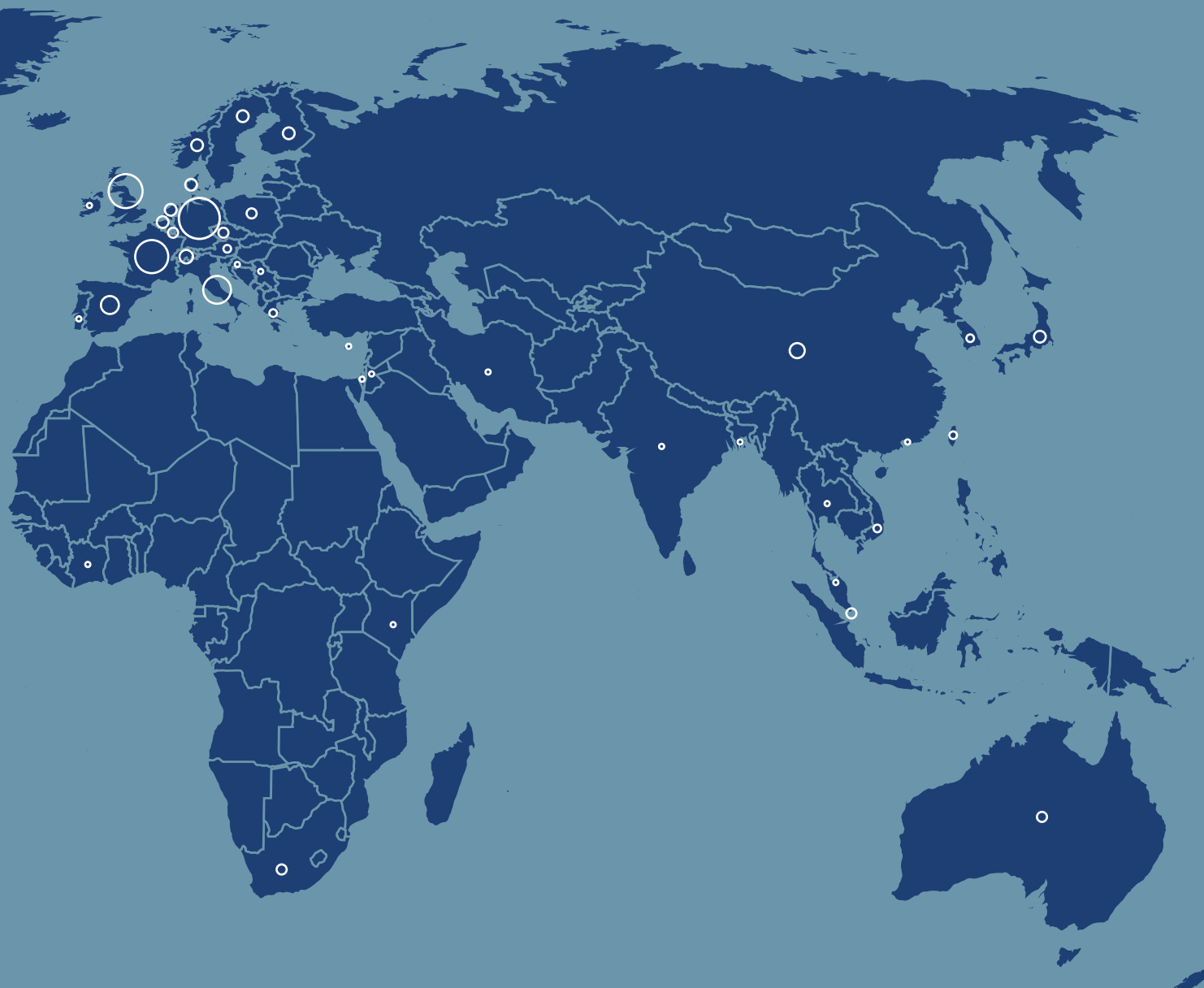
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- > NATIONAL INSTITUTES OF HEALTH
- > JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH
- > DUKE UNIVERSITY
- > BROWN UNIVERSITY
- > UNIVERSITY OF CALIFORNIA, BERKELEY
- > UNIVERSITY OF CALIFORNIA, SAN DIEGO
- > HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
- > BAKER HEART AND DIABETES INSTITUTE
- > CENTRE FOR DIABETES AND ENDOCRINE CARE
- > UNIVERSITY OF MAINE
- > UNIVERSITY OF MICHIGAN
- > WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

