



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

# 2018

## ANNUAL REPORT









Prof Ulf Nehrbass, Chief Executive Officer of LIH

## FOREWORD

### MESSAGE FROM THE CEO

The struggle between continuity and change is a challenge playing out in many different nuances: adaption over perseverance, disruption over stability, flexibility over stagnation. It appears to be an omnipresent theme. From the evolutionary strategies of simple living organisms to the travails of modern management, the challenge around change never appears simple and straight forward, and it always comes with a trade-off. Fact is, you simply have to get the decision right of how long to stay course and when to start turning.

“While the scientific quality of the research work and its originality has struck me from the day I set foot into the institute, it is now official: LIH has been ranked amongst the leading non-academic institutions in the world by the *Times Higher Education*.”



Why do I talk about that? 2018 has been a very successful year for LIH, even a year of coming out for our institute. While the scientific quality of the research work and its originality has struck me from the day I set foot into the institute, it is now official: LIH has been ranked amongst the leading non-academic institutions in the world by the *Times Higher Education*. Such ranking may be questionable if it were a performance indicator we actively pursue. It is very meaningful, however, if we pursue excellence and happen to be ranked number 7 in Europe and number 15 in the world, for those who have not been aware yet. Whoever may have held a remainder of doubt about the sheer scale of this excellence, 2018 also saw the Technopolis review, an evaluation by the Ministry of Higher Education and Research, analysing in depth and detail everything from past performance to future strategy of LIH. The outcome, again, was highly positive, obviously with improvements remaining to be made. And all the while these evaluations were ongoing, LIH researchers kept it coming with excellent publications in top ranking journals and the public press, as can be read in the “Research Progress” section of this annual report.

The obvious question then, in the face of so much success: why do we want to change a winning hand? In 2018, LIH started a range of restructuring from strategy to operations and budget processes. A simple answer is: because we can easily become even better by making current processes more effective, by finding a common focus and narrative of our work, by developing more synergies and by spending our budget more effectively. More pressing, however, is the fact that the context around us is changing, and it is changing fast. By and large, there is a heightened expectation by the public to see return from decades of fundamental research. There are tremendous new possibilities coming along with the emergence of Digital Health and human-based disease modelling that fundamentally change the approaches that will be used in biomedical research. Along with that comes an ever-increasing focus on disease prevention as a research and development goal, instead of a previous primary focus on therapy and cure. And there are ground breaking perils and opportunities coming along with the rapidly accelerating unleashing of Pharma from the R&D value chain.

In spite of our current success then, there is no alternative than adapting to our fast-changing environment. Importantly, a shared objective has been defined in putting the patient at the centre of our application-targeted research and establishing integrated bed-to-bench-to-bed processes for our projects. It will be reinforced by defining a synergistic disease focus and aligned innovative methodologies. Operational retro-planning enables us to approach our objectives in a stepwise and systematic fashion and in close alignment with our partners in Luxembourg. By systematically expanding from our current base of achievement, we can assure a strong element of continuity. Goal is to position the scientific excellence of LIH at the cutting edge of the evolving paradigm context to assure that LIH will be a leading institution for years to come. Success can be a risk if it prevents from the necessary adjustments. We are making sure this is not the case at LIH.

In the name of the stakeholders and partners, I would like to thank you all for a highly successful year 2018.

Prof Ulf Nehrbass  
CEO of LIH





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# MISSION & VISION



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

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





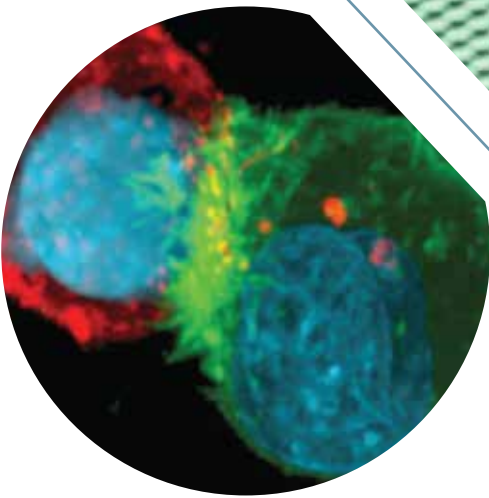
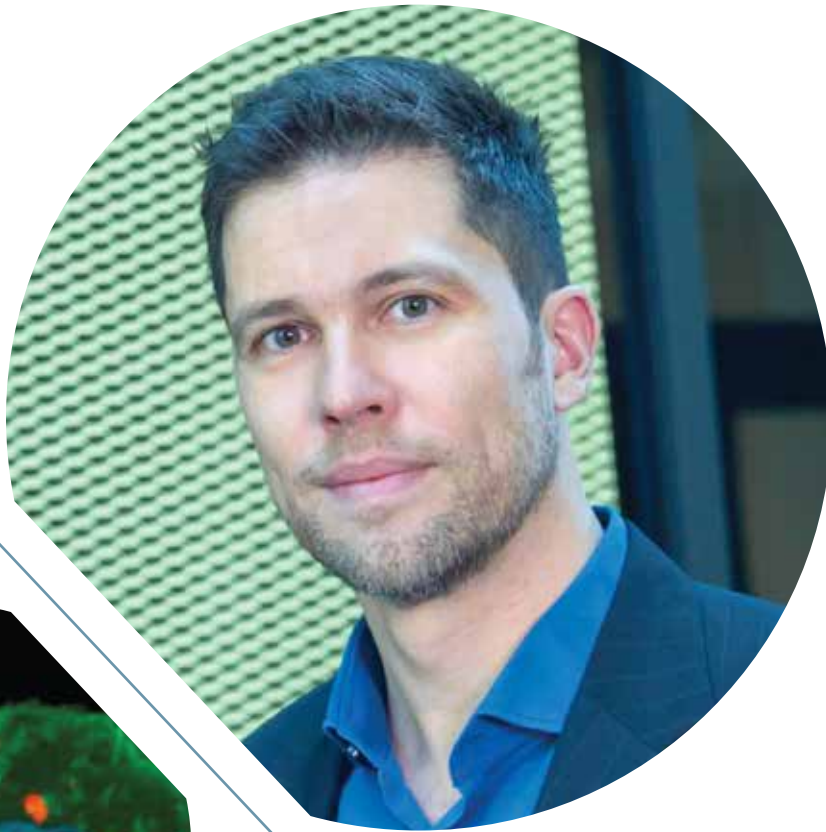


# RESEARCH PROGRESS

09



Dr Clément Thomas



Confocal microscopy image showing the actin response: accumulation of actin filaments (in green) at the immunological synapse of a resistant cancer cell in contact with a Natural Killer cell (in red). Cell nuclei are shown in blue.

# TUMOUR CELLS DEPLOY A MOLECULAR SHIELD AGAINST IMMUNE ATTACK

Actin cytoskeleton remodelling in breast cancer

Department of Oncology › Laboratory of Experimental Cancer Research › Cytoskeleton and Cancer Progression Research Group

Tumour cells can develop multiple strategies to protect themselves from the reactions of the immune system. LIH researchers have uncovered a brilliant defence strategy used by some breast cancer cells to block the attack of immune cells: they deploy a protective molecular shield to resist to Natural Killer cells.



