

RESEARCH DEDICATED TO LIFE
ANNUAL REPORT 2015



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

ANNUAL REPORT 2015

FOREWORD

RESEARCH DEDICATED TO LIFE

The Luxembourg Institute of Health (LIH) can celebrate its first year of existence as new structure resulting from the fruitful merger of the biomedical research institute “Centre de Recherche Public de la Santé” (CRP-Santé) and the research infrastructure and biobanking service provider Integrated BioBank of Luxembourg (IBBL).

LIH, with its new corporate identity and its more than 340 collaborators, became reality on 1st January 2015, following the entry into force of the new law on the organisation of public research in Luxembourg. This novel structure reflects the willingness of the Government to reinforce the national research centres by creating synergy of people and technology, thus enabling them to face the progression of a fast-evolving sector.

LIH's slogan expresses its mission clearly and concisely: “Research dedicated to life”. By conducting basic and translational research projects, our scientists aim to improve patients' lives, diagnosis and treatment, and implement personalised medicine. The change of identity went along with a refinement of our research strategy at the departmental and at the institutional level. We defined our key research areas in which we aim to gather a critical mass of outstanding workforce. The year 2015 was therefore marked by a profound internal restructuring crucial for LIH's future development.

The institute is now composed of three large thematic departments. Next to them, IBBL remains a clearly identified structure with management autonomy, enabling it to fully assume its specific role as service provider. The three departments reflect the research focuses of the institute: Infection and Immunity, Oncology, Population Health. Each one is headed by a scientific director having an excellent track record and an internationally recognised expertise in their field. The departments are further sub-divided into units and groups with specific research scopes, led by ambitious junior and senior principal investigators. This organisation guarantees an optimal training and supervision environment for early-stage researchers and students, essential for shaping their future career.

Numerous synergies were created between the two entities during the past year, in particular on the administrative level. Core administrative services were united, which permitted to efficiently centralise recruitment and human resources management, accounting and purchasing, as well as IT infrastructure and support. Furthermore, a harmonisation of procedures related to the quality management system was initiated.

The organisational changes were in no way a hindrance for our researchers to excel again in scientific production. In 2015, the research departments issued a total of 236 publications, including books, book chapters and PhD theses. Forty-seven publications appeared in acclaimed international peer-reviewed journals with an impact factor above 5. Of these, 11 were of outstanding scientific quality and were published in journals with an impact factor higher than 10.

LIH also succeeded in attracting substantial national and international competitive funding. Importantly, the institute is now participating in two plurennial EUROSARS projects funded by the

European Union, involving collaborations with international academic partners and industries. In 2015, LIH engaged in 39 public-private partnerships and signed 176 agreements. Seven of these contracts concern wet-lab applications.

We can thus look back on a scientifically active year and ahead to the challenges awaiting us. We wish to conclude by thanking all our employees and collaborative partners for their continuous commitment to drive research forward that serves health and healthcare, and to develop Luxembourg into an attractive and internationally known research location for biomedical sciences.

Dr Catherine Larue
CEO since 1st January 2016

Dr Jean-Claude Schmit
CEO until 31st December 2015



KEY FIGURES

2015

236 
PUBLICATIONS


171
RESEARCHERS


343
EMPLOYEES

36 
NATIONALITIES

10 
PHD
DEFENCES



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MISSION & VISION



LIH'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.



INTERVIEW

WITH DR GREGOR BAERTZ

Dr Baertz, you are Medical Director of “Hôpitaux Robert Schuman” and President of LIH’s Board of Directors. Can you tell us about the mission of the Board of Directors?

The Board of Directors acts as the control body for the institute’s activities. It is mainly in charge of defining the general organisation, endorsing strategic changes and approving the annual budget and accounts. It recruits the Chief Executive Officer, the Chief Financial and Administrative Officer and the directors of departments. It can also sign and terminate contracts and agreements with partners, and occasionally deals with issues like major security concerns and risk management.

The Board closely follows the activities of the institution thanks to quarterly dashboard reports that are presented during the Board meetings. With these reports, it can easily evaluate how LIH performs with regard to its objectives defined in the performance contract concluded with the Government from 2014 to 2017. This also allows to develop a long-term vision on how the institute’s activities should evolve in the coming years.

How would you describe the Board of Directors’ organisation?

The Board of Directors is composed of nine members. It comprises a president and a vice-president, Dr Nadine Martin who is Head of Innovation Management at sitem-insel, the Swiss Institute for Translational and Entrepreneurial Medicine. In addition, there is a Government Commissioner, Mr Xavier Poos, who has an advisory role and ensures that the laws and regulations are respected.

The members come from different countries and have diverse professional backgrounds providing the Board with expertise in law, finance, research, medicine, industry and technology transfer. This multiplicity of competences is very beneficial for the functioning of the Board.

In 2015, CRP-Santé and IBBL have been merged to become LIH. Can you tell us a bit more on the synergies that have been created since then?

There are evident synergies at the administrative level. The foremost is that there is a single Board of Directors governing the two entities. Moreover, all administrative services have been united to a sole administrative department headed by a newly designated Chief Financial and Administrative Officer. In the middle-term we will surely see a positive effect on the institute’s budget. Importantly, the merger also facilitates the scientific collaborations between the two entities and will increase the number and quality of common scientific publications.

LIH also underwent a major internal reorganisation in the first half of 2015. Instead of five research departments and several distinct competence centres, it now comprises three large thematic research departments. What are the benefits of this structural reorganisation?

The former organisation was very heteroclite and the departments and research units were rather small. We now focus on three key research areas highlighted by the names of the three departments: Infection and Immunity, Oncology, Population Health. We clearly gain in efficiency by gathering a critical mass of experts

in those three fields of research.

Our national and international visibility will also be enhanced. A coherent structure with larger departments makes us much more attractive as an employer. I am confident that we will be able to attract ambitious young scientists and established senior researchers from abroad more easily.

Which challenges do you see ahead for LIH?

I think that we can still improve the level of our research outputs to gain more international visibility. It is important to communicate on our achievements and to do networking with our stakeholders. This should be done at all levels. Information should be made available for the broad public and media, the researchers should promote their work within their scientific community, and the top management should interact intensively with decision makers.

The Board of Directors continuously advises to put more efforts in applying for external funding and thus be more successful in fund raising. National and European third-party funding is essential to become more independent from the financial support provided by the Government. Furthermore, we will have to focus more on economic value creation by filing patents, and be more proactive to engage in further public-private partnerships.

To finish, would you have a message to pass to the people through this annual report?

I would like to thank all employees of LIH for the great job they did in 2015. It was a very productive year, especially in terms of scientific output. We managed to achieve our key performance indicators on scientific production and even surpassed the expected number and quality of publications.

LIH's co-workers should continue to be very demanding to themselves. The institute must maintain its quest for excellence and further develop a culture of reward and recognition.



Dr Gregor Baertz

President of LIH's Board of Directors

RESEARCH DEDICATED TO LIFE

The background features several vertical bars in red, orange, and dark red at the top. At the bottom, there are several thin, curved lines in shades of grey, brown, and blue that sweep across the page.



L

LEAD KNOWLEDGE GENERATION

Unveiling disease mechanisms
to translate knowledge into
clinical applications for
the benefit of patients

I

INVEST IN NEW TALENTS AND INFRASTRUCTURE

Investing in human
talents and state-of-the-art
infrastructure

F

FOSTER KNOWLEDGE SHARING


Being instrumental in
breaking down barriers to
knowledge sharing,
enhancing scientific debate
and exchange of ideas

E

ENGAGE IN COLLABORATIONS

Building links between
scientists at an
international level





LEAD KNOWLEDGE GENERATION

Unveiling disease mechanisms
to translate knowledge into
clinical applications for the
benefit of patients

MANIPULATIVE LEUKAEMIA CELLS UNVEILED

Subverting the tumour microenvironment to promote tumour growth

Can cancer cells manipulate surrounding cells to their advantage? That's what Dr Jérôme Paggetti, Dr Etienne Moussay and co-workers have been studying, focusing their research on blood cancer.

On the trail of exosomes

The study more specifically examined the role of exosomes released by leukaemia cells into their close environment. From other cancer types, it is known that exosome uptake by surrounding healthy cells induces important changes that are favourable for tumour survival. For the first time, exosomes derived from chronic lymphocytic leukaemia (CLL) were analysed in detail and their effect on the tumour microenvironment investigated.

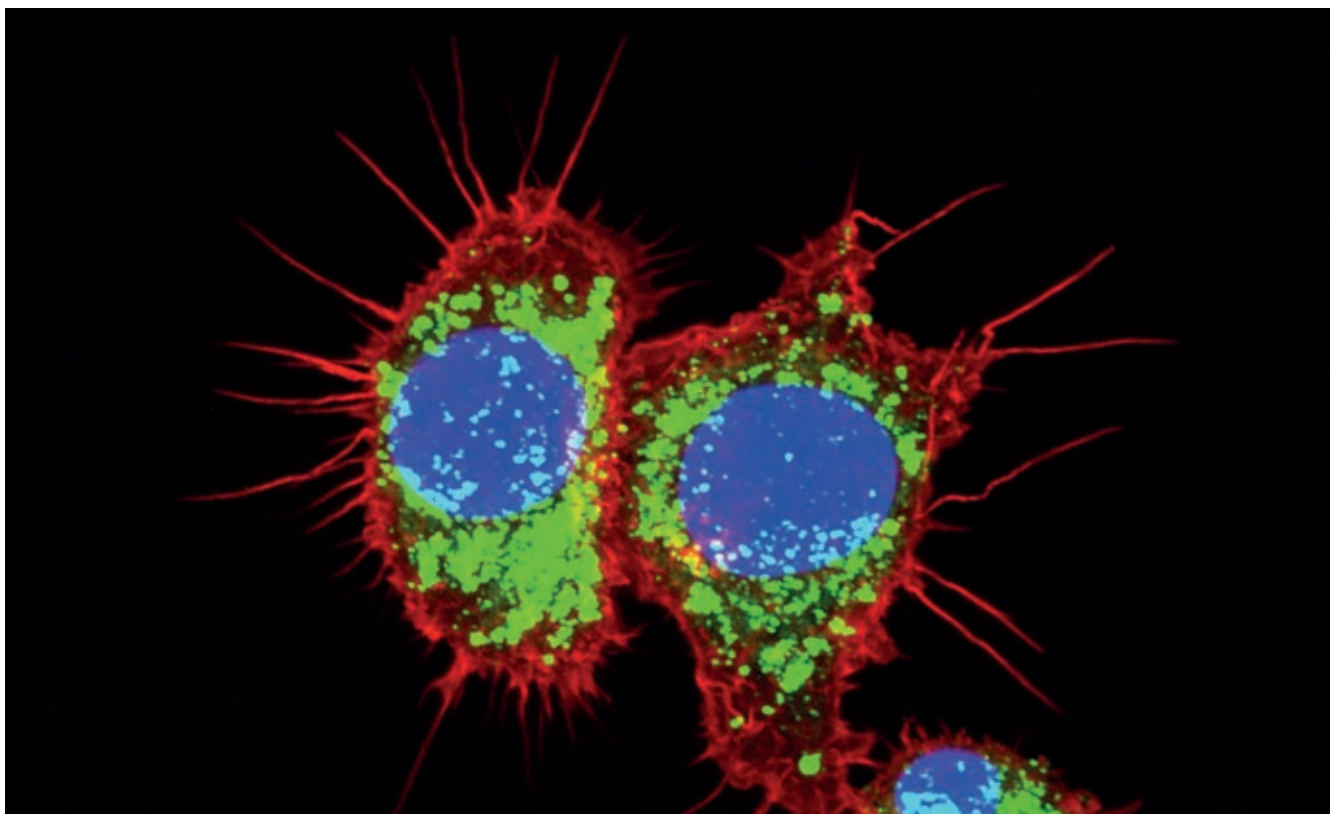
To carry out the experimental work, the research group used CLL cell cultures derived from patient samples. The researchers observed that exosomes released by CLL were internalised by stromal cells.

The molecules delivered with the exosomes were found to change the properties of the stromal cells to that of so-called cancer-associated fibroblasts.

"We saw that key signalling pathways are activated in the target cells upon uptake of exosomes", states Dr Moussay. The researchers could show that this activation led to increased production of cytokines that promote inflammation and consequently enhanced CLL cell survival. The data strongly suggest that exosomes stimulate tumour growth.

Testing the therapeutic potential

The team started to study whether targeting the interactions between exosomes and stromal cells could enforce the current therapeutic strategies. The researchers imagine to translate these discoveries into clinical treatments, able to either block the fusion of exosomes with stromal cells or to target the secretion or formation of exosomes by tumour cells.



“Our results provide a better understanding on how the tumour microenvironment is manipulated in leukaemia and reveal exosomes as a possible therapeutic target for this cancer.”

Dr Jérôme Paggetti

Publication, Collaboration & Funding

The findings were published in August 2015 in a research article (Paggetti *et al.*, 2015) in “Blood”, the most cited journal in field of haematology with an impact factor of 10.45.

The study is a collaborative work between the Laboratory of Experimental Cancer Research and the Genomics and Proteomics Research Unit at the Department of Oncology, involving also the Integrated BioBank of Luxembourg, the “Centre Hospitalier de Luxembourg” and two important internationally known cancer research centres: the “Deutsches Krebsforschungszentrum” in Heidelberg, Germany, and the Gustave Roussy Cancer Campus in Villejuif, France.

BIOCABULARY

Exosomes are small vesicles containing a complex mixture of biomolecules. They are released by cells into their immediate environment.

Chronic lymphocytic leukaemia (CLL) is a haematological malignancy that originates in the blood-forming cells of the bone marrow and spreads to other organs through the bloodstream.

Stromal cells are cells of the connective tissue, biological tissue that supports, connects or separates the organs.

MicroRNAs are small biomolecules encoded in the genome. They belong to the family of non-coding ribonucleic acids (ncRNAs), which means that they 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.

Fibroblasts are cells of the connective tissue that produce collagen and other fibres constituting the structural framework of tissues.

Cytokines are signalling molecules released by cells of the immune system. They ensure cell-to-cell communication and regulate immune responses.

A **(signalling) pathway** is a series of actions among molecules in a cell that leads to a certain cell function.

Inflammation is an immune response of the body's tissues to infection, injury or chemical irritants. A link between inflammation and cancer is known for many years.

Confocal microscopy image of CLL-derived exosomes stained in green, internalised by immune cells (macrophages). The actin cytoskeleton of the cells is shown in red and the nucleus in blue.

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TOWARDS PERSONALISED MEDICINE IN BRAIN TUMOUR THERAPY

A proteomics approach to assess the response to drug treatment

Glioblastoma is a highly aggressive brain tumour which rapidly invades brain tissues and is able to develop new blood vessels to ensure tumour cell proliferation. Due to the angiogenic trait of this tumour, anti-angiogenic drugs were recently evaluated as promising novel anti-cancer agents. Treatment efficiency remains however poor in most patients.

To better understand the response to drug treatments, a collaborative study was led at the Department of Oncology with the goal of identifying markers in the proteome that are altered by the molecule bevacizumab, a commonly administered anti-angiogenic drug.

A method to analyse complex biological samples

“We used a targeted mass spectrometry-based proteomics approach named Selected Reaction Monitoring and developed a specific optimised workflow for complex biological samples: patient-derived glioblastoma developed in the rodent brain”, tells Prof Simone Niclou, Head of the NorLux Neuro-Oncology Laboratory. The project allowed the identification and precise quantification of 32 differentially expressed proteins.