## **VENEZUELA**

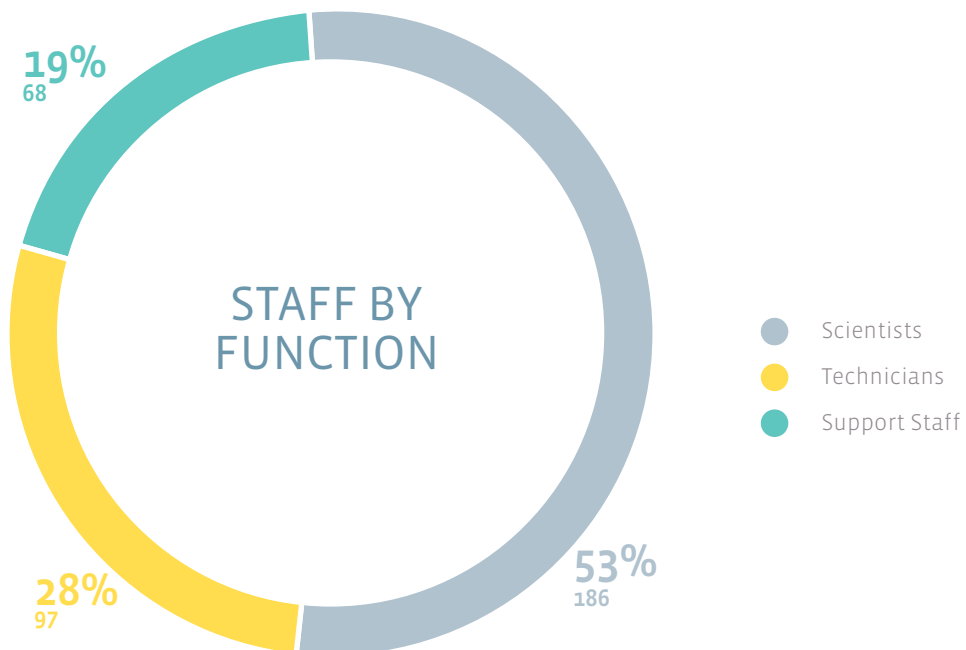
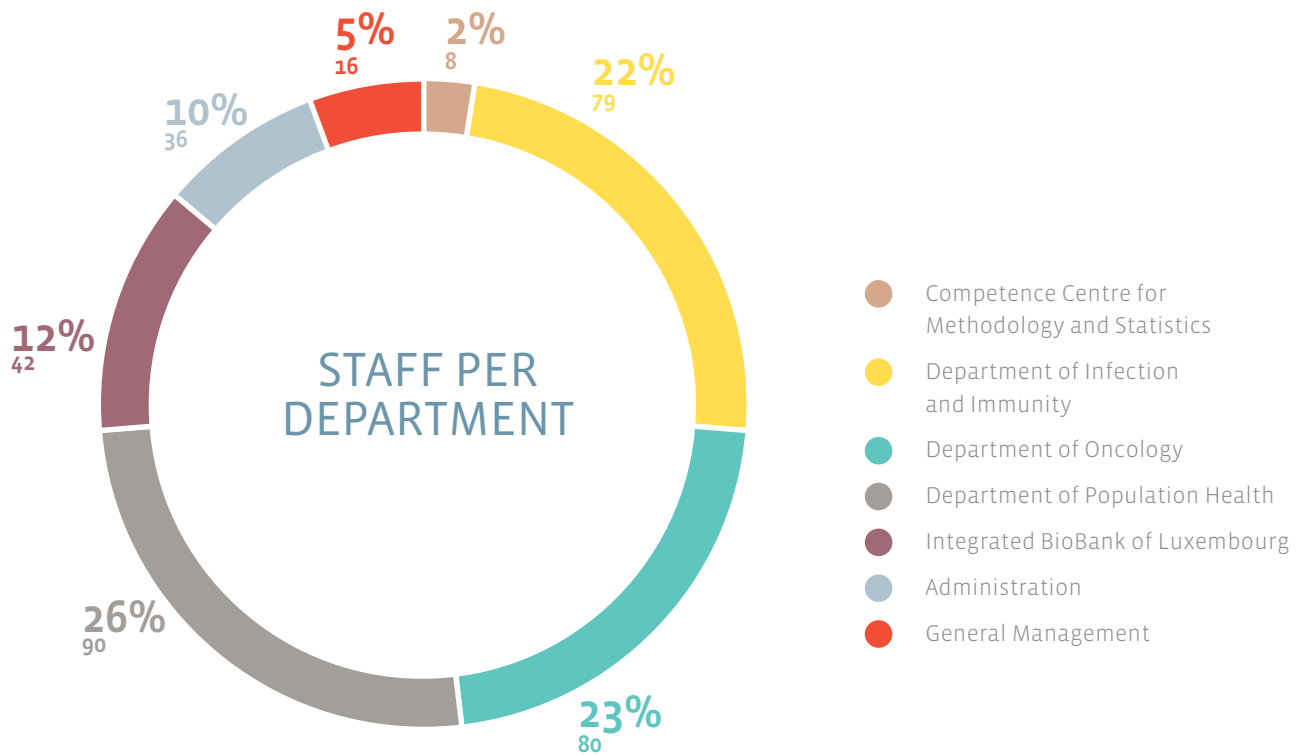
- > CENTRAL UNIVERSITY OF VENEZUELA
- > THE ANDES CLINIC OF CARDIO-METABOLIC STUDIES