Natural killer cells can detect abnormal characteristics of cancer cells by coming into contact with them before releasing toxic products to destroy them. In general, this attack kills cancer cells effectively and quickly. To ensure their survival and tumour growth, some cancer cells are though able to develop ingenious strategies to inhibit immune responses.

### Actin(g) as protection

Using advanced imaging techniques, LIH researchers monitored the contact point between tumour cells from breast cancer and Natural Killer cells, also known as “immunological synapse”. Doing so, they discovered that some cancer cells were able to resist the attack by Natural killer cells thanks to a very rapid remodelling of their actin cytoskeleton, dynamically concentrating at the level of the immunological synapse like a molecular shield.

Blocking this process termed the “actin response” in laboratory experiments was sufficient to restore effective destruction of cancer cells by Natural Killer cells. The researchers are thus convinced that this rapid and massive accumulation of actin filaments is associated with the resistance of cancer cells to Natural Killer cell attack.

The team now needs to understand how the actin response allows cancer cells to remain intact. The results indicate that cytoskeletal remodelling may result in a significant reduction in the amount of cytotoxic molecules transmitted from Natural Killer cells to target cells. Moreover, they aim to evaluate the possibility that the actin response also provides resistance against cytotoxic T cells.

#### IMPACTING ON PEOPLE’S HEALTH!

The discovery of the actin response opens up promising prospects for the development of new therapeutic strategies for breast cancer that could improve the effectiveness of currently applied immunotherapy. If the researchers unravel the molecular pathways that underlie the actin response, they could identify components serving as drug targets to overcome cancer cell resistance.

“ Our research work highlights a previously unknown fundamental process involved in the resistance of breast cancer cells. ”

*Dr Clément Thomas, Principal Investigator*

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#### Biocabulary:

**Actin** is a protein that forms microfilaments in the cell. It is one of the three types of filaments making up the cytoskeleton.

The **cytoskeleton** is an organised network of protein filaments inside the cell. It maintains the cell's shape and is crucial for movement of intracellular elements, cell division, muscle contraction and cell motility. It also plays critical roles in tumour cell invasion and metastasis.

A **drug target** is a molecule in the body that is intrinsically associated with a particular disease process and could be addressed by a drug.

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

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

**T cells** are white blood cells that play a central role in the immune system. A subset of T cells has cytotoxic properties similar to that of Natural killer cells.

#### Publication:

This study was published in August in an article titled *Actin cytoskeleton remodelling drives breast cancer cell escape from Natural Killer-mediated cytotoxicity* in the scientific journal *Cancer Research*, internationally recognised in the field of oncology.

#### Collaboration:

For the project, the Cytoskeleton and Cancer Progression Research Group worked in close collaboration with the National Cytometry Platform at LIH's Department of Infection and Immunity and the INSERM unit *Immunologie Intégrative des Tumeurs* at the Gustave Roussy Institute in Villejuif, France.

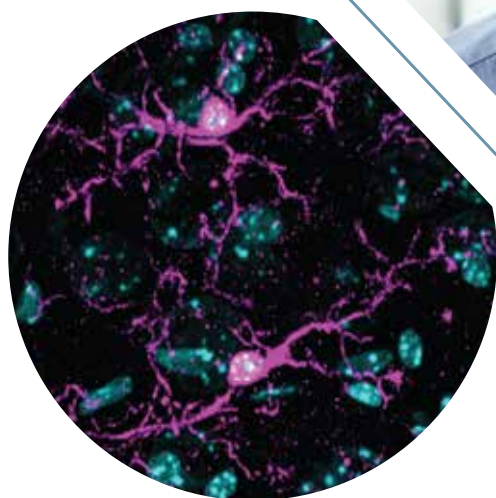
#### Funding:

This research work is a major part of the PhD thesis of Dr Antoun Al Absi who graduated in July and was supported by an AFR PhD grant from the Luxembourg National Research Fund (FNR). The research team is funded by further research grants from the FNR, F.R.S.-FNRS Télévie and *Fondation Cancer*, the Luxembourg Cancer Foundation.

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Dr Alessandro Michelucci



# MICROGLIA REACT DISTINCTIVELY DURING INFLAMMATION

Functional analysis of immune cells from the brain

*Department of Oncology > NorLux Neuro-Oncology Laboratory > Glioma Biology Research Group*

**LIH researchers have conducted a pioneering study to unravel the genetic programs that are triggered upon neuroinflammation in microglia, specialised immune cells of the central nervous system.**

## Immune control in the brain

The brain is a unique organ with its own “tailored” immune cells and mechanisms, distinct from those of the rest of the body. Microglia are resident cells that survey and modulate the neural environment, sense homeostatic perturbations and respond against infections, toxins or contaminants. They thus promote neuronal health and ensure normal brain function. Dysfunctional microglia have been observed in chronic neurological disorders such as Alzheimer’s disease, Parkinson’s disease, multiple sclerosis as well as brain cancer and are thought to worsen their outcome.

The activity of microglia during acute neuroinflammatory processes as those caused by infection remains largely elusive. Acute neuroinflammation represents the early phase of what could result in chronic inflammation and/or neurodegenerative processes. Therefore, microglial responses at this very early phase of perturbation should provide important insights into these cells’ role and adaptive capacities.



### Studying the effect of inflammation

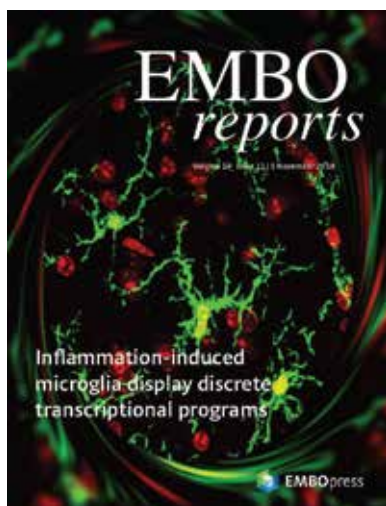
The aim of the study conducted at LIH was to uncover how microglia react during early acute inflammation. To do so, the researchers conducted experiments in mouse models\* in which they artificially induced inflammation. With state-of-the-art single-cell transcriptomics they then realised an in-depth profiling of microglia activation. This allowed to uncover distinct gene expression profiles under inflammatory conditions that greatly differ from the profiles observed in steady state conditions and in the context of neurodegenerative diseases.

Indeed, the researchers observed that the expression of genes involved in maintaining homeostasis was markedly reduced. Simultaneously, the expression of genes classically activated by inflammation was triggered. The gene expression pattern was however different from what is observed in chronic inflammation associated with neurodegenerative disorders. Importantly, they also noticed unforeseen heterogeneity among the activated cells that did not all react with the same intensity. They hypothesised that a subset of reactive microglia may be less sensitive to the inflammatory stimulus or recover more quickly from the activated state.

This research work thus revealed that microglia responses in inflammatory conditions are heterogeneous and clearly distinct from the responses described in the context of neurodegenerative diseases.

#### IMPACTING ON PEOPLE'S HEALTH!

The results obtained from single-cell transcriptomic profiling of microglia under inflammatory conditions is a first cornerstone which will contribute to the global understanding of the specific immune responses to brain disorders. This should boost the development of novel therapeutic strategies against diseases of the central nervous system.