Thinking further

This is the very first targeted proteomics study in glioblastoma addressing the identification of protein markers in response to anti-angiogenic treatment. The researchers aim to further investigate the biomarker potential of selected candidates, hoping that such biomarkers may serve as a short-term readout for success or failure of anti-angiogenic therapy and could thus guide therapeutic choices.

Publication, Collaboration & Funding

This study was published as a research article (Demeure *et al.*, 2016) which appeared in August 2015 as electronic version before print in the acclaimed journal “Molecular and Cellular Proteomics” having an impact factor of 6.56.

The research project, led by the NorLux Neuro-Oncology Laboratory, involved a tight collaboration with the Genomics and Proteomics Research Unit at the Department of Oncology.

The work was funded by a CORE grant from the Luxembourg National Research Fund.

BIOCABULARY

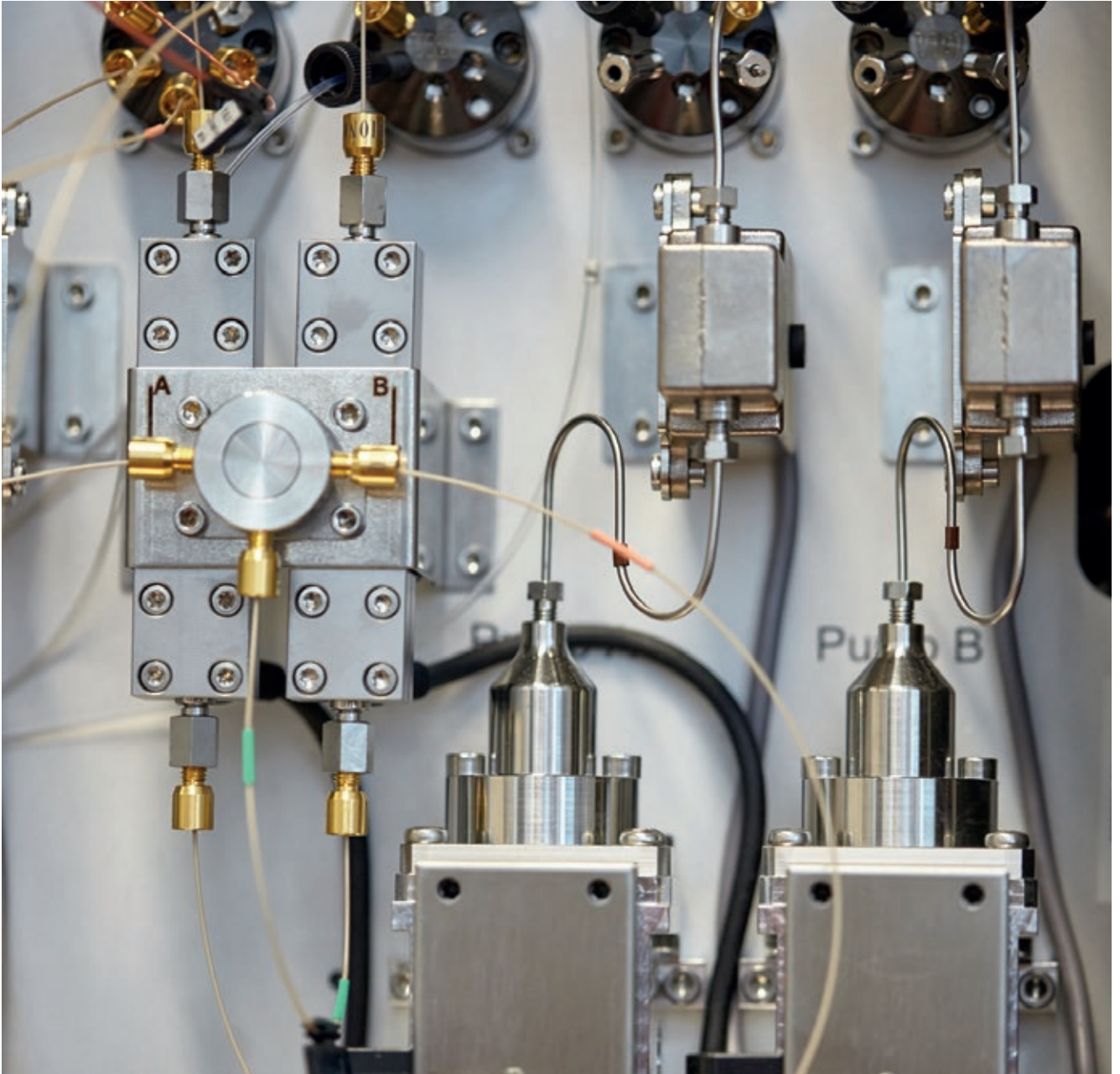
Proteomics is the large-scale study of protein production, (the proteome) in a biological sample (cell, tissue, organ, biological fluid or organism).

Angiogenesis is the physiological process through which new blood vessels are formed from pre-existing vessels.

The **proteome** is the entire set of proteins produced by an organism or biological system. Proteins are encoded in the genome and produced on the basis of the information contained in genes.

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

A **(bio)marker** 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.



“Being able to reliably identify even small protein concentration differences induced by treatment is remarkable, given the cellular complexity of brain tumour samples.”

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

BIOMARKER CANDIDATES FOR LUNG CANCER DIAGNOSIS

Research shall impact clinical practice

The Partnership of Personalised Medicine (PPM) is an initiative aiming at identifying molecular signatures of cancer that may be used to guide optimal therapy selection or early diagnostics. By developing proteomics-based approaches and integrating them with other omics data, PPM pursues the implementation of molecular diagnostics platforms with innovative biomarkers to make a direct impact on clinical practices in Luxembourg and enable personalised treatment for individual patients.

The PPM programme is divided into three parts for a bench-to-bedside approach: discovery, translation and validation. Work started on non-small-cell lung cancer (NSCLC), the most frequent form of lung cancer, but will be extended to other cancer types soon.

Potential biomarkers identified

Using a targeted proteomics approach, 95 potential tumour markers were tested in blood plasma samples from 72 early to late stage NSCLC patients in a pilot study. Seventeen proteins could be verified as potent biomarkers for early tumour diagnostics. The proteomics method, validated by this pilot study, will be applied to more than 500 biomarkers in a next step.

In addition, a NSCLC biomarker that differentiates lung cancer cell subtypes has been identified. The novelty of using this target for personalised therapy has been evaluated, and the statistical analysis is ongoing to support a patent application which is foreseen in 2016 by LIH's Research and Knowledge Transfer Office.

Besides the biomarker discovery and verification, a further prospect will be the exploration of the proteome of exosomes isolated from blood plasma and urine, with the long-term goal of developing non-invasive companion diagnostics.

Efficient teamwork

A multi-disciplinary team under the direction of Prof Rolf Bjerkvig, Head of the Department of Oncology, and coordinated by Dr Yeoun Jin Kim (Genomics and Proteomics Research Unit), conducts research for the programme. Further key players are Dr Guy Berchem (Laboratory of Experimental Cancer Research), Prof Bruno Domon (Genomics and Proteomics Research Unit), and also Prof Simone Niclou (NorLux Neuro-Oncology Laboratory).

To have access to patient samples, the team collaborates with the local hospitals, LIH's Clinical and Epidemiological Investigation Centre (Department of Population Health) and the Integrated BioBank of Luxembourg. For each patient, generated proteomic and genomic profiles as well as pathological and clinical data are internally available through a web-based data portal.



Publications & Funding

In 2015, the PPM co-workers published three articles, including the first outcome on the verification of NSCLC biomarkers which appeared in the "Journal of Proteome Research" having an impact factor of 4.25 (Kim *et al.*, 2015).

PPM is funded by the Ministry of Higher Education and Research from 2014 to 2017. It is an extension of the lung cancer programmes, which were part of the Luxembourg Life Science Initiative on personalised medicine.

BIOCABULARY

A **(bio)marker** is a biological characteristic that is objectively measured and evaluated as an indicator of normal biological or pathological processes, or of a response to a therapeutic intervention.

Proteomics is the large-scale study of protein production (the proteome) in a biological sample (cell, tissue, organ, biological fluid or organism).

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).

Bench-to-bedside is the process by which the results of research generated in the laboratory are directly used to develop new ways to treat patients.

Exosomes are small vesicles containing a complex mixture of biomolecules. They are released by cells into their immediate environment.

Molecular profiling is a method of testing that studies the genetic characteristics of a patient's tumour with the aim to develop a targeted therapy.

Genomics is the study of the genome, the genetic material of an organism.

Companion diagnostics are medical tests designed to predict if a person is likely to respond favorably to a specific treatment, or not.

HOLDING OUR BREATH FOR A NEW ASTHMA TREATMENT

Characterisation of the function of Neurturin

While investigating the immune mechanisms involved in allergic asthma, Dr Marion Mauffray, Dr Tatiana Michel and co-workers revealed an unexpected function for the protein Neurturin, a neurotrophic factor known to be involved in the development and survival of nerve cells.

Neurturin: a protective factor

In 2011, the research team reported that Neurturin, which is produced not only by neurons but also by immune cells, is involved in the bronchial inflammatory response in allergen-challenged mouse models. In the new follow-up publication, the same Neurturin-deficient mouse model was used to precisely dissect the response of type 2 T helper cells (Th2) known to orchestrate the immune response in allergic asthma.

In the absence of Neurturin and upon stimulation with allergens such as ovalbumin or allergenic extract from house dust mites, the researchers could measure an increased production and secretion of pro-inflammatory cytokines. When analysing microscopic lung tissue sections, they observed extensive thickening of bronchial walls and a stronger

infiltration of immune cells. From these findings they could conclude that Neurturin hinders the activation of Th2 cells and consequently the release of pro-inflammatory cytokines, and also prevents airway remodelling.

To test whether Neurturin provides direct protection against inflammation, the molecule was added together with ovalbumin to cultured cells. In these experiments, Neurturin appeared to have a pronounced anti-inflammatory effect as a consistently lower production of pro-inflammatory cytokines was monitored.

A potential drug target to treat allergic asthma

The findings reveal the potential of the Neurturin pathway as anti-inflammatory mechanism for asthma. The Neurturin molecule or analogues thereof may be an effective therapy to prevent the activation of T helper cells and consequently the release of pro-inflammatory cytokines. The results encourage to further investigate whether administration of Neurturin or analogues could efficiently lower asthma symptoms in humans.

“As several recent reports suggested the involvement of members of the neurotrophin family in airway inflammation, we had the idea to study Neurturin in the context of asthma.”

Dr Tatiana Michel

Publication, collaboration & funding

The work was published in February 2015 as a research article (Mauffray *et al.*, 2015) in the “Journal of Immunology” that has an impact factor of 4.92.

It involved a cooperation with the Blood Transfusion Centre-Alsace, France.

Dr Marion Mauffray was funded by an AFR PhD grant from the Luxembourg National Research Fund.

BIOCABULARY

Asthma is a chronic condition that causes inflammation and narrowing of the bronchial tubes, the passageways that allow air to enter and leave the lungs.

Neurotrophic factors are a family of proteins that support the growth, survival and differentiation of neurons.

Inflammation is an immune response of the body's tissues to infection, injury or chemical irritants.

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

Cytokines are signalling molecules released by cells of the immune system. They ensure cell-to-cell communication and regulate immune responses.

T helper cells are white blood cells that play an important role in the immune system. They promote the activity of other immune cells by releasing cytokines which activate, suppress or fine-tune immune responses. Type 1 and **type 2 T helper cells** are two cell subtypes.

Ovalbumin is the major protein from egg white, causing allergic reactions in some individuals.

A **(signalling) pathway** is a series of actions among molecules in a cell that leads to a certain cell function.

An **analogue** is a molecule having a chemical structure that only slightly differs from that of another molecule.



MULTILINGUALISM COULD PROTECT FROM DEMENTIA AND COGNITIVE COMPLAINTS

Conclusive results from the MemoVie study

The MemoVie study, initiated in 2008, reports for the first time reliable estimates on prevalence of dementia and cognitive complaints among seniors in Luxembourg and discusses the results in the national societal context.

Low dementia prevalence in Luxembourg

Using data collected from 438 seniors aged over 64 and living in Luxembourg, the researchers determined prevalence estimates of 3.8% (2.8 % to 4.8%) for dementia and 26.1% (17.8 % to 34.3%) for cognitive complaints.

These results are surprisingly low compared to other countries, as the estimated mean prevalence of dementia is 6.4% for Europe, 7.1% for Latin-America and 8% for Canada. There are only few field studies on cognitive complaints to date, but a representative Australian study reported, as an example, memory complaints for 33.5% of its participants.

The percentages determined in Luxembourg for both dementia and cognitive complaints are thus definitely lower, even if a bias or underestimation cannot be entirely excluded when analysing and comparing Luxembourg's national data.

Multilingualism protects the brain

Project leader Dr Magali Perquin and her colleagues think that the low occurrence of dementia and cognitive complaints among Luxembourg's seniors is

related to the high cognitive reserve observed in the population. "People with a high education level or those who practice several languages have a higher cognitive reserve", tells Dr Perquin. In Luxembourg, the native population is multilingual, as the country has three official languages that are taught at school from the youngest age and intensively used in daily life.

In a previous study, Dr Perquin and co-workers have already shown that multilingualism is strongly associated with protection against cognitive impairment.

A further hypothesis that rises from the study is that low occurrence of dementia may corroborate the longer life expectancy without disability observed in the country. Indeed, the indicator "healthy life years at age 65" is 2.5 years greater, on average, in Luxembourg than in several other European countries.

Investigating further

Dr Perquin will initiate a new research project in 2016, named MemoLingua, to better understand how multilingualism can delay the onset of cognitive impairment. With a novel neuroimaging approach developed in collaboration with the "Centre Hospitalier de Luxembourg" and the "Forschungszentrum Jülich" in Germany, she aims to determine the functional areas of the brain that are linked to cognitive reserve mediated by multilingualism.

"Given the findings, we believe that high cognitive reserve and consequently low levels of dementia most probably result from multilingualism."

Dr Magali Perquin

Publication, collaboration & funding

The results were published as research article (Perquin *et al.*, 2015) in the scientific open-access journal “PLOS One” in September 2015 (impact factor 3.23).

The study was conducted and coordinated by the Epidemiology and Public Health Research Unit in collaboration with the “Centre Hospitalier de Luxembourg” (Prof Nico Diederich), LIH’s Competence Centre for Methodology and Statistics and a number of other national and international partners (MemoVie group).

The work was supported by the Luxembourg National Research Fund.

BIOCABULARY

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

Prevalence is the proportion of a population found to have a certain condition.

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



GROWING ACTIVITY AND REPUTATION IN CLINICAL RESEARCH

LIH's Clinical and Epidemiological Investigation Centre 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. The centre stands for excellence in operational support in clinical research whilst striving to ensure respect of patient rights and data privacy, and offering the opportunity to access new, innovative therapeutic approaches otherwise inaccessible.

New patients and studies

In 2015, the centre ensured more than 1000 patient visits for clinical trials. Of these, 473 patients were newly enrolled. Eighteen new clinical studies were initiated. These include investigator-driven studies conducted with hospitals and universities, and trials developed by international pharmaceutical companies. Three of the studies were carried out in the framework of the European Clinical Research Infrastructure Network ECRIN (www.ecriin.org), a not-for-profit intergovernmental organisation that supports the conduct of multinational clinical trials in Europe.