## **VIETNAM**

- > UNIVERSITY OF MEDICINE AND PHARMACY OF HO CHI MINH CITY
- > VIETNAM NATIONAL HEART INSTITUTE

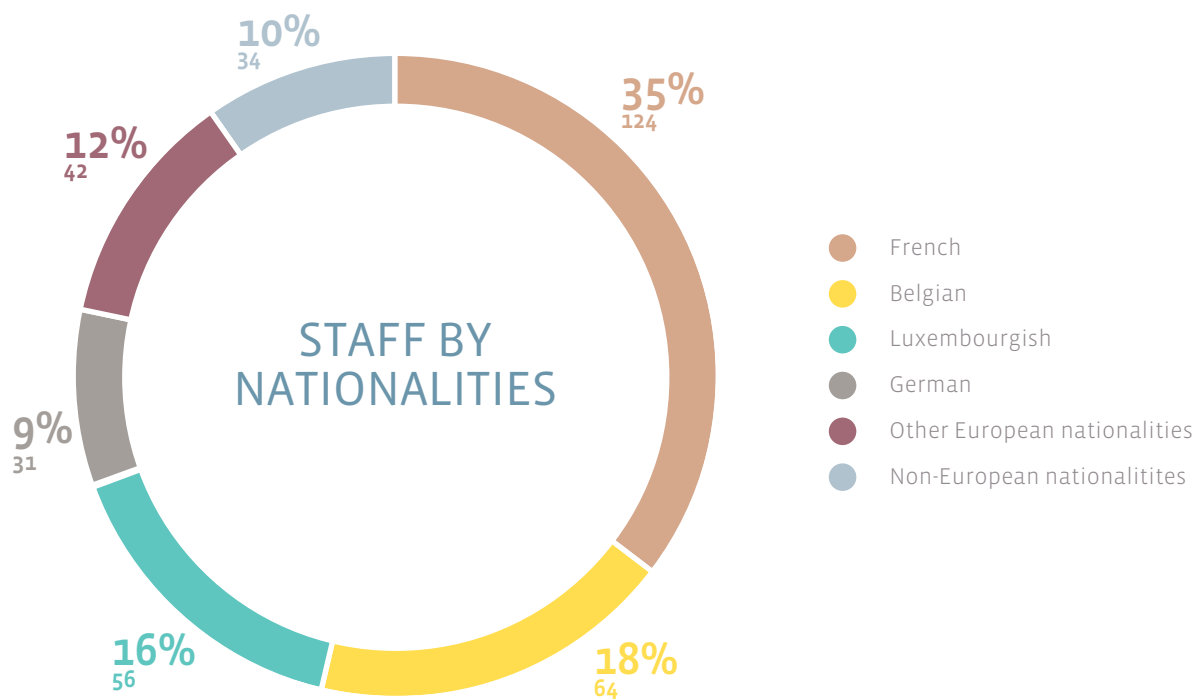
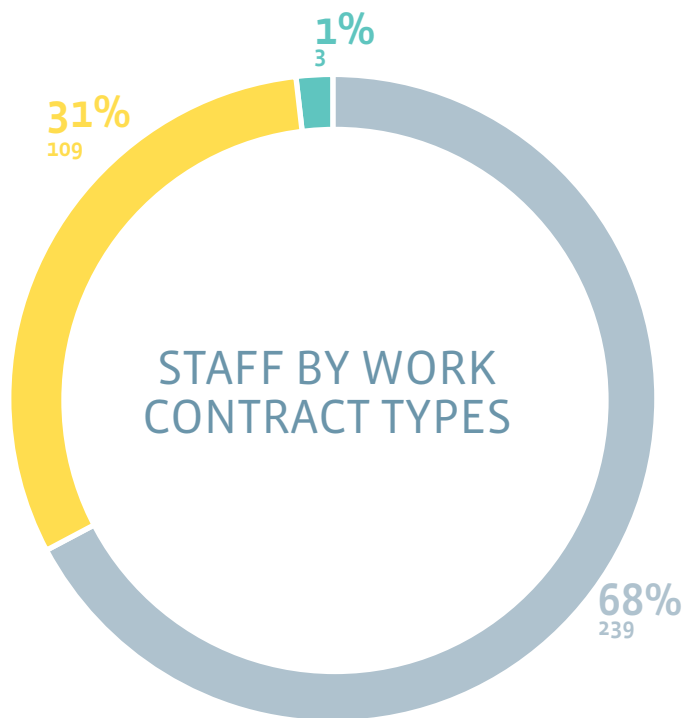