Cover of the November issue of EMBO reports showing a confocal microscopy image of microglia

“ Our findings could inspire future studies on potential therapies to restore normal microglia function at an early onset of inflammation to avoid entering into a chronic phase causing neurological disease. ”

*Dr Alessandro Michelucci, project leader*

#### Biocabulary:

A **genetic program** of a cell is a physiological change brought about by a temporal pattern of activation of a particular subset of genes.

**Homeostasis** is the state of steady internal physical and chemical conditions maintained by living systems. This equilibrium is the condition of optimal functioning at the level of the organism and at cellular level.

**Microglia** are non-neural resident cells of the central nervous system, located throughout the brain and spinal cord. They act in the immune defence as well as in the development and function of the adult brain.

**Neuroinflammation** refers to the inflammation of nervous tissue that can be triggered in response to a variety of cues such as infection or traumatic brain injury.

**Single-cell transcriptomics** is a high-throughput sequencing technique that examines the level of expression of genes of individual cells from a biological sample.

#### Publication:

The study was published as a scientific report in the November issue of the acclaimed journal *EMBO reports*. Featured on the journal cover, the report titled *Single-cell transcriptomics reveals distinct inflammation-induced microglia signature* stands out as the most read article of the issue since its online release in September.

#### Collaboration:

The project involved a fruitful collaboration of the Glioma Biology Research Group with scientists from the Proteome and Genome Research Unit at LIH's Department of Oncology as well as with teams from the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg.

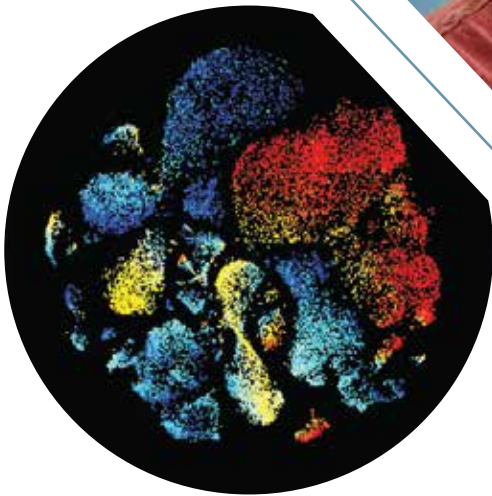
#### Funding:

This research work is a major part of the PhD thesis of Dr Carole Sousa who graduated in March, supported by an AFR PhD grant from the Luxembourg National Research Fund (FNR) and by funding from *Fondation du Pélican de Mie et Pierre Hippert-Faber*, a foundation under the aegis of *Fondation de Luxembourg*. The research team was supported by further research grants from the FNR and the National Institutes of Health.

\*National and European animal experimentation and animal welfare guidelines are strictly applied for all LIH research projects involving *in vivo* experiments.



*Dr Etienne Moussay*



*High-dimensional mass cytometry  
analysis of mouse spleen samples*

## TWO ARE BETTER THAN ONE: CONTROLLING LEUKAEMIA BY DUAL TREATMENT

Preclinical study of antibody-based immunotherapy

*Department of Oncology > Laboratory of Experimental Cancer Research > Tumour Stroma Interactions Research Group*

To ensure their survival and growth, tumour cells in chronic lymphocytic leukaemia are able to establish a microenvironment in which the body's immune response is suppressed. A team of researchers from LIH succeeded in characterising this microenvironment at the cellular and molecular level and proposes a dual treatment that can effectively inhibit the development of the disease.



Chronic lymphocytic leukaemia only develops in an environment that promotes tumour proliferation. When tumour cells infiltrate into tissue, they come into contact with healthy cells, including immune cells. To ensure their growth, tumour cells establish a protective microenvironment around them in which immune cells are hindered to become active.

### Mapping the tumour surroundings

As the tumour microenvironment is not well studied in leukaemia yet, LIH researchers analysed in detail the immune cell populations surrounding tumour cells with cytometry techniques. By comparing spleen samples from diseased mice with those from healthy mice\*, the researchers found out that the presence of tumour cells caused a significant reorganisation of the different immune cell types and subtypes.

For instance, the tumour microenvironment contains a larger quantity of immune cells that act as regulators and inhibit the immune response. Scientists also observed that immune cell types have a large number of molecules on their surfaces that act as immune checkpoints downgrading the immune response. Based on the newly gained knowledge on the composition and features of immune cells in the tumour microenvironment, the scientists explored whether treatments with antibodies that act as inhibitors of immune checkpoints could serve as immunotherapy to reboot the immune defence against leukaemia.

### Therapy with two antibodies

By testing several antibodies in single and double therapy in mice, the team found that only the simultaneous targeting of two specific immune checkpoints named PD1 and LAG3 effectively blocked tumour growth. This dual treatment is capable of changing the immune cell composition of the tumour microenvironment. The treatment caused a recruitment of more effector immune cells capable of attacking cancer cells. In addition, it reduced the abundance of regulatory cells that block the immune response.

#### IMPACTING ON PEOPLE'S HEALTH!

The dual immune checkpoint blockade could constitute a new therapeutic strategy against chronic lymphocytic leukaemia. The treatment may be tested in clinical trials with intravenous administration.

“ *Our preclinical study represents a significant advance in leukaemia research as it has broadened our knowledge of the tumour microenvironment.* ”

*Dr Etienne Moussay, Principal Investigator*

Dr Jérôme Paggetti



“ *Our work points to an effective immunotherapy based on immune checkpoint inhibitors.* ”

*Dr Jérôme Paggetti, co-Principal Investigator*

#### Biocabulary:

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

**Chronic lymphocytic leukaemia** is a blood cancer affecting adults over 50 years of age. It originates in the blood-forming cells of the bone marrow and spreads to other organs through the bloodstream. The disease is currently incurable, but various existing treatments can prolong life expectancy.

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

**Immune checkpoints** are molecules on the surface of certain immune cells that regulate the immune system. Cancer cells can find ways to use these checkpoints to avoid being attacked. The blockade of immune checkpoints by specific inhibitors is a therapeutic strategy.

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

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

#### Publication:

The findings were published in April in the acclaimed scientific journal *Blood*. The article, first-authored by PhD candidate Marina Wierz, is titled *Dual PD1/LAG3 immune checkpoint blockade limits tumour development in a murine model of chronic lymphocytic leukaemia*.

#### Collaboration:

For the study, the Tumour Stroma Interactions Research Group collaborated with researchers from the National Cytometry Platform at the Department of Infection and Immunity and from the NorLux Neuro-Oncology Laboratory at the Department of Oncology.

#### Funding:

The project was supported by grants from the F.R.S-FNRS Télévie, the Luxembourg National Research Fund and the European Regional Development Fund.

\*National and European animal experimentation and animal welfare guidelines are strictly applied for all LIH research projects involving *in vivo* experiments.



Dr Gloria Aguayo



# ASSOCIATING FRAILTY TO CARDIOVASCULAR DISEASE AND MORTALITY

Health outcome in elderly people

Department of Population Health > Epidemiology and Public Health Research Unit

Frailty is common in elderly people and goes along with elevated mortality. Many scores have been developed to assess frailty and evaluate health outcomes. LIH researchers analysed a wide range of existing frailty scores and revealed a link with future mortality and cardiovascular disease but not with cancer.