Become involved in more therapeutic areas

The clinical research team, led by Dr Anna Chioti and Dr Manon Gantenbein, was mainly involved in clinical trials in oncology, but also in the fields of pulmonology, cardiology and infectious diseases like hepatitis C. It is also giving support in epidemiological studies such as ORISCAV-LUX 2 (see next page). With the management of the recruitment and examination of healthy control subjects for the National Centre of Excellence in Research on Parkinson's Disease (see page 52), the centre is now extending its activities to neurodegenerative disorders.

Furthermore, end of 2015, the Clinical and Epidemiological Investigation Centre was designated as Lead Clinical Trial Unit for a project named DMD-Vision, financed by Horizon 2020, the European framework programme for Research and Innovation. A new treatment for Duchenne muscular dystrophy will be tested in 14 countries, with three to four patients at each of the 30 planned trial sites. This project allows LIH to develop expertise in trials on rare diseases and to widen its reputation in clinical research at the European level.

BIOCABULARY

Clinical research is a branch of healthcare science that determines the safety and efficacy of medications, devices, diagnostic products and treatment regimens intended for human use by conducting research studies named clinical trials.

Parkinson's disease is a progressive disorder of the nervous system that affects movement.

Duchenne muscular dystrophy is a genetic disorder starting in childhood and characterised by progressive muscle degeneration.





ORISCAV-LUX 2: CARDIOVASCULAR HEALTH IN LUXEMBOURG

In December 2015, the Epidemiology and Public Health Research Unit launched the second wave of the ORISCAV-LUX study (“Observation des Risques et de la Santé Cardiovasculaire au Luxembourg”). Its goals: assess the cardiovascular health of Luxembourg’s resident population and identify the potentially modifiable and non-classical risk factors to suggest efficient preventive health measures.

Cardiovascular risk factors

Cardiovascular disease is the primary cause of death worldwide. Myocardial infarction or stroke were accounting for 33% of deaths in Luxembourg in 2014. Yet, 80% of these deaths could most probably be prevented.

Gender, age, ethnicity and family medical history are non-modifiable factors. However, factors related to the environment and lifestyle such as smoking, dietary habits or physical inactivity can potentially be modified by a more conscious and healthy lifestyle. A better health prevention can have a major impact on reducing the social and economic burden of cardiovascular diseases.

Results from the first wave of the study

The first wave of the ORISCAV-LUX survey was conducted from 2007 to 2008 by recruiting a representative sample of more than 1,400 people from the resident population, aged between 18 and 69 years.

This first wave revealed that a number of pathological disorders affecting cardiovascular health such as diabetes, hypertension and lipid disorders are currently not diagnosed or treated. In addition, an important number of treated cases remains uncontrolled. For instance, over 60% of study participants suffering from high blood pressure were not aware of their condition.

Aiming for 1,000 participants

For the follow-up study ORISCAV-LUX 2, led by principal investigator Dr Ala’a Alkerwi, the same participants will be invited to take part to compare and monitor developments in cardiovascular health over time.

Recruitment started in December 2015, following a small-scale feasibility study, and will be conducted until March 2017. Approximately 1,000 subjects are expected to participate in the study which consists in lifestyle questionnaires as well as clinical tests on physical, cardiac and cognitive function.

The project represents a unique opportunity to collect reliable public health data and increase health awareness among the national population. In addition, this national databank constitutes a valuable research tool for scientists to address relevant questions about cardiovascular and metabolic risk.

More information on the study can be found on the ORISCAV-LUX website: **www.oriscav.lih.lu**.

Collaboration & funding

ORISCAV-LUX 2 is a collaborative work involving, next to the Epidemiology and Public Health Research Unit, also the Clinical and Epidemiological Investigation Centre and the Integrated BioBank of Luxembourg at LIH. External partners are the “Centre Hospitalier de Luxembourg”, University of Liège, “Ligue Médico-Sociale”, “Laboratoires Ketterthill” and BioLogistic SAS.

The project is supported by the Ministry of Higher Education and Research.



INVEST IN NEW TALENTS & INFRASTRUCTURE

Investing in human
talents and state-of-
the-art infrastructure



CREATION OF A NATIONAL CYTOMETRY PLATFORM

In 2015, following an internal reorganisation, a National Cytometry Platform has been created within the Department of Infection and Immunity. This platform, unique in Luxembourg's research landscape, will benefit from the long-term expertise in flow cytometry present at LIH. It provides services to the institute's researchers and aims to contribute to research projects in the context of national and international collaborations in the future.

New Head of National Cytometry Platform

On 1st August 2015, Dr Coralie Guérin was appointed Head of the National Cytometry Platform, as successor of the long-term former Head René Brons. Dr Guérin has over ten years of experience with flow cytometry and previously led a cytometry core facility at the Cardiovascular Research Centre in Paris, France.

Key missions

The main role of the platform is to advise and assist researchers in addressing their biological questions. It can give support in defining the experimental set-up, performing the experiment, analysing data and interpreting results. Dr Guérin and her team are able to respond to very specific demands, such as the isolation of certain cell subpopulations.

An important mission of the platform is also to provide individual training and course sessions about the principles of cytometry and the use of the equipment. In 2015, the facility hosted two major events open to Luxembourg's scientific community: the Flow Cytometry User Meeting on 7th May and the Flow Cytometry Course Day on 9th October, both organised in cooperation with flow cytometer manufacturers.

Cutting edge equipment

To extend the equipment composed of two flow cytometers for cell analysis and two for cell sorting, a CyTOF®2 mass cytometry instrument was acquired and put in place beginning of 2015. It is a pioneering time-of-flight mass cytometer allowing multi-parameter proteomics analysis of single cells. The instrument has a large number of detection channels and can resolve over 30 probes simultaneously. It should uniquely position LIH to advance the understanding of major biological questions in the field of infection, immunity and cancer.

BIOCABULARY

Cytometry is a technology to measure the characteristics of cells, including cell size, count, morphology and presence of specific surface molecules. **Flow** and **mass cytometry** are two cytometry techniques.



“Cytometry is a powerful transversal technique that has become an integral part in nearly all domains of cell biology research. Its applications are very diverse and the technique itself is in continuous evolution. I think that the platform will offer great opportunities to develop new big projects.”

Dr Coralie Guérin
Head of the National Cytometry Platform

STATE-OF-THE-ART ANIMAL FACILITIES

Animal experimentation provides essential information to understand disease mechanisms which are otherwise impossible to unravel and allows to perform pre-clinical studies on the effect of drug treatments.

In 2015, a brand-new facility of 400 m² for experimentation with rodents was installed, including specific pathogen-free work spaces as well as Biosafety Level 2 and 3 rooms for experiments involving pathogens. Thanks to these modern facilities, innovative research projects involving mice, rats and zebrafish as biological models are being conducted at LIH according to strict ethical and regulatory principles, giving the utmost importance to animal welfare.

An *in vivo* imaging platform for rodents complements these facilities including, amongst other new equipment, a Magnetic Resonance Imaging instrument which provides 2D and 3D anatomical and physiological tomographic images of rodent brain and whole body. This technology, which has applications in oncology, neurology and cardiovascular diseases, is the first animal scanner in Luxembourg and allows researchers to perform detailed real-time imaging. In addition, multimodal molecular imaging can be performed with the Positron Emission Tomography technology.

Over the past years, clinically relevant animal models that represent human pathology have been developed at LIH, including rodents engrafted with human tissue. These animal models allow the detailed study of the biology of cancer, inflammation and infectious diseases, the investigation of immune mechanisms as well as the identification of biomarkers and drug targets and are instrumental in the application-oriented research projects conducted at LIH.



BIOCABULARY

Biosafety is the maintenance of safe conditions in biological research to prevent harm to workers or the environment.

A **pathogen** (or infectious agent) is a biological agent that causes disease or illness to its host.

In vivo means in the living organism.

In vitro means outside the living organism and in an artificial environment (e.g. a test tube or culture dish).

The three Rs

LIH applies the principles of the three Rs for animal experimentation: Replacement, Reduction and Refinement. This means that *in vivo* experiments are only used to confirm a scientific hypothesis which was previously been tested *in vitro*, for example in cell culture. A fourth R standing for the word “Respect” can be added, as the personal trained in animal experimentation is made aware on the importance of respecting the animals as living beings which can experience stress, pain and fear.

All operational aspects for the maintenance and experimentation on small laboratory animals follow national and European regulations (EU Directive 2010/63/EU). LIH also has an internal code of ethics on animal testing and an Animal Welfare Structure evaluating all experimental protocols in accordance with the code and the law.

Dr Olivier Keunen
Head of the *in vivo* Imaging Platform

ECO-IMMUNOLOGY AND MICROBIOME: EXPLORING INTERACTIONS IN THE GUT

Dr Mahesh Desai, started his work at LIH on 1st October 2015 as a junior group leader, to establish the research group “Eco-Immunology and Microbiome” which will develop a new line of research at the institute on the human gut microbiome.

The gut microbiome has emerged as a broadly important and rapidly moving area of research, owing to important roles of the microbiota in health and disease. Dr Desai’s research mainly focuses on the connection of dietary fibre to intestinal diseases. “Although diet is a major driver of the microbiota physiology, the gut microbiota-mediated mechanisms that link diet to intestinal disorders and enteric infections are poorly understood”, he explains.

The work of the research group is focused on discerning these mechanisms and underlying eco-immunological processes which are arising from the interactions between the intestinal mucosal barrier and the gut microbiota. Since the modern diet of developed nations includes significantly reduced dietary fibre, the group seeks to understand how a fibre-deprived gut microbiota affects our health.

To mechanistically connect gut bacterial metabolism to disease, a multi-disciplinary approach is essential. The institute offers the possibility to liaise these studies on the gut microbiome with several other research domains such as allergy, inflammation, gastrointestinal infections, oncology and cardiovascular diseases, that have been recently linked to the gut microbiome.

“One of LIH’s strengths is the amalgamation of basic, pre-clinical and clinical research in biomedicine.”

Dr Mahesh Desai



Portrait: Dr Mahesh Desai, junior group leader

Dr Desai, originally from India, completed a PhD in Intestinal Microbiology at the Max Planck Institute for Terrestrial Microbiology in Marburg, Germany, and later worked as a postdoctoral researcher at the University of Göttingen, Germany, the University of Michigan Medical School, United States, and the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg. Shortly after starting in his new position, Dr Desai already obtained major third-party funding, with a CORE grant proposal having been accepted by the Luxembourg National Research Fund.

BIOCABULARY

Eco-Immunology is a recently emerged sub-discipline combining aspects of immunology with evolutionary and behavioural ecology.

The **microbiome** comprises all of the genetic material within a microbiota.

Microbiota is the entire collection of microorganisms in a specific niche, such as the gut.

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.

IMMUNE SYSTEMS BIOLOGY: MODELLING COMPLEX BIOLOGICAL SYSTEMS

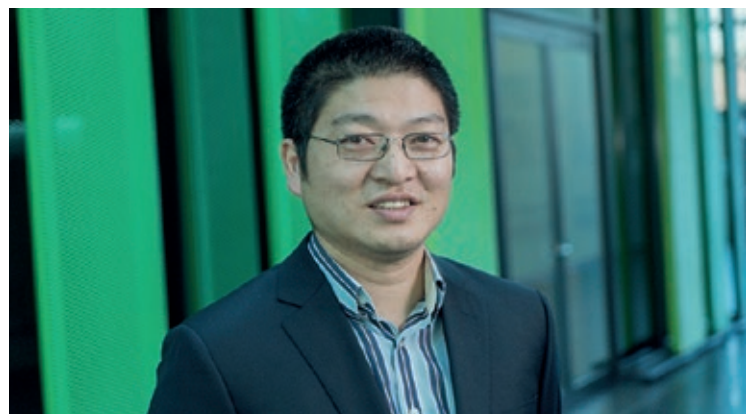
On 15th March 2015, Dr Feng He joined LIH to set up a new research group focussing on systems biology in the context of the human immune system. The group “Immune Systems Biology”, a team of six people, focuses on unravelling how the dynamic molecular networks of immune cells quantitatively respond to various genetic perturbations or mutations as well as to environmental factors. These factors include, amongst others, stresses under physiological or pathological conditions.

To this end, the research group develops and applies integrated computational and experimental systems biology strategies to predict and delineate the dynamic molecular networks of immune cells. With expertise in network inference and analysis, in contrast to the classical hypothesis-driven approaches, the team orchestrates major efforts on network-biology-guided experiments to accelerate biomedical discoveries. Currently, the research group focuses on unravelling the molecular networks of T lymphocytes, including regulatory and effector T cells.

The team closely collaborates with the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg, where researchers can get support from the theoretical computational experts and have access to IT infrastructure.

“The reasons for me to join LIH are its clinically orientated strategy, in line with my motivation to straightforwardly translate biomedical findings into a benefit for the patients, and its strong competences in basic and translational immunology.”

Dr Feng He



Portrait: Dr Feng He, junior group leader

The Chinese-born junior group leader holds a PhD from the Technical University of Braunschweig, Germany, and previously worked as postdoctoral researcher at the Helmholtz Centre for Infection Research in Braunschweig and as a research associate at the Luxembourg Centre for Systems Biomedicine. Since his arrival at LIH, Dr He has already received several competitive grants: an AFR PhD funding and a CORE grant from the Luxembourg National Research Fund as well as a Pump Prime Fund from the Personalised Medicine Consortium.

BIOCABULARY

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

T cells, also called **T lymphocytes**, are white blood cells that play a central role in the immune system. **Regulatory** and **effector T cells** are T cell subtypes.

EXPERIMENTAL AND MOLECULAR IMMUNOLOGY: TARGETING DISEASE

On 1st March 2015, a new research group named “Experimental and Molecular Immunology” was created by Prof Dirk Brenner, T cell and signalling specialist. The group will investigate the function of T cells in inflammatory diseases and hematopoietic malignancies. Prof Brenner has developed several mice models that can be used to identify factors altering the T cell response. The long-term goal of this research is to interfere with different disease pathways and pave the way for new immunotherapies targeting relevant human diseases.

The creation of this new research unit was made possible thanks to the allocation of a five-year term ATTRACT Consolidator grant from the Luxembourg National Research Fund of 2.14 million Euro, including funding for five positions.

The ATTRACT programme is designed for researchers who are not yet established in Luxembourg and offers the opportunity to set up an independent research team within a host institution. “This programme is a unique and attractive opportunity for young researchers who wish to proceed an academic career and develop their own research thematic”, stresses Prof Brenner. “What I particularly like about the programme is that it gives you a well-defined and well-funded framework to implement an internationally recognised research group within a department.”

Portrait: Prof Dirk Brenner, group leader

Prof Brenner carried out his PhD at the “Deutsches Krebsforschungszentrum” in Heidelberg, Germany, in the laboratory of Prof Peter H. Krammer, widely known for his important work on apoptosis. He then worked for six years as a postdoctoral fellow at the Campbell Family Cancer Research Institute in Toronto, Canada, in the group of Prof Tak W. Mak, highly recognised for his multiple ground-breaking discoveries in the fields of immunology and cancer research. Up to now, Prof Brenner already published more than 35 highly ranked articles in international journals and has acquired a considerable number of scientific awards.

BIOCABULARY

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

Hematopoietic malignancies are the types of cancer affecting blood, bone marrow and lymph nodes.

A **(signalling) pathway** is a series of actions among molecules in a cell that leads to a certain cell function.

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

Apoptosis is a mechanism of programmed cell death. It is a highly regulated and controlled process essential for an organism’s lifecycle.

“You clearly feel that things are moving forward at LIH. It is the perfect place to launch new challenging research projects and foster novel collaborations. I hope that my projects will contribute to enhancing the international recognition of the institute.”