\*Organisms, institutes and universities with which LIH co-authored publications in 2016

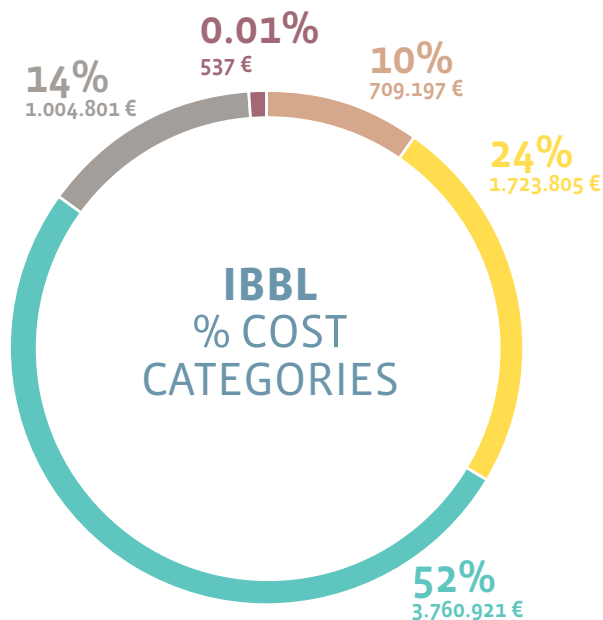
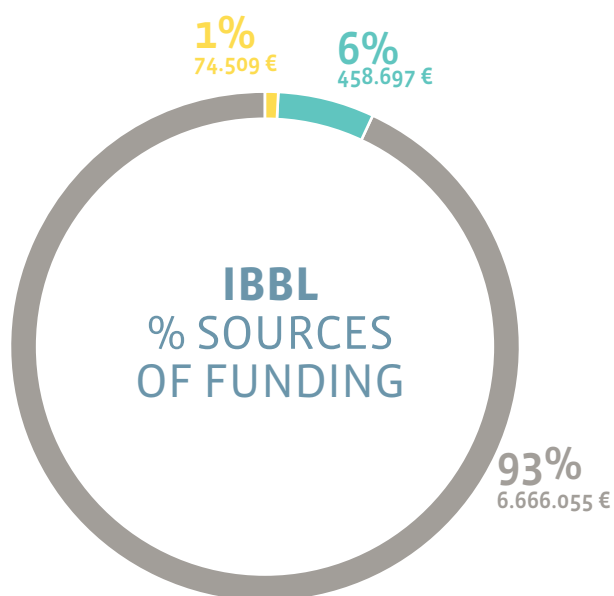
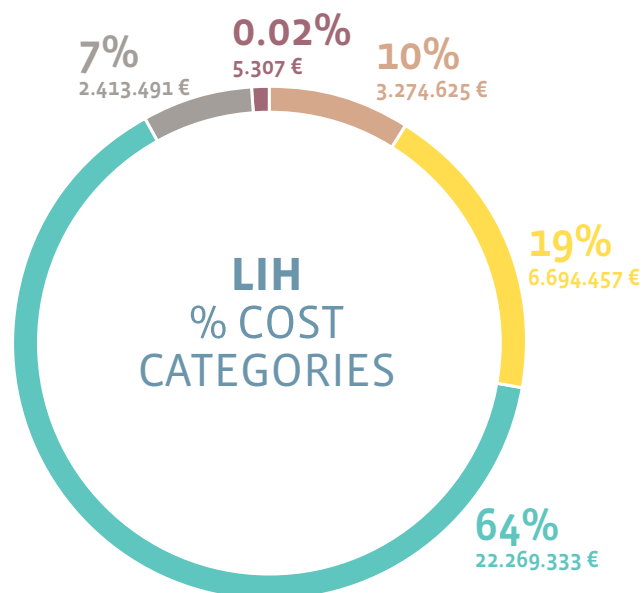