### More than 30 frailty scores evaluated

No consensus exists on the definition of frailty. There is no gold standard to assess it and to make predictions on disease and mortality. Researchers from LIH and collaboration partners therefore examined the predictive ability of 35 frailty scores-identified by a systematic literature review-on their ability to predict all-cause mortality, cardiovascular disease and cancer. Data was used from 5,294 adults aged 60 years or more and followed up over a period of seven years within the English Longitudinal Study of Ageing.

The researchers observed that all frailty scores were associated with mortality, some were also associated with the incidence of cardiovascular disease, but none were associated with cancer events. In models adjusted for demographic and clinical information, 33 out of 35 frailty scores showed significant added predictive performance for all-cause mortality. Certain scores outperformed others with regard to all-cause mortality and cardiovascular health outcomes in later life. Multidimensional frailty scores may have a more stable association with mortality and incidence of cardiovascular disorders.

### Clear added value

The study provides a direct comparison of the most complete list of frailty scores examined to date, using an advanced and reproducible methodology, in a well-characterised cohort representing the general elderly population. It is the first study to compare the performance of frailty scores with respect to cancer incidence. It highlights the vast heterogeneity in the composition and performance of existing frailty scores. The comparative evaluation of strength of associations between different frailty scores and major health outcomes made in this study provides a solid evidence base for researchers specialised in the field and of course for health professionals dealing with elderly patients.

#### IMPACTING ON PEOPLE'S HEALTH!

The findings of this study on frailty scores shall help clinicians in choosing the most appropriate instrument to assess frailty in their patients. A better prediction of associated health risks can help to prevent a rapid health decline in frail elderly people.

“ *This study addresses one of the most relevant issues in healthcare and research on ageing populations: how to diagnose and assess frailty.*”

*Dr Gloria Aguayo, project leader*

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#### Biocabulary:

**All-cause mortality** refers to the deaths that occur in a population, regardless of the cause.

**Cancer incidence** is the rate of new cases of cancer disease.

A **cohort** is a group of individuals from which samples and data is collected over a period of time.

**Frailty** is a state on vulnerability in the elderly that embodies an elevated risk of catastrophic declines in health.

**Frailty scores** express the degree of frailty of a person on a scale assessed with a combination of tests and questionnaires.

#### Publication:

The scientific article for this study, first-authored by Dr Gloria Aguayo, was published in March in a special issue on *Cardiovascular disease and multimorbidity* in the Open Access journal *PLOS Medicine*. It appeared as featured article in a press release by the journal. The title of the publication is *Comparative analysis of the association between 35 frailty scores and cardiovascular events, cancer, and total mortality in an elderly general population in England: An observational study*.

#### Collaboration:

The study is the result of a tight collaboration of researchers from the Epidemiology and Public Health Research Unit with LIH's Competence Centre for Methodology and Statistics, the University of Liège (Belgium), the VU University Medical Centre in Amsterdam (Netherlands), the University of Western Ontario (Canada) and the Aarhus University (Denmark).

#### Funding:

The research work was supported by intramural funding.

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Dr Michel Vaillant



# A NEW DRUG TO TREAT RIVER BLINDNESS IN AFRICA

Clinical trials for moxidectin

*Department of Population Health > Competence Centre for Methodology and Statistics*

LIH had been intensively involved in the phase 3 of a clinical trial for a new drug against the parasitic disease onchocerciasis, commonly known as river blindness. The trial was a success: the tested drug moxidectin reduces parasite levels in the skin better and for longer than ivermectin, the only drug currently registered for onchocerciasis.



Onchocerciasis is the second leading cause of infectious blindness and the fourth leading cause of preventable blindness worldwide. The drug ivermectin kills the early parasite life stage in the skin and eyes (microfilariae) causing the disease symptoms. It also reduces - but does not prevent - production of new microfilariae by the adult parasite life stage (macrofilariae). Mass drug administration with ivermectin, donated by the pharmaceutical company Merck & Co, is used to control onchocerciasis as a public health problem in Africa and may even eliminate parasite transmission in some areas.

### Comparing two drugs

A phase 3 clinical trial was initiated to test whether the drug moxidectin, a molecule from the same chemical group as ivermectin, is more powerful than the standard treatment. The randomised, double-blind study conducted in Ghana, Liberia and the Democratic Republic of the Congo, compared the efficacy and safety of a single oral dose of moxidectin and ivermectin in almost 1,500 participants included between 2009 and 2011. LIH took a central role in data management and statistical analysis which was essential to handle and interpret the large data sets generated by the trial.

The study found that microfilarial loads in the skin of patients suffering from onchocerciasis were lower after moxidectin treatment than after ivermectin treatment, often reduced to an undetectable level. Moreover, moxidectin appeared to be safe to be used in mass drug administration. As microfilariae cause the disease and are the source for transmission, the new drug is expected to reduce parasite transmission between treatment rounds more efficiently than ivermectin.

### Submission for drug approval

A new drug application for moxidectin as an oral treatment for river blindness was submitted by the not-for-profit organisation Medicines Development for Global Health (MDGH) to the Food and Drug Administration of the United States. It qualified for priority review and was accepted within six months.

#### IMPACTING ON PEOPLE'S HEALTH!

Today, patients can already benefit from the outcome of this clinical research study. In June, the Food and Drug Administration of the United States approved moxidectin tablets for oral treatment (8 mg single dose) of onchocerciasis in patients aged 12 years and older.

“ *The use of moxidection could accelerate the progress towards elimination of river blindness and thus be beneficial for a significant part of the world's population.* ”

Dr Michel Vaillant,  
Head of the Competence Centre for Methodology and Statistics

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#### Biocabulary:

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

**Onchocerciasis** or **river blindness** is a tropical disease caused by the parasitic worm *Onchocerca volvulus* that is transmitted through the bites of black flies. The disease symptoms include severe skin inflammation, intense itching, enlarged lymph nodes and visual impairment that can ultimately lead to blindness.

The **phase 3** of a clinical trial compares a new treatment with the best currently available standard treatment.

#### Publication:

The clinical trial results are reported in an article that was released in January in the high-impact journal *The Lancet*. It is entitled *Single dose moxidectin versus Ivermectin for Onchocerca volvulus infection in Ghana, Liberia, and the Democratic Republic of the Congo: a randomised, controlled, double-blind phase 3 trial*.

#### Collaboration:

The project was led by TDR, the Special Programme for Research and Training in Tropical Diseases hosted at the World Health Organisation. Multiple scientists and collaborating organisations from different countries were involved in the clinical studies leading to final drug approval. Dr Michel Vaillant from LIH's Competence Centre for Methodology and Statistics was responsible for supervising data management and conducted the statistical analysis in collaboration with Dr Christine Halleux and Dr Annette Kuesel from TDR. LIH also contributed to the submission of the drug application while working together with Syne Qua Non, a Contract Research Organisation contracted by MDGH.

#### Funding:

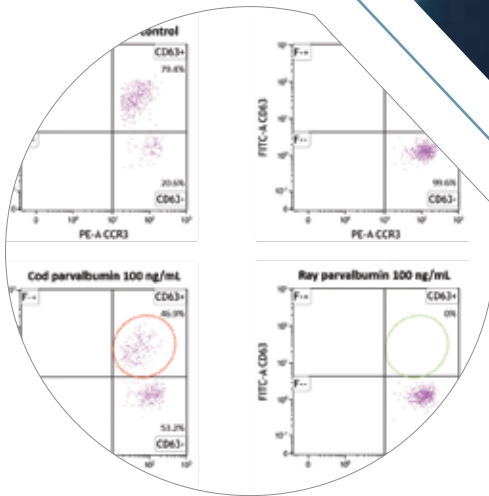
This study was funded by TDR. It utilised contributions from the African Programme for Onchocerciasis Control, the pharmaceutical company Wyeth/Pfizer and TDR donor countries.