Prof Dirk Brenner



ON THE WAY TO EXCELLENCE IN CANCER RESEARCH



In 2015, the Department of Oncology, headed by Prof Rolf Bjerkvig, underwent significant structural changes with the purpose to achieve further excellence in cancer research that will have an impact on reducing the cancer burden within the Luxembourg population and beyond, and drive the concept of personalised medicine forward.

Research activities focus on the cellular and molecular mechanisms of tumour progression by employing a wide range of state-of-the-art technologies including *in vitro* and *in vivo* imaging modalities that use specific animal models for cancer research.

In the period from April to June 2015, the department was reorganised by a merger of specific research groups into stronger research units. This included the incorporation of the technological platform “Luxembourg Clinical Proteomics Centre” into the department. Expertise in omics analysis is presently grouped within a single unit, the Genomics and Proteomics Research Unit.

“With the new department structure, excellence can be developed within basic, translational and clinical cancer research.”

Prof Rolf Bjerkvig
Director of the Department of Oncology

These platforms are working in close collaboration with the NorLux Neuro-Oncology Laboratory, partnering with a laboratory of the same name in Norway, and the Laboratory of Experimental Cancer Research.

The reorganisation allows to have a critical mass of researchers within prioritised research areas in which international competitiveness can be achieved. It is also in line with the research strategy of the National Cancer Plan (see page 54).

BIOCABULARY

In vivo means in the living organism.

In vitro means outside the living body and in an artificial environment (e.g. in a test tube or culture dish).

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).

OUTSTANDING PHD THESES: THE NEXT GENERATION OF PROMISING TALENTS

*PhD candidates are the next generation of leading researchers and managers.
In 2015, ten doctoral candidates at LIH successfully defended their PhD thesis.
Zoom on three of them...*

Department of Population Health > Sports Medicine Research Laboratory

Dr Robert Mann



Luxembourger



School for Nutrition, Toxicology and Metabolism at the University of Maastricht, the Netherlands



Supervisors: Prof Daniel Theisen (LIH), Dr Laurent Malisoux (LIH), Prof Matthijs Hesselink (Maastricht), Dr Meijer Kenneth (Maastricht)



PhD defence on 6th July 2015



“A new approach to running style analysis using a pressure-sensitive insole device: a small step towards injury prevention”



AFR PhD grant, Luxembourg National Research Fund



Five publications, of which four as first author in high-ranking sports medicine journals



Presentations at the annual European College of Sport Science Conference and at the International Olympic Committee World Conference on Prevention of Injury and Illness in Sport

Major achievements during the PhD

- Validation of a pressure-sensitive insole device designed to measure spatio-temporal parameters during running
- Commercialisation of the device by a company created in 2014 and currently developing the next prototype
- Submission of developed algorithms to the Benelux Office for Intellectual Property for an i-Depot (legal means of proof issuing a date stamp for an idea or creation)
- Other: National Badminton Champion

Robert Mann

PhD defence at the University of Maastricht



Dr Marion Mauffray



French



Doctoral School of Life and Health Sciences at the University of Strasbourg, France



Supervisors: Dr Tatiana Michel (LIH), Dr Daniel Hanau (Strasbourg)



PhD defence on 23rd November 2015



“Influence of the neurotrophic factor Neurturin in nerve and immune cells during airway inflammation”



AFR PhD grant, Luxembourg National Research Fund



One publication as first author, one a co-author



Oral presentation at the Allergy and Asthma 2013 congress in Bruges, Belgium, six poster presentations



Major achievement during the PhD

Detailed characterisation of the function of Neurturin in asthma and revelation of its therapeutic potential (see page 24)

Marion Mauffray

PhD defence at the University of Strasbourg

Dr Yue Zheng



Chinese



Doctoral School of Life and Health Sciences at the University of Strasbourg, France



Supervisors: Dr André Steinmetz (LIH), Dr Carole Devaux (LIH)



PhD defence on 3rd December 2015



“Purified compounds derived from *Cassia abbreviata* (tropical tree) inhibit Human Immunodeficiency Virus 1 (HIV-1) entry”



AFR PhD grant, Luxembourg National Research Fund



One publication as first author, one a co-author, two under revision



Poster presentations at the European Meeting on HIV & Hepatitis, the International Conference on Antiviral Research and at the Annual International Conference on the Science of Botanicals

Major achievement during the PhD

Identification of *Cassia abbreviata* as an African plant with a broad spectrum of antiviral activities having the potential to deliver new drug candidates against HIV



Yue Zheng

PhD defence at the University of Strasbourg

A NEW VISION FOR THE DEPARTMENT OF POPULATION HEALTH

In April 2015, Prof Saverio Stranges has been appointed Scientific Director of the Department of Population Health. He coordinates the department together with Dr Anna Chioti who acts as Operational Director. Within a few months, he has developed a new research strategy that should increase the recognition of Luxembourg as a research hub for epidemiology and public health and have a true impact on the population's health culture.

Taking advantage of a dynamic research landscape

The Department of Population Health has stayed for several years without scientific leadership. Accepting the position as new Director of Department thus represents a great challenge. Prof Stranges now has the essential task of defining priority research areas, uniting the department and promoting the cooperation between the different research units. He also has the ambition to develop the department, which does not have many PhD candidates at present, into a training centre for young researchers in epidemiology and public health.

When being asked about his reasons to come to Luxembourg, Prof Stranges' answer comes promptly: "I was looking for further professional development at a senior management level. I also wanted to come back from the United Kingdom to Continental Europe. When informing myself about research focuses and funding opportunities in Luxembourg, I discovered a dynamic and rapidly developing research landscape. It was very appealing to me to take a new role in this country which offers wider opportunities for new research projects and collaborations than the much more rigid British research system."

Five years to get recognition

Prof Stranges expects that within five years' time the Department of Population Health, by fostering collaborations and joining international partnerships, will be more widely known within the international scientific community. He also hopes that the future research outcomes will have a socio-economic impact and truly affect health behaviours and life styles.

Communication to the public at large is another important concern for the scientific director. "Public health topics are attractive subjects to communicate", he stresses. "Communication is indispensable to create health awareness. Therefore, the department will become more proactive in promoting scientific culture and research results."

Portrait: Prof Saverio Stranges, Scientific Director of the Department of Population Health, and Head of the Epidemiology and Public Health Research Unit

Prof Saverio Stranges, originally from Italy, previously worked at the University of Warwick Medical School (United Kingdom) as an Associate Professor of Cardiovascular Epidemiology for nearly nine years and at the State University of New York at Buffalo (United States) for over four years, before joining LIH. He has a medical background and is an expert in public health, preventive medicine and chronic disease epidemiology.

Throughout his career, Prof Stranges has been involved in a range of international epidemiological projects, clinical trials, secondary data analyses and systematic review work. He has published extensively in the area of chronic disease epidemiology, with over 130 publications consisting of scientific articles, reviews and book chapters.



“My vision is to switch from the traditional disease-focused research approach to a more global approach centred on general health and well-being as well as on healthy ageing. The Department of Population Health has the required multidisciplinary expertise to implement this vision.”

Prof Saverio Stranges

*Scientific Director of the Department of Population Health,
and Head of the Epidemiology and Public Health Research Unit*

HEALTH ECONOMICS AND EVIDENCE SYNTHESIS: OPTIMISING HEALTHCARE

Since July 2015, the newly created Health Economics and Evidence Synthesis Research Unit, aims at developing and promoting the application of state-of-the-art economic methods to improve health and healthcare in Luxembourg. The unit will provide research expertise to support Luxembourg's health sector developments and shall advise the Government in assessing new health technologies, fill evidence gaps regarding major health issues and help to render the national healthcare system more cost-effective.

Prof Ngianga-Bakwin Kandala, Head of this new research unit, works in close collaboration with Prof Andrea Manca from the Centre for Health Economics of the University of York, United Kingdom, and Prof Maarten IJzerman from the University of Twente, the Netherlands. He aims to build his team at LIH with the recruitment of two postdoctoral researchers, and further recruitments will follow in the coming years.

Portrait: *Prof Ngianga-Bakwin Kandala,
Head of the Health Economics
and Evidence Synthesis*


Prof Kandala, originally from DR Congo, previously worked as an Associate Professor in Health Technology Assessment at the Universities of Oxford and Warwick, United Kingdom. Next to his research activities, he was appointed as full professor at Northumbria University, Newcastle Upon-Tyne, United Kingdom, in September 2015. He holds further strong links with the Northumbria University through a collaboration aiming at building capacity in biostatistics in developing countries. The research programme DELTAS - Developing Excellence in Leadership, Training and Science, he is one of the principal investigators of, is supported by a 5-year grant from the Wellcome Trust (2016-2021).



“Together we will take up the challenge of developing a solid research programme in health economics in Luxembourg with a focus on personalised medicine.”

*Prof Ngianga-Bakwin Kandala
Head of the Health Economics
and Evidence Synthesis*





FOSTER KNOWLEDGE SHARING

Being instrumental in
breaking down barriers
to knowledge sharing,
enhancing scientific debate
and exchange of ideas

SPORT-SANTÉ: FIGHT DISEASE WITH SPORT



Numerous studies have demonstrated the positive impact of regular exercise in the treatment of a range of diseases: cancer, depression, neurological disorders, heart and lung diseases, metabolic diseases as well as muscle, bone and joint diseases.

Since 2013, “Œuvre Nationale de Secours Grande-Duchesse Charlotte” shows its interest in this important topic and accordingly assigned the Sports Medicine Research Laboratory and postdoctoral researcher Dr Alexis Lion the mission to develop and carry out a project called “Sport-Santé” with its support. It was launched on 22nd April 2015 during a press conference, in the presence of the Minister of Sports.

Developing the offer of therapeutic courses

A preliminary study, conducted in the first half of 2014, allowed to assess the offer of existing initiatives and the patients’ needs with regard to the practice of therapeutic physical exercise. The main findings were that the therapeutic groups were under-attended at that time point and some were affected by a lack of resources and structural functioning. In addition, some sectors were not represented or appeared to be under-developed in Luxembourg.

The project “Sport-Santé” therefore has three main objectives: to rise the number of participants in existing groups offering therapeutic physical exercise, to increase the offer of therapeutic sports, and to durably maintain this offer.

Raising national awareness

The objectives are pursued through a national awareness campaign (website, flyers, information conferences, presence at sports and health events), advocacy and logistical support for the existing therapeutic groups and support for the further development of the offer on the national territory.

Showcase of the project is the website **www.sport-sante.lu** available in French, German and English, created to provide complete, detailed and objective scientific information on the recommended physical activities, for different types of disease. Moreover, it provides patients with a practical guide to finding therapeutic exercise groups suited to their needs, listing the organiser, the activities practiced as well as the locations and dates of all registered courses in Luxembourg.

The success of the project “Sport-Santé” depends on the involvement of all stakeholders: patients, trainers, health professionals and public authorities. This mobilisation must be supported over time in order to both develop innovative practical solutions and render the project sustainable.



Press conference for the launch of the project “Sport-Santé” and its website www.sport-sante.lu. From left to right: Dr Alexis Lion (project leader, Sports Medicine Research Laboratory), Prof Daniel Theisen (Head of the Sports Medicine Research Laboratory), Dr Jean-Claude Schmit (CEO of LIH until 31st December 2015), Romain Schneider (Minister of Sports) and Pierre Bley (President of “Œuvre Nationale de Secours Grande-Duchesse Charlotte”).

“The project aims at supporting the promotion in Luxembourg of physical activity as a therapeutic adjuvant and a means for health protection after an illness or an accident.”

Dr Alexis Lion

RETRACE REPORT ON INJURIES AND ACCIDENTS: INFORM TO PREVENT



Accidents and intentional injuries are one of the major causes of death, hospital admissions and disabilities in the country. The Ministry of Health, in the framework of the European Injury Data Base network and in collaboration with LIH's Department of Population Health has committed itself to an injury prevention policy. At the national level, the programme is called RETRACE, standing for "Recueil de données sur les TRAumatismes et ACCidents au Luxembourg". Dr Dritan Bejko, epidemiologist, is in charge of the RETRACE project at LIH.

Extensive data collection

In accordance with the common European Injury Data Base methodology, the national injury monitoring system RETRACE collects a detailed set of information on causes, circumstances and objects involved in the process producing injury, from one of the local hospitals: the "Centre Hospitalier de Luxembourg". This detailed level of information called Full Data Set is highly useful for conceiving injury prevention measures.

At the other hospitals of the country ("Centre Hospitalier Emile Mayrisch", "Centre Hospitalier du Nord" and "Hôpitaux Robert Schuman"), a less detailed level of information called the Minimum Data Set is collected. The information from all hospitals is combined to estimate the burden of injuries in terms of morbidity by prevention domain, age, gender, mechanism of injury, etc.

Injuries: 4th cause of death in Luxembourg

In May 2015, the first RETRACE report co-authored by the Ministry of Health and LIH was published, presenting the national statistics on accidents and injuries from 2013 and comparing them at the international level.

The report reveals that, on average, 261 people die from a traumatic event each year in Luxembourg, which makes injuries the fourth cause of death in the country. In 2013, more than 60,000 cases of injury were registered at the emergency departments of Luxembourg's hospitals. This represents 170 visits per day and concerns one out of ten residents. On average, 7% of those patients had to be hospitalised. The annual costs for hospitalisation are currently estimated to 50 million Euro.

Data collected from the injury surveillance system will be analysed on a yearly basis to provide information on the burden of injuries and select population groups which are at higher risk. Effectiveness of prevention actions targeting the groups at risk will also be evaluated using injury data of the following years.

"A large number of injuries could be avoided by effective and appropriate prevention measures, but for this, information on the causes and circumstances must be collected and analysed."

Dr Dritan Bejko

SUPPORT AND TRAINING IN METHODOLOGY AND STATISTICS

The Competence Centre for Methodology and Statistics, headed by Prof Stephen Senn, provides methodological support in statistical planning of clinical, epidemiological and laboratory studies as well as in data analysis and handling. It is engaged in training activities and also proposes support in writing publications.

Internal support and external consultancy

An important objective in 2015 was to provide LIH's departments with a full support in methodology and statistical analysis. Major proposals for national third-party funding were all discussed with researchers regarding project design and planning. Since the beginning of the year, an internal "statistics clinic" has been held once a week for which researchers can request appointments to ask questions about the methodology of their projects.

Furthermore, the team offers consulting services for the pharmaceutical industry in Europe and the United States, attends Data Safety Monitoring Boards worldwide for randomised clinical trials, and engages in collaborative research with external partners, for instance with the World Health Organisation and foreign universities.

Training in Luxembourg and beyond borders

In 2015, the centre has been energetically involved in giving courses and lectures. Three courses were given in the framework of LIH's annual Training & Workshops series of which most courses are open as well to external Luxembourg-based researchers. Prof Senn gave a workshop on the use of a statistical software and two general two-day statistics courses for participants with a basic or intermediate level.

Training courses were also held just beyond the country's borders in Thionville and Metz (France), further away in Verdun (France), Basle (Switzerland), Edinburgh (Scotland), London (Great Britain) and Siena (Italy), and as far away as in Dakar (Senegal) and Libreville (Gabon). In addition, a dozen invited lectures were given in locations ranging from Beijing in China to New York in the United States, also including several European locations.

*Prof Stephen Senn
Head of the Competence Centre
for Methodology and Statistics*





A woman and a man in a laboratory setting, with a red overlay and vertical bars.