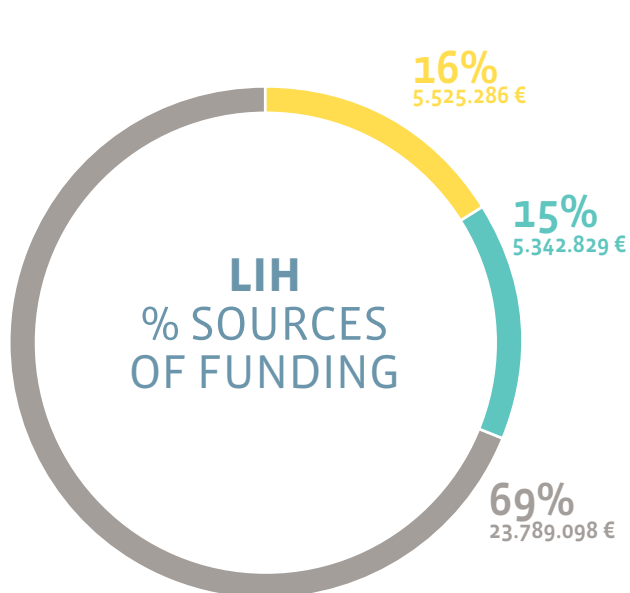


## HUMAN RESOURCES







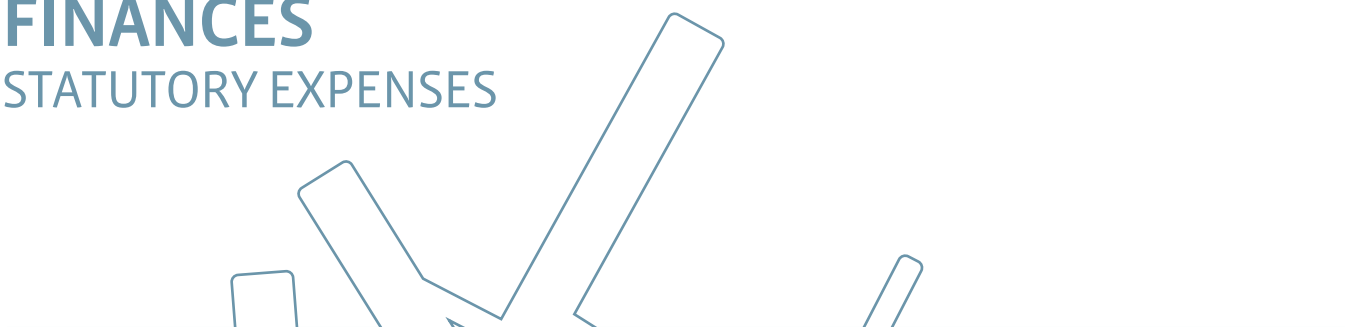


- Contractual research
- Ministry of Higher Education and Research
- Competitive research