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Dr Annette Kuehn



Cytometry analysis showing immune cells activated by cod parvalbumin but not ray parvalbumin

# NEW HOPE FOR FISH ALLERGY SUFFERERS

Ray consumption can be safe

Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Molecular and Translational Allergology Research Group

**Fish allergy is one of the most dangerous food allergies as it can cause potentially life-threatening symptoms such as anaphylactic shock. A research team involving scientists from LIH discovered that fish allergy sufferers can tolerate cartilaginous fish.**

Fish is a healthy nutrient source providing easy digestible protein and omega-3 fatty acid. People who do not eat fish need to pay attention to consume certain seeds and nuts to get sufficient amounts of the essential fatty acid.



“ Our findings indicate that those suffering from fish allergy do no longer have to exclude fish from their diet.”

Dr Annette Kuehn, Principal Investigator

### Possible food alternative

In a new study, an international research team focused on the protein parvalbumin, responsible for triggering fish allergy. They found that the parvalbumin contained in the flesh of cartilaginous fish has a lower allergenicity than that of bony fish, which is consumed much more often. The thornback ray (*Raja clavata*), a cartilaginous fish, was identified as a possible food alternative for fish allergy sufferers. In the study, almost all subjects were able to consume the ray without any allergic reaction, despite proven and sometimes severe allergy to fish.

The thornback ray can thus be a nutritional alternative for people with fish allergy. The ray is found in the Eastern Atlantic, around Norway, the North Sea and even Namibia and is available in food stores in Luxembourg. It is currently enjoying a resurgence as edible fish delicacy. The wing-like pectoral fins are cooked as a filet.

The research findings have far-reaching potential. The team plans to globally expand the study, which initially focused on the European population, to ultimately significantly improve the quality of life of many people suffering from fish allergy. The range of tested fish species shall also be enlarged.

### IMPACTING ON PEOPLE'S HEALTH!

People allergic to fish do not need to avoid a particularly healthy food source, as they may be able to eat thornback ray without developing any allergic symptoms. They should however first consult an allergy specialist and be tested for tolerance to this fish type.

### Biocabulary:

**Allergenicity** refers to the potential of triggering an allergic reaction.

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

An **anaphylactic shock** is a serious, life-threatening allergic reaction affecting the whole body.

**Parvalbumin** is a small globular protein of the family of albumins.

### Publication:

The study co-authored by Dr Annette Kuehn, Dr Christiane Hilger and Prof Markus Ollert was issued online in November in the *Journal of Allergy and Clinical Immunology: In Practice* with the heading *Fish-allergic patients tolerate rays based on the low allergenicity of its parvalbumin*.

### Collaboration:

The Molecular and Translational Allergology Research Group worked in close collaboration with partners from the *Centre Hospitalier de Luxembourg* (CHL), the Medical University of Vienna (Austria), the University Hospital St. Pölten (Austria) and the James Cook University in Townsville (Australia). All allergy and control subjects were enrolled at the CHL and the clinical samples were processed at LIH.

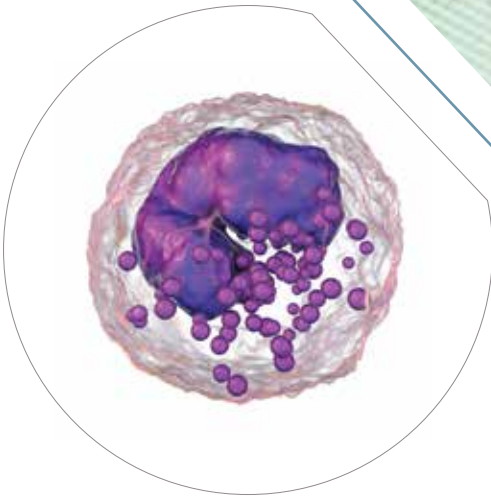
### Funding:

The project was funded, amongst others, by the Austrian Science Fund and the Luxembourg National Research Fund.





*Dr Christiane Hilger*



*Model of a basophil*

# WHO IS 'AT STEAK'? NEW DETECTION METHOD FOR RED MEAT ALLERGY

## Diagnosis of alpha-gal syndrome

*Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Molecular and Translational Allergology Research Group*

**Alpha-gal syndrome is a rare allergy related to red meat consumption. With substantial involvement of LIH, a German-Luxembourgish research team developed a new diagnostic method, a blood test that is based on the activation of immune cells named basophils.**

### **Singular allergy**

Biting down into a juicy grilled steak can be dangerous. In 2009, American scientists confirmed that humans can develop an allergy to mammalian meat. In particular, for those who have once suffered a severe inflammatory response to a tick bite, red meat consumption becomes a serious risk. Possible consequences of eating red meat then include symptoms like skin rashes, shortness of breath, or even anaphylactic shock.



“ When the basophils from blood samples strongly react to alpha-gal, they light up in our test.”

Dr Christiane Hilger, Principal Investigator

The direct trigger for this rare condition, known as alpha-gal syndrome, is a carbohydrate named galactose-alpha-1,3-galactose, or shortly alpha-gal, residing on the surface of mammalian cells but absent in humans. The allergic reaction does not start as soon as the food is chewed – as is the case with apple allergy for example – but in most cases only after a delay of two to six hours when alpha-gal reaches the bloodstream. It is therefore not easy to attribute the allergic symptoms to the consumption of meat.

### Safe and efficient test

So far, the only way to diagnose the allergy has been to perform a provocation test, where allergy sufferers would eat increasingly large amounts – under medical supervision – until an allergic reaction occurred. Because of the time delay, this test is very elaborate and not without risks. It is also possible to identify a sensitisation to alpha-gal, by detecting the presence of antibodies specific to alpha-gal. However, this method has never helped to estimate the actual severity of an allergic reaction. The team of scientists and clinicians has developed further a far more efficient test for diagnosing alpha-gal syndrome.

For their work, the researchers analysed the behaviour of basophils. These react strongly to various allergens, including alpha-gal, if an allergy exists. The team set up a test kit that contains, among other things, the allergen alpha-gal and certain fluorescent cell markers. Blood is drawn from the patient and brought into contact with the substances of the test kit. Next, basophils are monitored by a cell analysis technique named flow cytometry. The research team studied blood samples from more than 50 patients. From the fluorescence signal, the researchers were able to identify very clearly those persons who have developed a meat allergy.

### IMPACTING ON PEOPLE'S HEALTH!

The oral provocation test currently used in clinical settings may be replaced by this novel detection method that is based on basophil activation and flow cytometry and simply requires a blood sample to be taken from the patient. This safer and quicker test will make it possible to diagnose much more easily a rare but dangerous allergy.

### Biocabulary:

An **allergen** is a substance capable of triggering an allergy.

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

An **anaphylactic shock** is a serious, life-threatening allergic reaction affecting the whole body.

**Basophils** are a type of immune cell that play a role in inflammation and allergy. They belong to the granulocytes, a cell type containing granules with active molecules to be secreted.