ENGAGE IN COLLABORATIONS

Building links
between scientists
at an international
level

LIH TAKES PART IN THE NATIONAL CENTRE OF EXCELLENCE IN RESEARCH ON PARKINSON'S DISEASE

On 11th April 2015, at the occasion of the World Parkinson Day, a new funding programme of the Luxembourg National Research Fund was launched: the National Centre of Excellence in Research on Parkinson's Disease, shortly NCER-PD. The aim of the programme, which involves all national actors in biomedical research, is to identify new methods for the early diagnosis of Parkinson's disease, the second most common neurodegenerative disease of the brain, and for the stratification of patients in sub-groups.

LIH's involvement

LIH is part of this long-term clinical Parkinson's disease study. More specifically, the Clinical and Epidemiological Investigation Centre is in charge of recruiting the healthy control subjects to allow a comparison of their results from clinical tests and specific laboratory measurements with those of Parkinson patients. In the coming years, 800 healthy controls are to be recruited for the study from Luxembourg and the Greater Region, a major undertaking!

The Competence Centre for Methodology and Statistics is also involved in the project and will be doing statistical design and analysis. A further internal collaborator is the Integrated BioBank of Luxembourg (IBBL). In spring 2015, IBBL started collecting biospecimens and clinical data for the programme, generating almost 10,000 aliquots of

blood, urine, saliva and their components from just over 200 patients and healthy donors.

NCER-PD: a multi-partner consortium

Dr Marc Schiltz, Secretary General of the Luxembourg National Research Fund explains the motivation behind the new funding initiative NCER: "We want to support high quality research with impact and the cooperation of national research actors. Through the creation of a common research programme in a domain that is strategically important for Luxembourg, we can unite existing competencies to work efficiently on a relevant socio-economic problem."

The NCER-PD consortium, coordinated by Prof Rudi Balling, Director of the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg, has been allocated eight million Euro for a first phase of four years. The total budget estimated for the eight-year programme amounts to 20 million Euro.

Within the consortium, the national actors are the Luxembourg Centre for Systems Biomedicine, the "Centre Hospitalier de Luxembourg" and LIH. International partners are the Oxford Parkinson's Disease Centre, the "Hertie-Institut für klinische Hirnforschung" in Tübingen, Germany, the "Paracelsus-Elena-Klinik" in Kassel, Germany, and the National Institutes of Health in the United States.



Press conference to launch NCER-PD National Centre of Excellence in Research on Parkinson's Disease. From left to right: Prof Ludwig Neyses (University of Luxembourg), Prof Nico Diederich ("Centre Hospitalier de Luxembourg"/Luxembourg Centre for Systems Biomedicine), Dr Romain Nati ("Centre Hospitalier de Luxembourg"), Dr Marc Schiltz (Luxembourg National Research Fund), Prof Rudi Balling (Luxembourg Centre for Systems Biomedicine), Prof Rejko Krüger ("Centre Hospitalier de Luxembourg"/Luxembourg Centre for Systems Biomedicine), Dr Jean-Claude Schmit (LIH), Dr Nikolai Goncharenko (IBBL).

INTERVIEW WITH DANY, THE 100TH HEALTHY CONTROL SUBJECT FOR NCER-PD AT LIH

Dany, 58 years, Luxembourger

How did you hear about the Parkinson study, and what motivated you in participating?

I read about it on the Facebook page of **www.science.lu**. I always read the posted articles because I find them really interesting. That's where I got to know about the study.

What motivated me? I've somehow always been interested in medicine, and seeing that such a study is taking place in Luxembourg caught my attention. It has never been done before, and it is really something important. I could get sick from Parkinson tomorrow, and I know some people who have been living with the disease for years. I can see it's very difficult not to have control on yourself anymore. I guess you must feel a bit trapped in your own body.

I already volunteered for Omega 90 and "Médecins du Monde", I just find it natural to help. So if I can contribute in any way to help researchers in understanding what happens and finding new treatments for Parkinson, I'm more than happy to do so!

How was your day here?

Very good! People are very nice, and I could ask a couple of questions to the doctor who came for the examination, so I even got to learn a few new things!

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

It doesn't hurt (laughs)! Don't be afraid! We can't stand waiting and not doing anything - you've got to do something too!

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

Go on and ... find something! The job you do is really important, even if you don't always get the recognition you owe. So don't stop and don't drop the ball. What you're doing is great and we're counting on you!

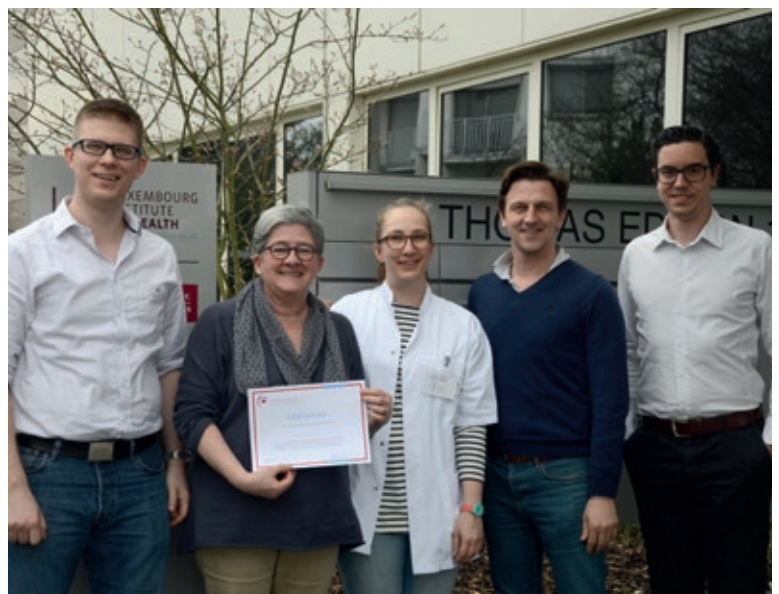
And to the Parkinson's disease patients?

Keep hoping! And don't forget to enjoy the little things in life!

From left to right: Dr Christian Stallinger (Parkinson Clinic, "Centre Hospitalier de Luxembourg"), Parkinson study participant Dany, Anne-Marie Hanff (Clinical and Epidemiological Investigation Centre, LIH), Jean-Yves Ferrand (Clinical and Epidemiological Investigation Centre, LIH) and Dr Pierre Kolber (Parkinson Clinic, "Centre Hospitalier de Luxembourg").



THE NATIONAL CENTRE OF EXCELLENCE IN RESEARCH (NCER) IS AN INITIATIVE OF THE LUXEMBOURG NATIONAL RESEARCH FUND





WORKING TOGETHER FOR THE NATIONAL CANCER PLAN AND REGISTRY

The National Cancer Plan 2014-2018 is developed under the patronage of the Minister of Health, Lydia Mutsch, with the support of the Direction of Health. It is a tool for structuring the fight against cancer on a national level and allows bringing together all involved stakeholders to reach major objectives over a period of five years.

LIH has been part of the project since its initiation, along with national stakeholders. Its implication in 2015 impacts on several levels.

Research strategy of the National Cancer Plan

In the course of 2015, a working group chaired by Dr Catherine Larue, at that time CEO of the Integrated BioBank of Luxembourg, managed to work out a common strategy on cancer research focused on personalised medicine, and involving all biomedical research institutions of the country. This strategy will be presented to the National Cancer Platform in 2016. The chairing of the working group is taken over in 2016 by Dr Anna Chioti, Operational Director of LIH's Department of Population Health.

Creation of the National Cancer Institute

A virtual institute, the National Cancer Institute was created in the form of a non-profit organisation, under the presidency of Dr Guy Berchem, Head of the Laboratory of Experimental Cancer Research in LIH's Department of Oncology. The institute's objective is to ensure that all cancer patients have access to a structured, standardised and quality clinical follow-up and will benefit from the most efficient and secure treatment. It will also control health expenditure in oncology.

National Cancer Registry

The National Cancer Registry, for which LIH is responsible, aims at providing transparent and standardised patient data to reliably follow cancer incidence, treatment, follow-up and patient survival in Luxembourg. In 2015, quality indicators for the care of breast cancer were established by the National Cancer Registry team. The development of these indicators revealed the crucial importance of traceability and completeness of recorded data in clinical documentation.

In the framework of the National Cancer Registry, a working group of specialised clinicians also selected the clinical practice guidelines to be used in Luxembourg for breast, colorectal, lung and prostate cancer. Following an intense review of existing guidelines from different countries, those which are most adapted to the expectations and needs of the Grand-Duchy were chosen and submitted to the "Conseil Scientifique dans le Domaine de la Santé" for approval and dissemination.

Finally, basic and advanced training courses on how to codify and introduce data from patient files into a hospital-based cancer registry were provided to data entry operators working at the hospitals (Data Managers Cancer). These training courses were held by Dr Sophie Couffignal, Associate Head of the Epidemiology and Public Health Research Unit and Operational Director of the National Cancer Registry, and by Stéphanie Saleh, epidemiologist of the National Cancer Registry.

EXPANSION OF THE RESEARCH NETWORK CARDIOLINC



The Cardiolinc network (www.cardiolinc.org) was founded and is coordinated by Dr Yvan Devaux, Associate Head of the Cardiovascular Research Unit. It is a platform bringing together research institutions working on the function of long non-coding ribonucleic acids in the heart.

Major achievements

Cardiolinc is the prime example of a multiparty international collaboration initiated by LIH. While it had 21 members at the end of 2014, it could extend the membership to 31 research institutions and five industrial partners in 2015. More than ten countries are now involved, including the United States.

One of the highlights for Cardiolinc in 2015, demonstrating its recognition by the international scientific community, was the invitation by the renowned scientific and medical publisher Nature Publishing Group to write a review on long non-coding RNAs. The article entitled “Long non-coding RNAs in cardiac development and ageing” appeared in July in Nature Reviews Cardiology, an international journal with an impact factor of 9.18.

It provides a detailed definition and classification of cardiac long non-coding RNAs to the reader and gives a comprehensive overview on their diverse mechanisms of action as regulators of gene expression in the context of the healthy and diseased human heart. The review was jointly produced by network members from Luxembourg, Germany, the Netherlands, Switzerland and the United States.

It ought to be mentioned as well that the Cardiolinc name and visual identity has been filed as a trademark in December 2015.

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.

Gene expression refers to the conversion of genetic information into functional gene products (e.g. synthesis of proteins or lncRNAs).



COLLABORATING WITH THE UNIVERSITY OF SOUTHERN DENMARK FOR EARLY ALLERGY DIAGNOSIS

Since the beginning of 2015, the Department of Infection and Immunity, headed by Prof Markus Ollert, has established a strong strategic partnership with the Odense Research Centre for Anaphylaxis (ORCA), a clinical centre of excellence of the Odense University Hospital at the University of Southern Denmark (Syddansk Universitet, SDU). This collaboration in allergy research will allow combining the department's expertise in immune cell function with ORCA's widely recognised experience in clinical allergology.

Complementary competences

ORCA has a unique and very large repository of biological samples from highly characterised allergy patients, in particular anaphylactic patients, and an outstanding potential to conduct clinical research. In the Department of Infection and Immunity there is in turn a strong expertise in immunology and molecular allergology research, namely in dissecting molecular structures, T cell function and immune signalling pathways.

"We also possess the required equipment and knowhow for large-scale data analyses", tells Prof Ollert. "Using the samples from ORCA, we therefore aim at developing an omics approach to unravel the mediators of anaphylactic shock". The joint research efforts could ultimately facilitate early diagnosis and clinical care of anaphylaxis.

First fruitful outcomes

A bilateral collaborative agreement, has been signed beginning of 2015. Since then, both institutions have submitted two major joint grant proposals in Denmark and have already published jointly authored articles.

Moreover, Prof Ollert and Prof Dirk Brenner, principal investigator in the department, were both appointed as professors at SDU during a ceremony at an inaugural mini-symposium on allergy research in November 2015. "The professorship appointment involves future teaching duties and confers us supervision rights to train doctoral candidates affiliated to SDU at LIH," explains Prof Brenner. "We have even agreed on developing a joint doctoral degree between SDU and the University of Luxembourg, with which our department is also working closely together", adds Prof Ollert.

BIOCABULARY

A **(signalling) pathway** is a series of actions among molecules in a cell that leads to a certain cell function.

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).

Anaphylaxis or **anaphylactic shock** is an extreme, often life-threatening allergic reaction to a substance to which the body has become hypersensitive.

Ceremony at the inaugural seminar "Frontiers in Allergy Research" organised at SDU. From left to right: Prof Knut Brockow (Technical University Munich), Prof Kirsten Ohm Kyvik (SDU), Prof Dirk Benner (LIH), Prof Markus Ollert (LIH), Prof Tilo Biedermann (Technical University Munich) and Prof Carsten Bindslev-Jensen (Odense University Hospital, SDU).

“The chief aim of our collaboration is to build a bridge between basic immunological research and clinical work.”

Prof Markus Ollert

Director of the Department of Infection and Immunity



IBBL WITHIN LIH

Biobanking and bioservices for applied medical research

Since 1st January 2015, IBBL, the Integrated BioBank of Luxembourg (IBBL), is an autonomous institute organised within LIH. This allows IBBL and LIH's research departments to work even closer together. In 2015, IBBL has reached several milestones: the biobank gained ISO accreditation, won a national prize for its quality, launched several new large-scale research projects, increased its third-party funding and even organised the world's largest microbiome conference in Luxembourg.

IBBL's mission

Since its creation in 2008, IBBL has substantially expanded its activities on a mission to provide biospecimen-related services and a biobanking infrastructure for applied medical research. As a research support infrastructure, IBBL offers bioservices, including the collection, processing, analysis and storage of biological samples, such as blood, tissue, urine, saliva and stool, as well as the data associated with these samples. IBBL works closely with its partners to promote and support research in the following priority areas: cancer, Parkinson's disease, diabetes, microbiome, general population. In addition, IBBL carries out in-house research to optimise biospecimen processing and to qualify biospecimens.

Hand in hand

Following the merger with CRP-Santé, IBBL operates under the responsibility of the same Board of Directors. Within LIH, IBBL has a certain autonomy as it kept its own CEO, management committee, budget and performance contract with the Ministry of Higher Education and Research.

Even before the merger, the biobank and the departments of LIH collaborated on a number of projects, for example on lung cancer or type 2 diabetes. In particular, the Clinical and Epidemiological Investigation Centre (Department of Population Health) and IBBL work hand in hand on the recruitment of patients and collection of samples and data for multiple studies. The collaboration on these projects has continued in 2015, while the merger led to the creation of additional synergies on various operational levels, particularly within the administrative department.

One new collaboration between the two entities, as well as other local and international partners, is the National Centre of Excellence in Research on Parkinson's Disease (see page 52), an 8-year research programme with the aim of diagnosing and stratifying Parkinson's disease better and earlier.

Luxembourg takes centre stage

Luxembourg took centre stage in March 2015, when IBBL organised the fifth International Human Microbiome Congress, attracting more than 500 researchers, engineers and clinicians from 32 countries. Over the last few years, IBBL has become deeply invested in microbiome research, the field that studies the interactions between the human body and the billions of microorganisms that share it. In 2015, the biobank continued on this path by studying the best ways to process and annotating gut microbiome samples and preparing to launch the first Luxembourg gut microbiome cohort.





Quality hat-trick

As a service provider, IBBL has - since the beginning - put an enormous emphasis on quality and built its whole operations around a formal Quality Management System (QMS). This strategy paid off on three levels in 2015. IBBL gained ISO 17025:2005 accreditation (general requirements for the competence of testing and calibration laboratories) and is now one of only a handful of biobanks worldwide to be accredited according to this norm. In addition, IBBL successfully passed the follow-up audits for its ISO 9001 and NF S96-900 certifications.