- Raw materials and consumables
- Other operating costs
- Staff costs
- Depreciations
- Interests and other financial charges

## FINANCES

### STATUTORY EXPENSES



**PROFIT AND LOSS ACCOUNT (EUR), incl. IBBL**

	<b>2016</b> 01.01 - 31.12.16	<b>2015</b> 01.01 - 31.12.15
<b>A. CHARGES</b>		
1. Use of merchandise, raw materials and consumable materials	3.983.822	3.791.423
2. Other expenses	8.418.262	7.150.680
3. Staff costs	26.030.254	26.044.118
4. Value adjustment on intangible and tangible fixed assets	3.418.292	2.984.178
5. Interests and other financial charges	5.844	11.046
6. Profit for the financial year	0	0
<b>TOTAL CHARGES</b>	<b>41.856.474</b>	<b>39.981.445</b>
<b>B. INCOME</b>		
1. Net turnover	1.539.165	2.818.877
2. Subsidies	40.133.531	36.932.741
3. Other income	130.945	145.961
4. Interests and other financial income	52.833	83.866
5. Loss for the financial year	0	0
<b>TOTAL INCOME</b>	<b>41.856.474</b>	<b>39.981.445</b>

# FINANCES

## PROFIT AND LOSS ACCOUNT

**ASSETS** (EUR), incl. IBBL**2016**  
01.01 - 31.12.16**2015**  
01.01 - 31.12.15**FIXED ASSETS**

Intangible fixed assets	695.070	583.912
Tangible fixed assets	9.110.073	9.410.281
Financial fixed assets	424.555	424.205
<b>TOTAL FIXED ASSETS</b>	<b>10.229.698</b>	<b>10.418.398</b>

**CURRENT ASSETS****Debtors**

<b>1. Trade debtors</b>	<b>1.080.984</b>	<b>1.419.926</b>
a. Becoming due and payable within one year	1.062.440	1.419.926
b. Becoming due and payable after more than one year	18.544	0
<b>2. Other debtors</b>	<b>3.936.571</b>	<b>3.308.948</b>
a. Becoming due and payable within one year	3.936.571	3.308.948
Cash at bank and in hand	<b>21.804.458</b>	<b>26.064.559</b>
<b>TOTAL CURRENT ASSETS</b>	<b>26.822.013</b>	<b>30.793.433</b>

**Prepayments**

<b>TOTAL ASSETS</b>	<b>37.575.571</b>	<b>41.660.668</b>
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# FINANCES