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

A **fluorescent cell marker** is a molecule that binds to specific proteins on the cell surface. By emitting fluorescence after excitation the marker allows the detection of the specific proteins.

**Galactose-alpha-1,3-galactose**, shortly termed **alpha-gal**, is a carbohydrate (sugar) present in most mammalian cell membranes. It is not found in primates, including humans, as the gene necessary for its synthesis was lost during evolution.

### Publication:

The findings were published online in August in the *Journal of Allergy and Clinical Immunology*. The research article, co-authored by Dr Christiane Hilger, Kyra Swiontek and Prof Markus Ollert, is available under the title *The basophil activation test differentiates between patients with alpha-gal syndrome and asymptomatic alpha-gal sensitisation*.

### Collaboration:

The Molecular and Translational Allergology Research Group worked with scientists from the Technical University of Munich (Germany) who led the project and partners from the *Centre Hospitalier de Luxembourg* and the Eberhard Karls University of Tübingen (Germany).

### Funding:

This research work was financed with intramural funding.



*Dr Brice Appenzeller*



*Hair sample for biomonitoring*

# MULTIPLE PESTICIDE EXPOSURE DURING PREGNANCY

Biomonitoring in hair samples of pregnant women

*Department of Population Health > Human Biomonitoring Research Unit*

**Currently used and banned pesticides can have adverse effects on future mothers and their unborn children. LIH researchers assessed the exposure to pesticides using hair samples from a French birth cohort and revealed the exposure to multiple pesticides.**

## **Hair as biomonitoring matrix**

In contrast to blood and urine samples, hair samples allow to get data on long-term exposure to chemicals. As hair grows on average one centimetre per month, one centimetre of a hair strand contains information on one month of exposure.

The present study, conducted in France and Luxembourg, aimed to monitor the cumulative exposure of pregnant women to different pesticides by analysing hair samples collected shortly after delivery. Hair strands from more



than 300 subjects were collected in French maternities from a cohort for a large health study named ELFE. The women were aged 30 years on average and living in south-western or north-eastern parts of France, representing two different agricultural environments.

### Striking pesticide contamination

The LIH researchers used advanced methods of analytical chemistry to discriminate between 140 components from more than 20 chemical classes of pesticides. The median number of different chemicals detected in the hair samples was 43, the minimum being 25 and the maximum 65. Overall, 122 compounds were detected at least once and 28 of them even in over 70% of the samples. The most frequently detected pesticides were organochlorines, organophosphorus compounds, pyrethroids (insecticides) and acidic herbicides. The highest median concentrations were found for permethrin, an insecticide mostly used in stays against mosquitoes, p-nitrophenol, a metabolite of organophosphorous pesticides, and pentachlorophenol, a broadly used pesticide and disinfectant.

The team was also able to observe inter-trimester differences in the exposure when segmenting the hair in three parts representing the hair growth during the three trimesters of pregnancy.

This study is the largest ever carried out in France with pregnant women in terms of number of simultaneously tested compounds. Several chemical groups had been rarely or even never included in previous human biomonitoring studies.

#### IMPACTING ON PEOPLE'S HEALTH!

This project is of high relevance for public health as several pesticides are suspected to have detrimental health effects on the child, such as prematurity, increased risk of congenital malformation, impairment in neurodevelopment, or to act as endocrine disruptors interfering with the hormone system of the mother and the foetus. Further studies are necessary to link hair contamination to health outcome and to assess the full implications of pesticide exposure on the human body.

“ With our research work we provide new knowledge to an understudied topic: presumably every pregnant woman is exposed to a large range of pesticides.”

*Dr Brice Appenzeller, Principal Investigator*

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#### Biocabulary:

**Biomonitoring** is the measurement in blood, urine, tissue or hair samples of the presence of toxic chemical compounds or their metabolites, reflecting the body's exposure to harmful substances.

A **cohort** is a group of individuals from which samples and data is collected over a period of time.

In statistics, the **median** is a measure of central tendency. It separates the higher half from the lower half of a data sample.

A **pesticide** is a chemical that prevents, destroy or controls pests, or protects plants as well as plant products.

#### Publication:

This study was published in July in the journal *Environmental International* under the title *Multiple pesticide analysis in hair samples from pregnant French women: Results from the ELFE national birth cohort*. It is second-authored by Emilie Hardy and last-authored by Dr Brice Appenzeller.

#### Collaboration:

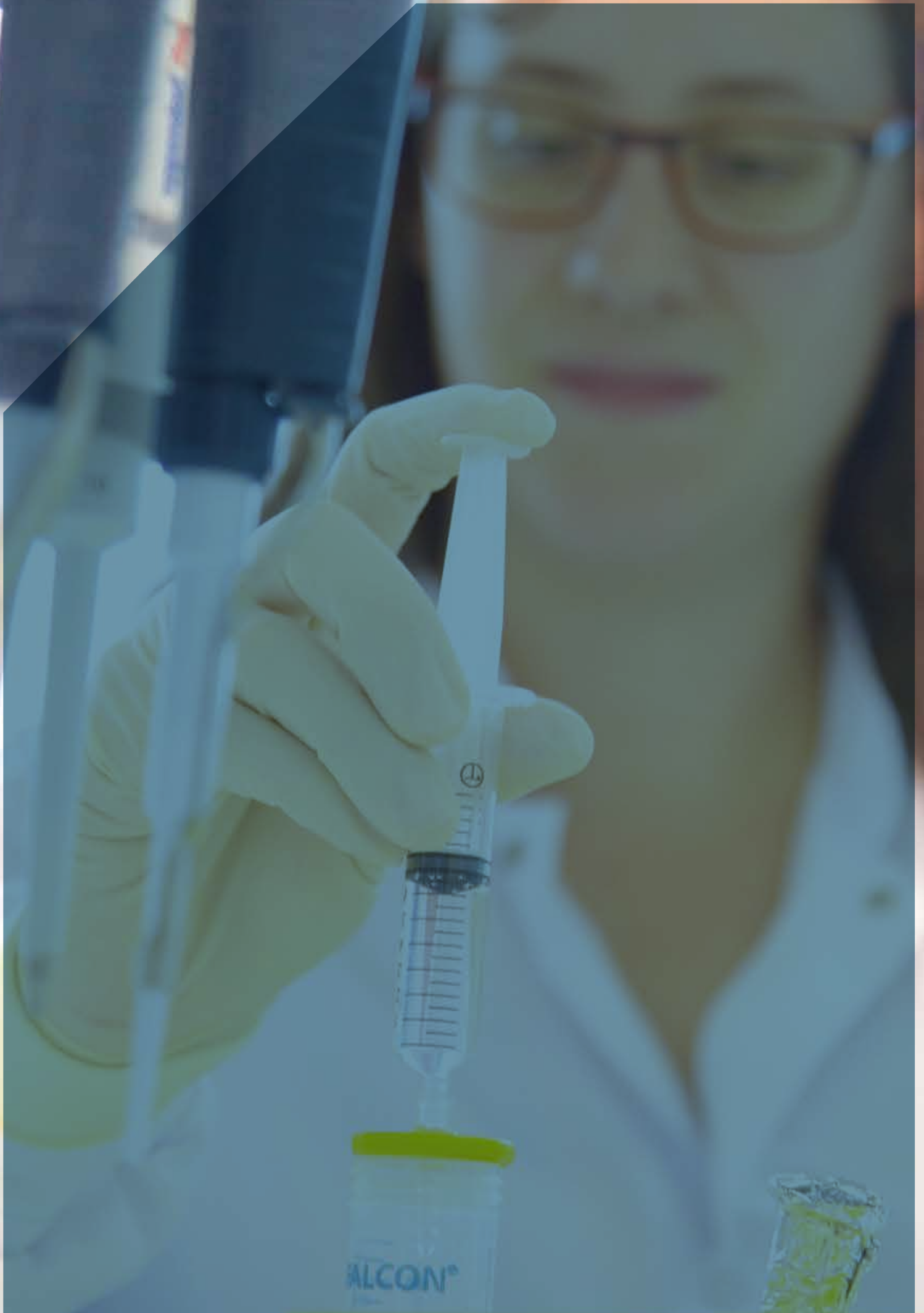
The research work resulted from a collaboration between the Human Biomonitoring Research Unit, the University of Rennes, Inserm - *Institut national de la santé et de la recherche médicale* and the European Food Safety Authority, France.