However, the cherry on the cake was the Luxembourg Quality and Excellence Award, which IBBL received in the category for small enterprises as a recognition for its QMS as well as its efforts in terms of sustainability. The ultimate goal of the QMS is to ensure IBBL's clients are satisfied and their needs are met. This is also the reason IBBL reformulated its service offer in 2015 and introduced a new service for the pre-clinical validation of biomarkers. Overall, with 16 new service contracts, substantially increased participation in the Proficiency Testing programme and great feedback from the students of the University Biobanking Certificate, the year proved fruitful for IBBL's bioservices.

Prestigious research partnerships

Another big success for IBBL in 2015 was its membership in the CANCER-ID consortium, funded by the Innovative Medicines Initiative, a collaboration between the European Union and the European pharmaceutical industry. IBBL joined the ranks of 33 partners from prestigious academic and clinical research institutions, small-and-medium-sized enterprises and the pharmaceutical industry with the goal of validating the use of blood-based biomarkers for cancer.

Within the CANCER-ID consortium, IBBL works on the validation of laboratory methods, the development of standard operating procedures and of a proficiency testing programme. One reason why IBBL has become part of this consortium is the international recognition of IBBL's Biorefinery Department as one of the leading research groups focusing on the quality of biospecimens. In addition to their contribution to CANCER-ID, IBBL's researchers focused primarily on the evaluation of new technologies to improve the processing of tissue biospecimens. Overall, IBBL's various biospecimen research projects led to ten scientific publications.

A look ahead

For the coming years, IBBL has a number of exciting and challenging new projects in the pipeline, including new tissue collections in France and Vietnam, the Luxembourg gut microbiome cohort and the National Cancer Plan. At the same time, IBBL will continue its efforts to increase third-party funding by gaining new service contracts and grants from national and European research funding agencies. Last but not least, the biobank plans to expand the scope of its accreditation to more testing methods, while maintaining its current certifications.

Dr Sabine Lehmann, Quality Manager of IBBL (left), and Dr Catherine Larue, CEO of IBBL in 2015 (right), accept the Luxembourg Quality and Excellence Award in the category for small enterprises.







HIGHLIGHTS

2015

Events, Visits, Discoveries,
Patents, Awards & News

HIGHLIGHTS

2015

JAN

CRP-Santé becomes LIH

On 1st January 2015, following the law of 3rd December 2014 on the organisation of public research in Luxembourg, CRP-Santé and Integrated BioBank of Luxembourg merged to become the Luxembourg Institute of Health. Both entities operate under the responsibility of a single Board of Directors and share common administrative services. Within LIH, the biobank remains a clearly identified corporate structure with management autonomy.

EUROSTARS funding for medical device development

A EUROSTARS grant from the European Commission of 312,000 Euro was approved on 16th January for the project DYNEELAX involving the Sports Medicine Research Laboratory (Department of Population Health). Together with public and industry partners from France and the Czech Republic, a new medical device for computer-assisted assessment of knee ligaments tears and associated soft tissues status will be developed and clinically validated. It will be composed of an automated arthrometer to measure knee laxity (elasticity) and a data analysis software.

Cancer Foundation supports a research project

The Luxembourg Cancer Foundation funds a research project of the NorLux Neuro-Oncology Laboratory (Department of Oncology), which aims at unravelling the mechanisms underlying cancer cell invasion in malignant brain tumours. If successful, this should ultimately lead to new therapeutic approaches that effectively inhibit tumour growth. On 28th January, the Cancer Foundation, represented by its President and Director, handed over a check of 397,104 Euro.



From left to right: Dr Carlo Bock (President of the Cancer Foundation), Dr Anne Schuster (postdoctoral researcher at the NorLux Neuro-Oncology Laboratory), Prof Simone Niclou (Head of the NorLux Neuro-Oncology Laboratory), Dr Gregor Baertz (President of LIH's Board of Directors) and Martine Neyen (Director of the Cancer Foundation).

FEB

Science Club visits the NorLux Neuro-Oncology Laboratory

LIH aims at promoting science to the broad public, in particular to the young generation. On 12th February, the Science Club of the National Museum of Natural History, a group of teenagers interested in science and technology, was invited to the NorLux Neuro-Oncology Laboratory (Department of Oncology). Eight young people could discover the projects of a cancer research unit and apply a classical molecular biology technique during a hands-on workshop.

Researcher Dr Fred Fack explains the research scope of the NorLux Neuro-Oncology Laboratory to the Science Club members.



MAR

EACR conference gathers the international oncology research community in Luxembourg

The conference “Precision Medicine for Cancer”, which is part of a new conference series of the European Association for Cancer Research (EACR), was held from 1st to 4th March at the Neumünster Abbey in Luxembourg-City. Gathering top-level scientists together with 116 participants from the field of oncology, early-stage researchers to a large majority, the conference was highly appreciated by all attendees. Prof Simone Niclou, Head of the NorLux Neuro-Oncology Laboratory (Department of Oncology) was a member of the scientific organising committee.

EACR European Association
for Cancer Research

Excellence in Human Resources honoured by the European Commission

During the celebration of the 10th anniversary of the European Charter and Code of Conduct for the Recruitment of Researchers in Brussels on 3rd March, the European Commission awarded LIH for having attained the fifth and final step of the setting-up of improved human resources policies. LIH was the first Luxembourgish research institution to receive the label “Human Resources Excellence in Research” in 2010, and is now also the first to pass all required steps for this award.



APR

Two directors for the Department of Population Health

Prof Saverio Stranges and Dr Anna Chioti were respectively appointed as Scientific and Operational Directors of the Department of Population Health. Prof Stranges, who took office on 1st April, also holds the position of Head of the Epidemiology and Public Health Research Unit, one of the six research units composing the department. Dr Chioti remains the Head of the Clinical and Epidemiological Investigation Centre, also integrated in the department.

MAY

Inauguration of LIH's facilities at the House of BioHealth

Following the relocation of one third of LIH's staff to the House of BioHealth in Esch-sur-Alzette beginning of the year, the premises were officially inaugurated on 4th May in the presence of numerous invitees. The brand-new laboratories host the Department of Infection and Immunity and the Human Biomonitoring Research Unit (Department of Population Health). The infrastructure better suits the researchers' needs and allows the development of novel research groups and collaborations.



From left to right: Dr Jean-Claude Schmit (CEO of LIH until 31st December 2015), Marc Hansen (Secretary of State for Higher Education and Research) and Lydia Mutsch (Minister of Health) cut the ribbon to inaugurate LIH's premises at the House of BioHealth.

Prize for the best conference presentation from the Society of Hair Testing

PhD candidate Caroline Chata from the Human Biomonitoring Research Unit (Department of Population Health) was awarded the prize of the best oral presentation at the annually held international meeting of the Society of Hair Testing. The 20th edition of this meeting took place in São Paulo, Brazil, from 3rd to 6th May. She presented the first promising results of her PhD project on the potential of hair as human biomonitoring matrix for pesticides.

Open Day at the Clinical and Epidemiological Investigation Centre

On 19th May, the Clinical and Epidemiological Investigation Centre (Department of Population Health) opened its doors to the public on the occasion of the International Clinical Trials Day. With the help of presentations, posters, interactive educational games and a quiz, visitors could learn about the purpose of clinical research and the different phases to conduct a clinical trial.



Dr Lamia Skhiri, Junior Clinical Research Associate at the Clinical and Epidemiological Investigation Centre, introduces a game on the principles of clinical trials to the participants.

Prof Rolf Bjerkvig rewarded by the King of Norway for his lifework in cancer research

Prof Rolf Bjerkvig, who is Director of LIH's Department of Oncology and at the same time leading the Kristian Gerhard Jebsen Centre for Brain Tumour Research in the Department of Biomedicine at the University of Bergen, Norway, was awarded the King Olav V Cancer Research Prize on 8th June. This prestigious distinction, bestowed by His Majesty King Harald V of Norway on behalf of the Norwegian Cancer Society, honours his exceptional achievements in brain cancer research.



From left to right: Anne Lise Ryel (General Secretary of the Norwegian Cancer Society), His Majesty King Harald V, Prof Rolf Bjerkvig and Carl Otto Løvenskiold (Deputy Chairman of the Norwegian Cancer Society).

Training in Good Clinical Practice

One of the key objectives of the Clinical and Epidemiological Investigation Centre (Department of Population Health) is to promote clinical research activities according to international standards of Good Clinical Practice (GCP). On 10th June, the centre partnered up with the "Centre Hospitalier de Luxembourg" to organise its yearly interactive and certified GCP training for clinical investigators and site personnel. The half-day course focused on risk-based monitoring in clinical research.

Award for two young scientists at an international sports medicine congress

Two members of the Sports Medicine Research Laboratory (Department of Population Health), PhD candidate Caroline Mouton and research assistant Paul Gette, were awarded for the convincing presentation of their research projects on the optimisation of clinical intervention after knee soft tissue injuries during the 30th annual congress of the GOTS, the Society for Orthopaedic-Traumatologic Sports Medicine. This congress was held from 12th to 13th June in Basel, Switzerland.

EUROSTARS funding for the development of a prognostic test for heart failure

Members of the Cardiolinc Network, coordinated by the Cardiovascular Research Unit (Department of Population Health), received 1.75 Million Euro funding through the EUROSTARS programme for a 3-year project aiming at developing an *in vitro* diagnostic assay for prognostication of patients with acute myocardial infarction. The research programme MiPROG, involving biotech companies in France and Spain as well as the Medical School of Hannover, Germany, was accepted on 24th June and launched on 4th December.

World Hepatitis Day organised with the Red-Cross Luxembourg

On the occasion of the World Hepatitis Day on 27th July 2015, LIH together with “HIV Berodung” of the Red-Cross Luxembourg informed about prevention, diagnosis and treatment of hepatitis as well as LIH’s research projects on hepatitis B and C viruses conducted at the Infectious Diseases Research Unit (Department of Infection and Immunity). A booth at which flyers and condoms were distributed was set up at the train station in Luxembourg and in Esch-sur-Alzette. 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).



HRH Princess Tessy of Luxembourg visits LIH for a short-term traineeship

During two weeks in August, HRH Princess Tessy of Luxembourg did a training period at LIH related to her Master's degree studies in International Studies and Diplomacy at the School of Oriental and African Studies of the University of London, United Kingdom. A tour through all three departments gave her the opportunity to get an overview on all research activities and their relevance for scientific progress and healthcare.



HRH Tessy of Luxembourg with Dr Jean-Claude Schmit (CEO of LIH until 31st December 2015).

A grant for knowledge and innovation transfer support

LIH's Research and Knowledge Transfer Office received a Knowledge and Innovation Transfer Support (KITS) grant of 177,000 Euro from the Luxembourg National Research Fund. The project, accepted on 28th August, will allow to put into practice LIH's strategy of including the reflection on economic and societal value creation into research projects right at their start. A Research Impact Officer will be hired and a lecture series with speakers from industry will be organised to increase awareness on the importance of technology transfer among LIH's researcher community.

Famous immunologist Prof Tak W. Mak gives a lecture on anti-cancer targets

The annual Lecture Series and Workshops in Infection and Immunity, organised by the Department of Infection and Immunity, brought ten internationally renowned speakers to Luxembourg in 2015. The highlight of the year was the lecture given by Prof Tak W. Mak from the University of Toronto, Canada, on 9th September. He is known for his pioneering work in the genetics of immunology, in particular for the discovery of the T cell receptor in 1984.



Prof Tak W. Mak right before giving his lecture “Future anti-cancer targets: put the cart before the horses” at the Amphitheater of the “Centre Hospitalier de Luxembourg”.

Award for the best PhD in Life Sciences at the University of Lorraine

On 29th September, Dr Emeline Goretti received an award for having prepared the best PhD thesis of the academic year 2014-2015 within the Doctoral School of Biological, Health and Environmental Sciences of the University of Lorraine. She had carried out a 4-year PhD project at the Cardiovascular Research Unit (Department of Population Health) and defended her thesis in October 2014.



Dr Emeline Goretti (centre) and other PhD graduates from the University of Lorraine at the PhD diploma ceremony. PhD supervisor Dr Yvan Devaux is standing on the left of the awardee and Prof Patrick Menu, Director of the Doctoral School of Biological, Health and Environmental Sciences, on the right.

Numerous visitors at LIH's Open Day

LIH invited the public to an Open Day at the House of BioHealth in Esch-sur-Alzette on 20th September. The Department of Infection and Immunity presented its research activities and gave insights into the complex techniques used to address major questions in immunology. At seven stations, the 240 visitors could get information about research projects on Human Immunodeficiency Virus (HIV), allergies, Lyme disease, epigenetics, molecular modelling and much more.



Patent application for biomarkers of heart failure

The Cardiovascular Research Unit (Department of Population Health) filed a patent application on 15th September at the Office for Intellectual Property in Luxembourg on the use of circular RNAs for predicting the development of heart failure after myocardial infarction. This is the fourth patent application for biomarkers of heart failure made by the research unit.

Healthcare Research Award for the NorLux Neuro-Oncology Laboratory

On 6th October, the NorLux Neuro-Oncology Laboratory (Department of Oncology) was rewarded with the Healthcare Research Award at the second edition of the Luxembourg Healthcare Summit. The award jury considered the research unit's work on malignant brain tumours as a major contribution to national excellence in health research.



Dr Olivier Keunen, researcher at the NorLux Neuro-Oncology Laboratory, and Prof Simone Niclou, Head of the NorLux Neuro-Oncology Laboratory, at the Luxembourg Healthcare Summit 2015. © Farvest Group

Three CORE grants for LIH

The Luxembourg National Research Fund finances multi-annual thematic research programmes with its central funding instrument CORE. Three projects submitted by LIH received the third-party funding in 2015. The successful applicants announced end of October were Prof Dirk Brenner and Dr Mahesh Desai from the Department of Infection and Immunity, and Prof Bruno Domon from the Department of Oncology.

Launch of a new corporate website: www.lih.lu

To better present the new corporate identity as well as the departmental and intra-departmental reorganisation that LIH underwent in 2015, a new website was launched on 22nd October. It is intended to inform the local and international scientific community on research activities, news and events, and to promote the institute's attractiveness for collaborations with public and private partners. A second website to specifically target the lay public is under development.



Translational Research Award for two LIH scientists at the Medical Research Day

The Medical Research Day, organised by the "Centre Hospitalier de Luxembourg", jointly with LIH and the University of Luxembourg, was held on 28th October. More than 200 attendees had the opportunity to get informed about the challenges and prospects of clinical research. At this occasion, Dr Victoria El-Khoury (Laboratory of Experimental Cancer Research, Department of Oncology) and Melanie Vausort (Cardiovascular Research Unit, Department of Population Health) were given the Translational Research Award for their research projects carried out in collaboration with clinicians.



Conference on an unprecedented year of Ebola research

“Médecins sans Frontières” and LIH co-organised a conference on the Ebola epidemics that hit West Africa in 2014-2015. The conference entitled “Twelve months of Ebola research: an unprecedented year” was held on 4th November at the Amphitheater of the “Centre Hospitalier de Luxembourg”. In the presence of Lydia Mutsch, Minister of Health, findings from epidemiological and anthropological field research were presented, and lessons learnt from the Ebola outbreak were discussed.



Allocution by Lydia Mutsch, Minister of Health, at the conference “Twelve months of Ebola research: an unprecedented year”.

LIH maintains its ISO 9001:2008 certification

LIH’s administrative services, several research groups and its animal facility which were ISO 9001:2008 certified in 2013 and 2014, successfully maintained their certification following an external audit of the Quality Management System on 23rd November. The certification scope was successfully extended to the recently formed unit “Doctoral Training” that is in charge of overseeing and organising doctoral training-related activities at the institute.