## BALANCE SHEET

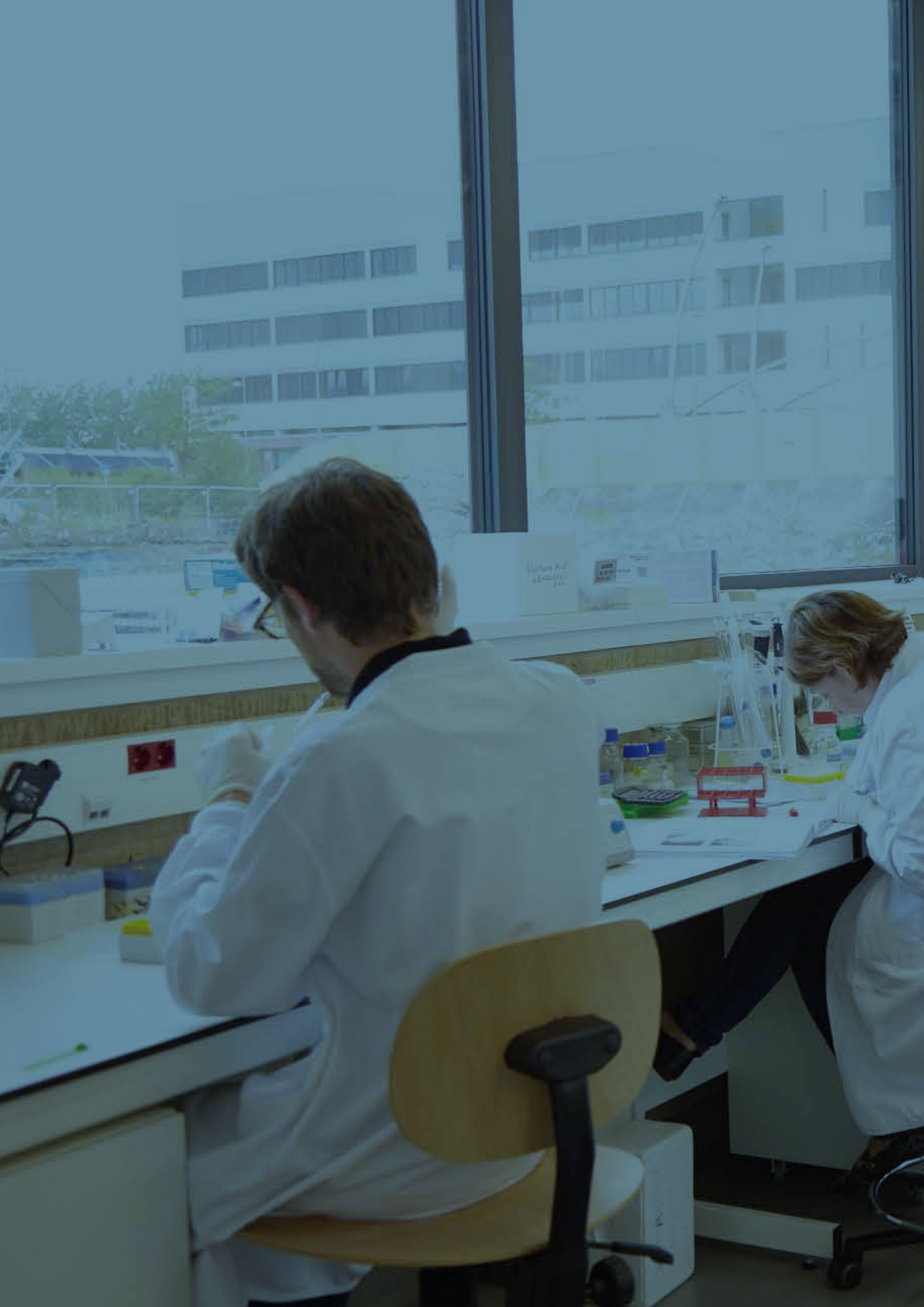


**LIABILITIES (EUR), incl. IBBL****2016**  
01.01 - 31.12.16**2015**  
01.01 - 31.12.15**CAPITAL AND RESERVES**

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	0	0
Capital investment subsidies	9.490.224	8.763.389
<b>TOTAL CAPITAL AND RESERVES</b>	<b>23.570.628</b>	<b>22.843.793</b>
<b>Available reserve for projects</b>	<b>9.150.822</b>	<b>13.760.352</b>
<b>Provisions</b>	<b>1.441.957</b>	<b>719.964</b>