Personalised Medicine Consortium Meeting held at LIH

The Personalised Medicine Consortium, composed of the national biomedical research institutions, aims to foster new synergies between clinicians and researchers from Luxembourg. The annual meeting of the consortium was organised by LIH on 13th November and took place at the House of BioHealth in Esch-sur-Alzette. About 60 researchers gathered to discuss current collaborative research projects amongst others in the field of cancer, immunology and cardiometabolic diseases.



Dr Anna Chioti honoured with the Award of Economic Diplomacy

On 26th November, Dr Anna Chioti was rewarded by the International Diplomatic and Consular Society CIDIC with the Award of Economic Diplomacy for her role as Head of the Clinical and Epidemiological Investigation Centre (Department of Population Health) and her active contribution in promoting fruitful collaborations between the pharmaceutical and the academic sectors in Belgium and Luxembourg. The award was given on the occasion of an official diplomatic, economic and academic delegation visit in Luxembourg under the High Patronage of HRH Princess Léa of Belgium.



Engagement in the European Health Parliament

Dr Xianqing Mao, postdoctoral researcher at the Laboratory of Experimental Cancer Research (Department of Oncology), was selected in December to join the European Health Parliament during six months to be part of a lively discussion about Europe's major challenges in health and healthcare. The European Health Parliament is an initiative from Johnson & Johnson, Google, POLITICO, College of Europe and EU40. It engages 55 young professionals from different backgrounds.



Dr Xianqing Mao interviewed at the European Parliament in Brussels in her function as European Health Parliament delegate.

Patent application on biomarkers for bladder cancer

The Genomics and Proteomics Research Unit (Department of Oncology) filed a patent application on 23rd December at the European Patent Office. Dr Elodie Duriez and Prof Bruno Domon, co-inventors on the patent, were able to identify and validate novel biomarker proteins for bladder cancer using a proteomics-based approach.



GOVERNANCE, HUMAN RESOURCES & FINANCES

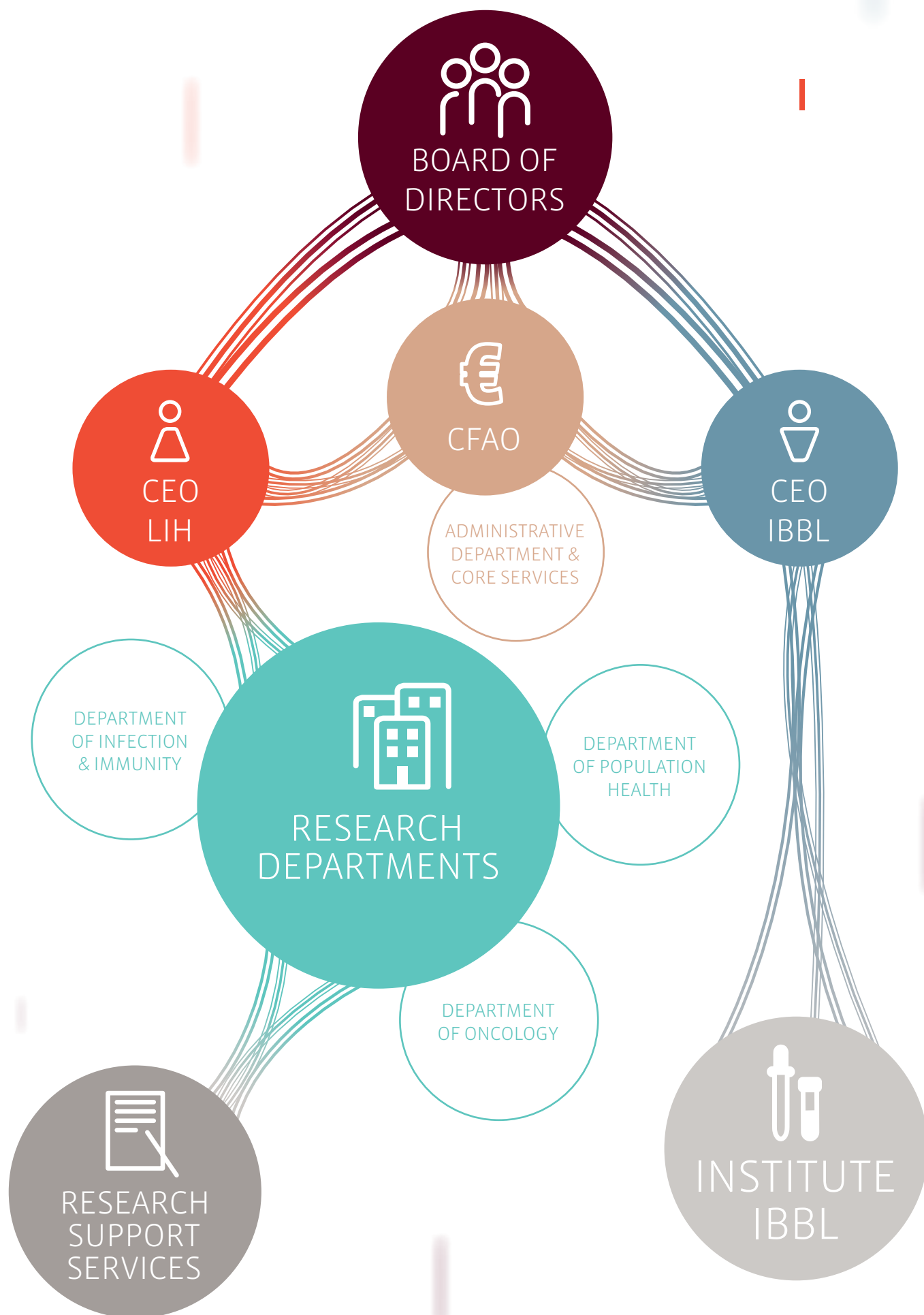
GOVERNANCE BOARDS

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.

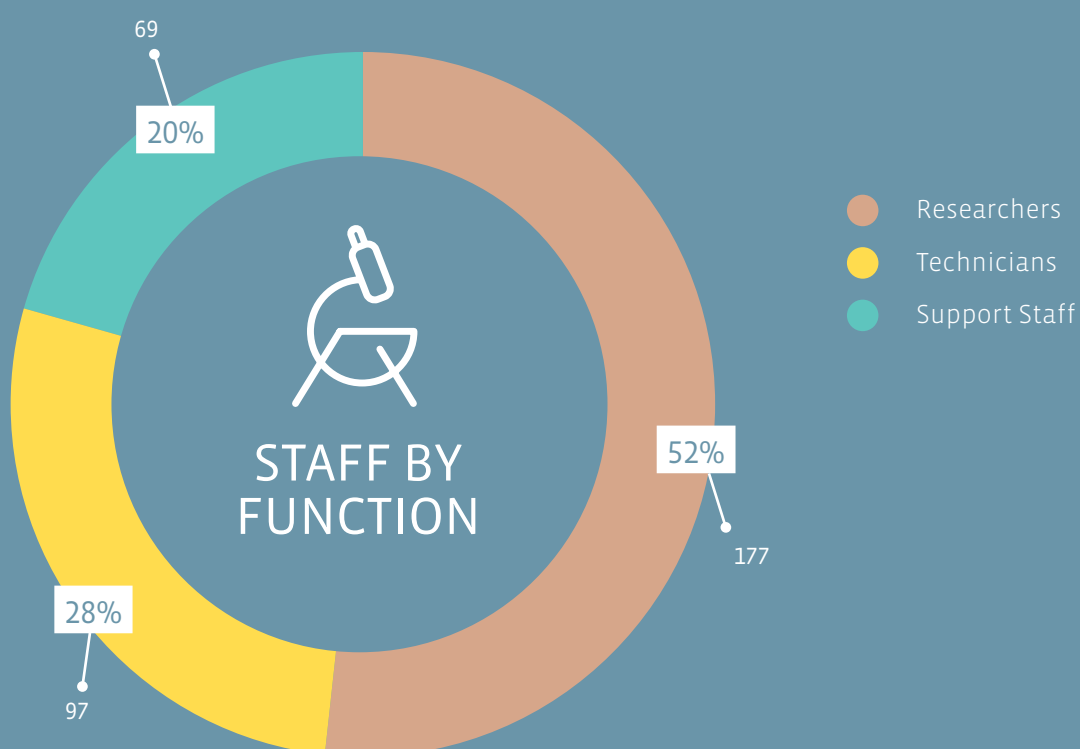
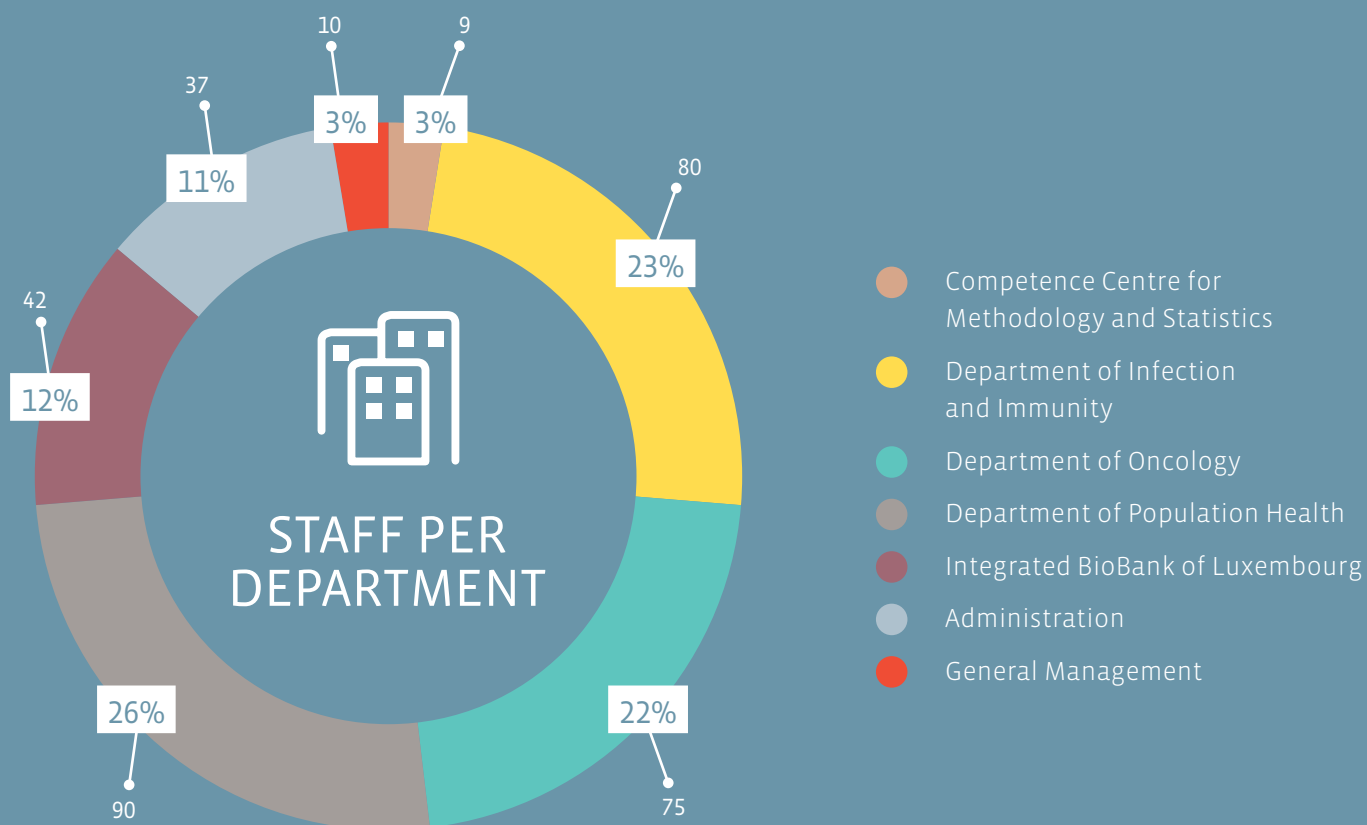
The **Executive Committee**, composed of the Chief Executive Officer, the Chief Financial and Administrative Officer and the directors of the three research departments, is responsible for the implementation of the strategy approved by the Board of Directors and for day-to-day management of the institution.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

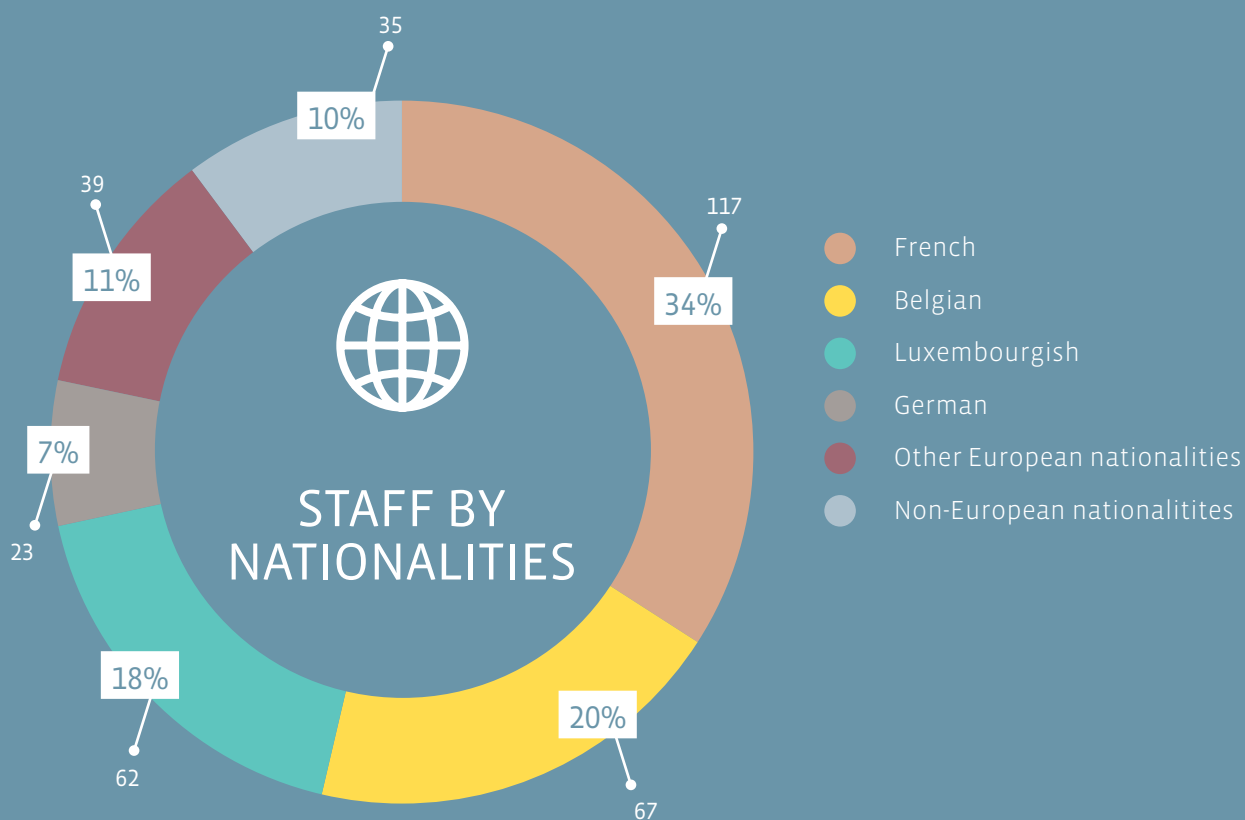
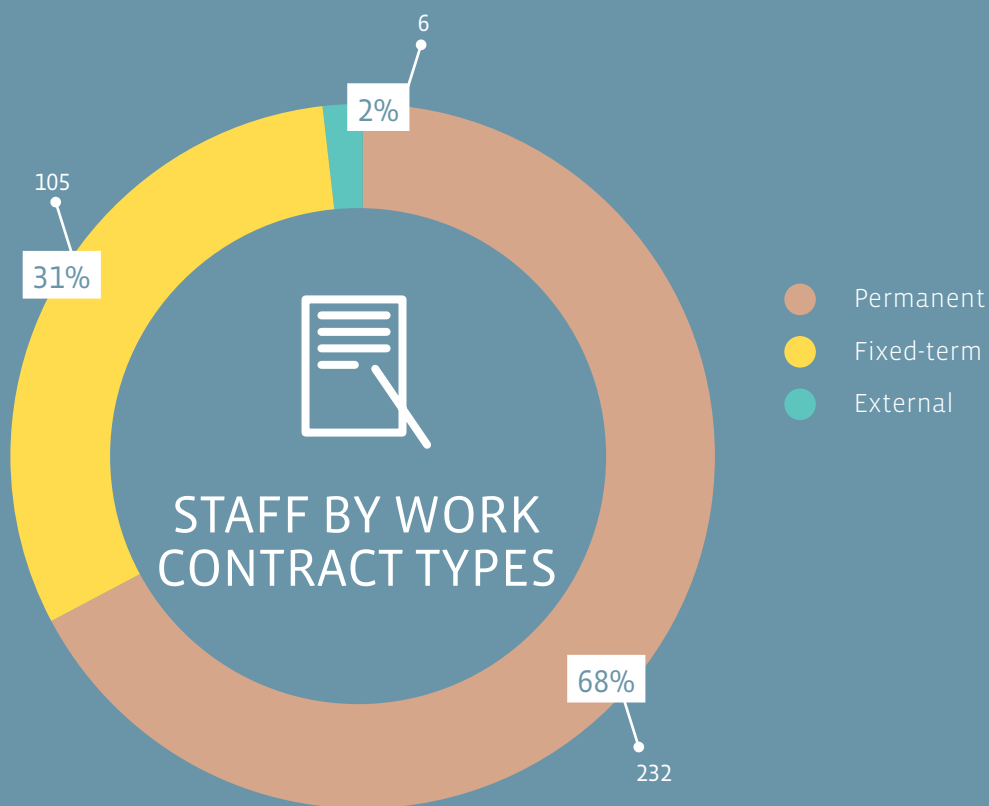
The **Collaborative Council** is a consultative body composed of internal representatives of the research staff, the personal delegation and the research and innovation support personnel. It issues advisory opinions to the Board of Directors regarding research policy, development and innovation. It will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



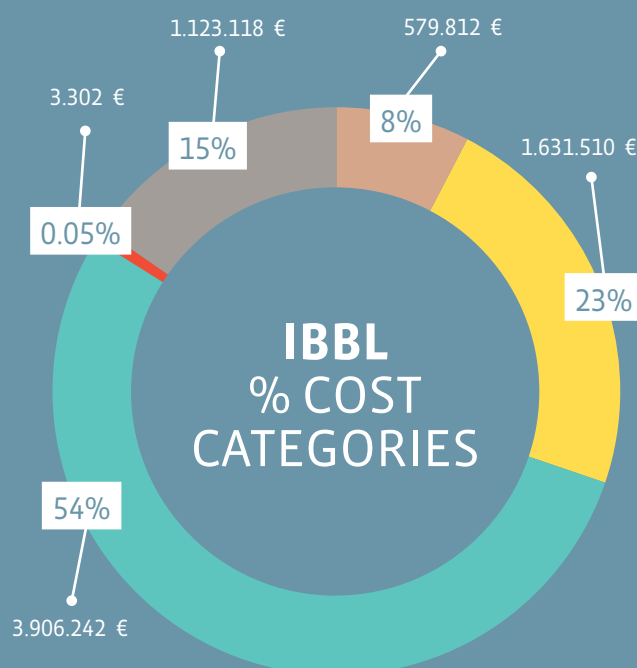
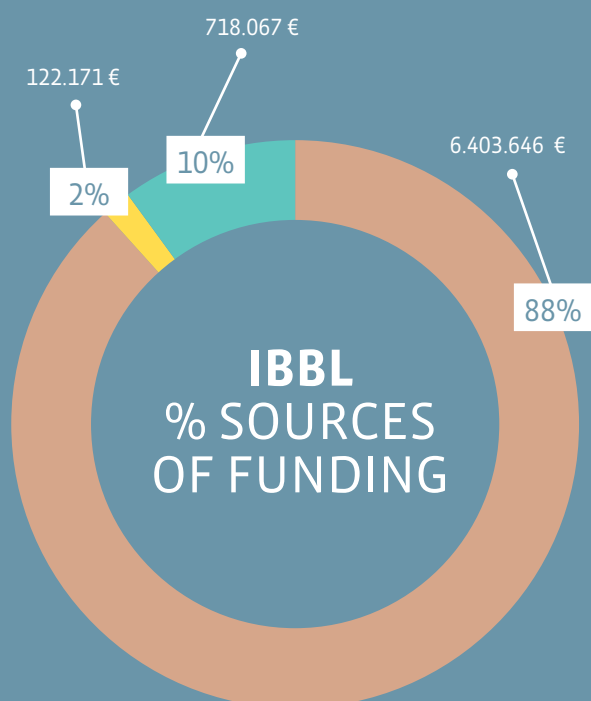
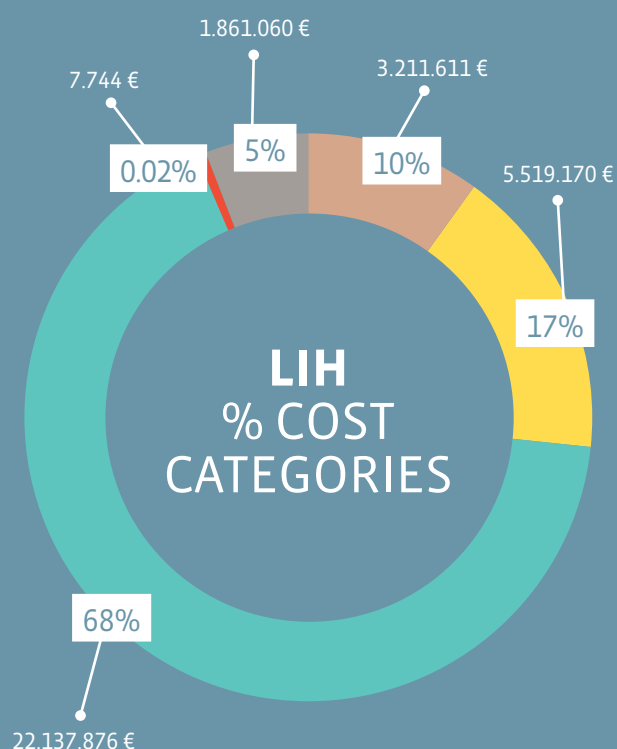
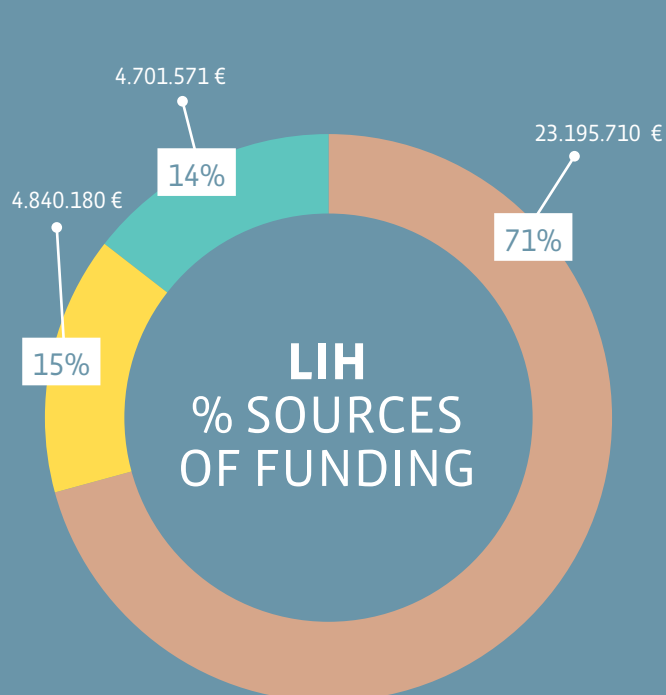
HUMAN RESOURCES





FINANCES

STATUTORY EXPENSES



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

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

PROFIT AND LOSS ACCOUNT

(31st December 2015, incl. IBBL)

PROFIT AND LOSS ACCOUNT (EUR)

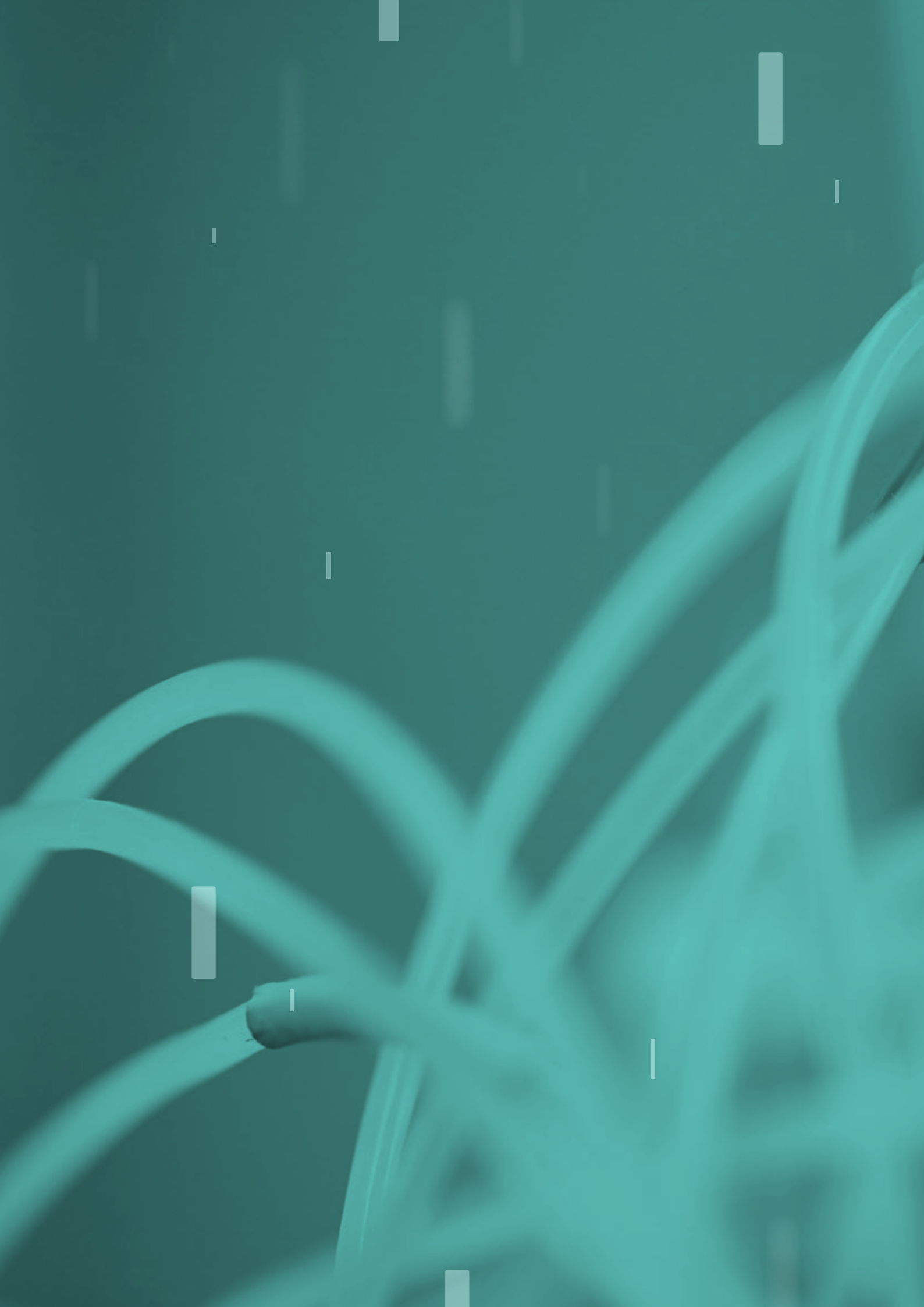
	2015 01.01. - 31.12.15	2014 01.01. - 31.12.14
A. CHARGES		
1. Use of merchandise, raw materials and consumable materials	3.791.423	3.139.078
2. Other expenses	7.150.680	7.406.185
3. Staff costs	26.044.118	25.504.660
4. Value adjustment on intangible and tangible fixed assets	2.984.178	2.178.587
5. Interests and other financial charges	11.046	7.973
6. Profit for the financial year	0	1.295.814
TOTAL CHARGES	39.981.445	39.532.297
B. INCOME		
1. Net turnover	2.818.877	3.019.888
2. Subsidies	36.932.741	35.997.456
3. Other income	145.961	406.152
4. Interests and other financial income	83.866	108.801
5. Loss for the financial year	0	0
TOTAL INCOME	39.981.445	39.532.297

BALANCE SHEET

(31st December 2015, incl. IBBL)

ASSETS (EUR)	2015 01.01. - 31.12.15	2014 01.01. - 31.12.14
FIXED ASSETS		
Intangible fixed assets	583.912	862.029
Tangible fixed assets	9.410.281	7.280.250
Financial fixed assets	424.205	384.008
TOTAL FIXED ASSETS	10.418.398	8.526.287
CURRENT ASSETS		
Debtors		
1. Trade receivables	1.419.926	1.251.346
a. Becoming due and payable within one year	1.419.926	1.251.346
2. Other receivables	3.308.948	2.618.991
a. Becoming due and payable within one year	3.308.948	2.618.991
Cash at bank, cash in postal cheque accounts, cheques and cash in hand	26.064.558	28.536.856
TOTAL CURRENT ASSETS	30.793.433	32.407.194
Prepayments	448.837	449.658
TOTAL ASSETS	41.660.668	41.383.139

LIABILITIES (EUR)	2015 01.01. - 31.12.15	2014 01.01. - 31.12.14
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	7.198.551
Profit or loss for the financial year	0	1.295.814
Capital investment subsidies	8.763.389	5.799.714
TOTAL CAPITAL AND RESERVES	22.843.793	19.880.118
Available reserve for projects	13.760.352	17.046.148
Provisions	719.964	409.088
NON-SUBORDINATED DEBTS		
1. Trade creditors	1.975.285	2.906.413
a. Becoming due and payable within one year	1.197.211	2.906.413
b. Becoming due and payable after more than one year	778.074	0
2. Tax and social security debts	1.600.313	833.374
a. Tax debts	729.711	4.194
b. Social security debts	870.602	829.179
3. Other creditors	760.431	307.711
a. Becoming due and payable within one year	760.431	307.711
TOTAL NON-SUBORDINATED DEBTS	18.816.345	21.502.734
Deferred income	530	288
TOTAL LIABILITIES	41.660.668	41.383.139



The background is a teal-tinted photograph of a laboratory setting. It features various pieces of glassware, including a large Erlenmeyer flask in the foreground and several test tubes in the background. A crumpled piece of white paper is visible on the right side. The overall aesthetic is clean and scientific.

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Note: The Centre also contributed significantly to several studies published by the different research departments (listed in the following sections).

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