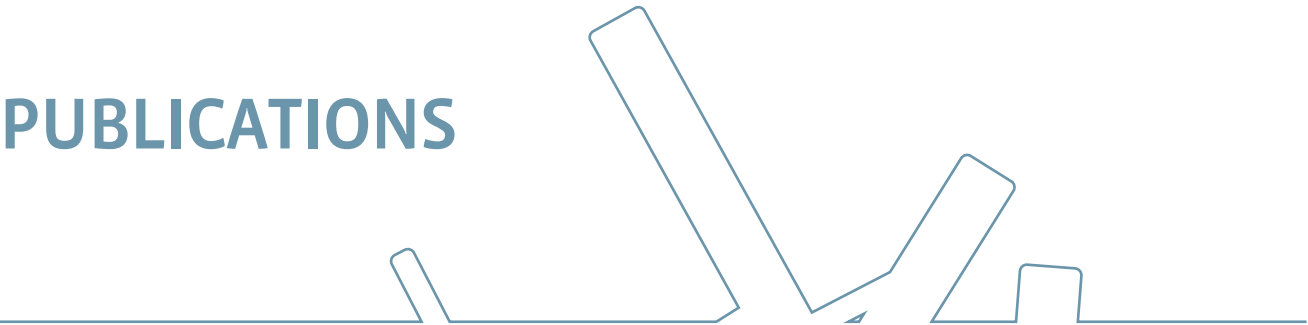
**NON-SUBORDINATED DEBTS**

<b>1. Trade creditors</b>	<b>2.478.806</b>	<b>1.975.285</b>
a. Becoming due and payable within one year	2.457.845	1.197.211
b. Becoming due and payable after more than one year	20.961	778.074
<b>2. Tax and social security debts</b>	<b>895.219</b>	<b>1.600.313</b>
a. Tax debts	12.384	729.711
b. Social security debts	882.835	870.602
<b>3. Other creditors</b>	<b>37.990</b>	<b>760.431</b>
a. Becoming due and payable within one year	37.990	760.431
<b>TOTAL AVAILABLE RESERVE FOR PROJECTS, PROVISIONS AND CREDITORS</b>	<b>14.004.794</b>	<b>18.816.345</b>
<b>Deferred income</b>	<b>149</b>	<b>530</b>
<b>TOTAL CAPITAL, RESERVES AND LIABILITIES</b>	<b>37.575.571</b>	<b>41.660.668</b>





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# COMPETENCE CENTRE FOR METHODOLOGY AND STATISTICS

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Collignon O, Vesely R. **Should baseline-dependent cut-offs really be used to define disease improvement in juvenile idiopathic arthritis? And few other considerations.** Rheumatology. 2017; 56(1): 165-167. Epub 2016 Oct 22. *IF: 4.524 (2015)*

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Cunningham SG, Carinci F, Brillante M, Leese GP, McAlpine RR, Azzopardi J, Beck P, Bratina N, Bocquet V, Doggen K, Jarosz-Chobot PK, Jecht M, Lindblad U, Moulton T, Metelko Z, Nagy A, Olympios G, Pruna S, Skeie S, Storms F, Di Iorio CT, Massi Benedetti M. **Core Standards of the EUBIROD Project. Defining a European Diabetes Data Dictionary for Clinical Audit and Healthcare Delivery.** Methods of Information in Medicine. 2016; 55(2): 166-76. *IF: 2.248 (2015)*

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Gewandter JS, McDermott MP, McKeown A, Hoang K, Iwan K, Kralovic S, Rothstein D, Gilron I, Katz NP, Raja SN, Senn S, Smith SM, Turk DC, Dworkin RH. **Reporting of cross-over clinical trials of analgesic treatments for chronic pain: Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks systematic review and recommendations.** Pain. 2016; 157(11): 2544-2551. *IF: 5.557 (2015)*

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Greenland S, Senn SJ, Rothman KJ, Carlin JB, Poole C, Goodman SN, Altman DG. **Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations.** European Journal of Epidemiology. 2016; 31(4): 337-50. *IF: 7.105 (2015)*

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Grun D, Pieri V, Vaillant M, Diederich NJ. **Contributory factors to caregiver burden in Parkinson disease.** Journal of the American Medical Directors Association. 2016; 17(7): 626-32. *IF: 6.616 (2015)*

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Lonergan M, Senn SJ, McNamee C, Daly AK, Sutton R, Hattersley A, Pearson E, Pirmohamed M. **Defining drug response for stratified medicine.** Drug Discovery Today. 2017; 22(1): 173-179. Epub 2016 Nov 3. *IF: 5.625 (2015)*

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Sauvageot N, Leite S, Alkerwi A, Sisanni L, Zannad F, Stranges S, Donneau AF, Albert A, Guillaume M. **Association of empirically derived dietary patterns with cardiovascular risk factors: A comparison of PCA and RRR methods.** PLoS One. 2016; 11(8): e0161298. *IF: 3.057 (2015)*

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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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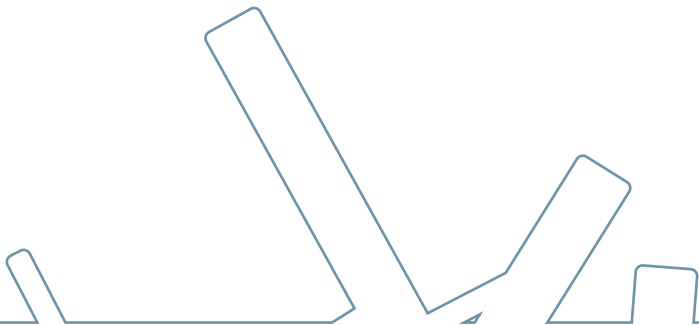
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