#### Funding:

The project was funded amongst others by the French Agency for Food, Environmental and Occupational Health & Safety.

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SCIENTIFIC  
EXPERTISE



Dr Manon Gantenbein



# A RELIABLE PARTNER FOR CLINICAL RESEARCH IN LUXEMBOURG

10<sup>th</sup> anniversary of CIEC

Department of Population Health › Clinical and Epidemiological Investigation Centre

**In 2018, the Clinical and Epidemiological Investigation Centre (CIEC) celebrated its 10<sup>th</sup> anniversary. The centre supports physicians and researchers in Luxembourg in clinical research projects and assists pharmaceutical companies in implementing clinical trials in the country.**

## Creation of the centre

Ten years ago, when clinical research was being built in Luxembourg, the idea of developing a “national clinical research centre”, independent of the local hospitals, came up. This centre should enable the development of high-quality clinical research, bringing together the essential skills and acting as a coordinator in national or international projects. Thus, in 2008, the CIEC was created, at the initiative of Dr Jean-Claude Schmit, at that time Chief Executive Officer of the CRP-Santé, which later became LIH. For more than five years, Dr Anna Chioti led the CIEC. Presently, Dr Manon Gantenbein is the Head of the centre. She supervises a team of 19 people including clinical research coordinators, associates and nurses.

## Supporting and promoting clinical research

One of the main missions of the CIEC is to provide logistical and operational support to health professionals as well as to pharmaceutical companies for the planning and implementation of clinical trials. The centre pays particular attention to protecting the rights and data of the volunteer study participants. Its staff is always up to date on regulations and good clinical practices. The centre thus offers the necessary regulatory framework for the implementation of any research project involving human participants. By participating in innovative research projects, the CIEC offers the opportunity to many patients to access the latest generation of treatments that are more effective and have fewer side effects than conventional treatments.



The centre is also involved in international networks such as the European Clinical Research Infrastructure Network (ECRIN), which allows the participation to multinational projects in part funded Horizon 2020, the European Framework Programme for Research and Innovation. This activity contributes to placing Luxembourg on the world map of clinical research.

The promotion of clinical research to the lay public and especially young people is also part of the centre's missions. Each year the CIEC holds events that raise awareness on clinical research such as the Medical Research Day jointly organised with the *Centre Hospitalier de Luxembourg* since 2015. At the Medical Research Day, researchers and clinicians present their current projects to an audience of over 200 high school pupils.

Every year, the CIEC organises a training session in Good Clinical Practice provided by external experts, so that any health professional involved in the conduct of a project with human participants is adequately trained. The centre also annually welcomes students for visits or internships to give them insights into the activities and present them the different clinical research professions.

### Clinical trials organised step by step

The CIEC assists researchers from the very beginning of a clinical research project. This includes assisting in the writing of a project proposal, advising on study design and methodology in collaboration with LIH's Competence Centre for Methodology and Statistics, and informing on the regulations and the deadlines for obtaining authorisations. In close interaction with the medical investigator, the CIEC evaluates the feasibility of a study by analysing in particular whether the necessary equipment is available and whether the potential population of patients concerned by the project is large enough.

The centre next manages the regulatory phase of the project, from the authorisation applications at the National Research Ethics Committee and at the Ministry of Health to the set-up of agreements between the various parties involved. Through its privileged contacts with project stakeholders such as radiology departments, analytical laboratories and hospital pharmacies, the CIEC can ensure the logistical implementation. Throughout the study, the team then organises the visits with patients or healthy participants, carries out the examinations as defined in the trial protocol, collect samples and data and securely transfers them to the project leader.

Thanks to its network of more than 70 medical investigators, the CIEC has been involved in more than 140 research projects in ten years, covering many therapeutic areas such as oncology, pulmonology or infectious diseases. In total, 7,000 participants have been included in clinical or epidemiological research projects in the ten years of existence of the CIEC.

### Digital revolution in clinical research

One of the challenges of the coming years will be the use of digital technologies for the benefit of clinical research and patients. These include for example remote consent for clinical trials, the sharing of digital medical data and the selection of personalised treatments. The CIEC must position itself as a recognised player in clinical research connecting researchers and health professionals and demonstrate its ability to use novel technologies to efficiently manage the clinical research projects of the future.

#### IMPACTING ON PEOPLE'S HEALTH!

Clinical research is defined as any medical research conducted on humans subjects. Its purpose is to evaluate the safety and efficacy of new diagnostic methods or potential new treatments to make them available to patients. The development of a new drug is a very long process starting with basic research projects, evolving to preclinical research studies and continuing in clinical trials that may, if successful, ultimately lead to drug approval. Clinical research is thus a key step in making initial laboratory results improve healthcare.

#### Biocabulary:

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

**Epidemiology** is the study of the distribution and determinants of health-related states or events, and the application of this study to the control of diseases and other health problems.

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

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

“The centre is ready to meet the upcoming challenges brought about by translational research as well as personalised and digital medicine”

*Dr Manon Gantenbein, Head of the Clinical and Epidemiological Investigation Centre*



# REPORTING KNOWLEDGE, TRENDS AND CHALLENGES IN KEY RESEARCH AREAS

High-profile scientific reviews published

Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Experimental and Molecular Immunology Research Group

## // Deregulated metabolism in immune cells

The review *B-cell Metabolic Remodelling and Cancer* that appeared in the journal *Trends in Cancer* gives insights into the metabolic changes that B cells undergo when transiting from a resting to an activated state and when differentiating to plasma cells or memory B cells. An imbalance in these tightly regulated processes can lead to the formation of malignant cells and thus to cancer. The authors point to key questions to be addressed in the recently emerged research field of immunometabolism and to possible anti-cancer strategies targeting B cell metabolism.

Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Experimental and Molecular Immunology Research Group

## // Immune cells tuned by Reactive Oxygen Species

In the review *Reactive Oxygen Species: Involvement in T Cell Signalling and Metabolism*, published in the journal *Trends in Immunology*, the authors provide a detailed overview on signalling inside T cells mediated by Reactive Oxygen Species (ROS). ROS is well known to be associated with stress responses and cell damage, but was found to also play an important role in fine-tuning T cells functions. Open questions on ROS production and the mechanisms by which it contributes to T cell activation and metabolic reprogramming are highlighted in the review.

Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Eco-Immunology and Microbiome Research Group

## // Microbiome - friends and foes in our gut

How does the gut microbiome interact with our intestinal mucosal barrier, which is the first line of innate defence that protects us from invading microbes? The review *Interactions of commensal and pathogenic microorganisms with the intestinal mucosal barrier* in the journal *Nature Reviews Microbiology* sheds more light on this question. The pathogenic and beneficial bacteria in the gut employ numerous molecular mechanisms to either traverse or disrupt the intestinal mucosal barrier, which can cause infectious or chronic diseases. The review assembles comprehensive literature to highlight the immense complexity of functional interactions taking place at the intestinal mucosal barrier in health and disease.

Department of Oncology > NorLux Neuro-Oncology Laboratory > Glioma Biology Research Group

## // How to perform genetic screens

In research, genetic screens are powerful tools to reveal genes responsible for specific biological functions. The choice of the best method among existing technologies for screens is not easy and the experimental set-up can be a challenge. The review titled *RNAi/CRISPR Screens: from a Pool to a Valid Hit* published in the journal *Trends in Biotechnology* serves as a comprehensive overview on RNA interference and CRISPR/Cas9 gene perturbation technology used for screens. It provides a critical assessment of different approaches at hand and advice on how to get robust and reproducible results and how to analyse data.

Department of Oncology > NorLux Neuro-Oncology Laboratory > Glioma Biology Research Group

## // Fascinating brain immune cells

LIH contributed to the edition of a research topic-specific issue of *Frontiers in Immunology* titled *Microglia in Health and Disease: A Unique Immune Cell Population*. It gives multiple interesting insights into the biology of microglia, a specialised resident immune cell type of the central nervous system. The issue, available as an e-book, comprises four original articles and four reviews covering different aspects of microglial biology. These depict the current understanding of different cellular and molecular mechanisms in microglia within the healthy central nervous system as well as under inflammatory, neurodegenerative and tumorigenic processes.



Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Innate Cellular Immunity and Chronic Inflammation Research Group

## // Harm potential of Natural Killer cells

The review with the title *Revisiting the Functional Impact of NK Cells* in the journal *Trends in Immunology* gives a critical overview on the current knowledge of the positive and negative functions of Natural Killer (NK) cells. These immune cells were found to not only play a protective role in immunity. They can potentially have deleterious effects by interfering with the normal immune response. Harmful activities were observed in different pathologies such as autoimmunity, infectious diseases, inflammation and cancer. The review highlights amongst others the use of NK cells in immunotherapy and argues that a deeper understanding of the harmful functions should be acquired to improve the safety of NK cell-based treatments.

Department of Infection and Immunity > Allergology-Immunology-Inflammation Research Unit > Immuno-Pharmacology and Interactomics Research Group

## // 30 years of research and paradigm shifts around an allergen

Der p 1, a protease from the house dust mite that can cause allergy of the airways, was the very first allergen to be identified by biologists. The cloning of the gene in 1988 marked the emergence of a new investigation field in allergy research: molecular allergology. At the occasion of the 30<sup>th</sup> anniversary, a review with the title *Emerging roles of the protease allergen Der p 1 in house dust mite-induced airway inflammation* summarising past and future research and open questions on Der p 1 function was edited in the *Paradigms and Perspectives* section of the *Journal of Allergy and Clinical Immunology*.

### Biocabulary:

An **allergen** is a substance capable of triggering an allergy.

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

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

**B cells** are a type of white blood cell with a major role in the immune system. Amongst other functions, they produce antibodies that can neutralise pathogens. B cells can mature and specialise to become plasma cells or memory B cells.

Molecular **cloning** refers to the process of creating copies of DNA fragments in a host organism such as bacteria.

**Commensal microorganisms** are non-harmful microbes that inhabit parts of the human organism, such as the gut.

**CRISPR/Cas9** is a recent method in molecular biology to precisely cut and edit DNA allowing to add, remove or alter genes.

**Der p 1** is the most abundant allergen contained in faecal pellets of the house dust mite. It is introduced into the body by inhalation and causes inflammation of the airways.

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

**Microglia** are non-neural resident cells of the central nervous system, located throughout the brain and spinal cord. They act in the immune defence as well as in the development and function of the adult brain.

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.

The **mucus layer** lubricates the intestine and serves as a physical and chemical barrier, in the latter case, by acting as a reservoir of anti-microbial molecules.

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

**Proteases** are enzymes degrading proteins.

**Reactive Oxygen Species** are chemically reactive chemical species containing oxygen. They are formed as a natural by-product of the cell metabolism and are produced in larger amounts under cellular stress conditions.

**RNA interference** is a regulatory system in cells that controls the activity of genes. In research, this system is used to suppress the expression of genes to study their function.

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

**Tumorigenic** means being capable of forming or tending to form tumours.





# USING BUSINESS INTELLIGENCE FOR BIOLOGY

Interview with Dr Antonio Cosma

In November, Dr Antonio Cosma joined LIH as the new Head of the National Cytometry Platform. He replaces Dr Coralie Guerin who has been in this position for three years. With more than 15 years of experience in managing core facilities, Dr Cosma has extensive expertise in developing cytometry-based assays and data analysis.

In an interview, the Italian national tells about his background, his scientific interests, the role of the National Cytometry Platform, his responsibilities and his vision for new developments.

## *Could you tell us about your educational and professional background?*

I hold a PhD in Human Biology from the Ludwig Maximilian University in Munich, Germany, and a habilitation from the University Paris-Saclay in France. I have already been working in various institutions in Italy, Germany and France before arriving in Luxembourg. During my PhD, I studied a HIV vaccination strategy, which made me specialise in the field of virology and immunology.

Over time, I became highly interested in cytometry technology, especially in the aspects on single cell analysis and data handling. My last position, which I held for nine years, was at the CEA in France – the Alternative Energies and Atomic Energy Commission – where I was in charge of managing the cytometry core facility FlowCyTech.



### ***Why are you passionate about cytometry and what challenges you in this domain?***

Cytometry is a powerful transversal technology that is in continuous evolution. It is widely used in cell biology research to tackle a diverse range of research questions. The techniques are complex and require advanced skills, especially for data analysis. I am fascinated about this complexity.

Cells can be analysed for multiple physical, chemical and biological features, each sample contains millions of cells, and a big number of samples can be processed in a single experiment. Cytometry therefore generates very large, multi-dimensional data sets. I am continuously in search of new ways to improve workflows and data management.

*A few years ago, I had the idea that business intelligence tools, normally employed by companies to analyse business information, could be an appropriate solution to analyse cytometry data. And yes, these tools can indeed be used!*

I am also passionate about mathematics and try to incorporate this knowledge into my work. As an example, I recently proposed a new method for the annotation of cell types based on prime numbers and the fundamental theorem of arithmetic.

### ***What is the mission of the National Cytometry Platform and your role as the Head?***

The National Cytometry Platform is a shared resource facility that assists researchers with cytometry experimental design, data acquisition, cell sorting and data analysis. We offer state-of-the-art equipment for flow, mass and imaging cytometry. My role is – together with my team – to advice researchers on how to address their biological questions with cytometry technology. If there is a new research project with cytometry assays, I would like the team to be involved right from the project's onset, helping to prepare

the work plan and set up protocols. I aim to create a strong connection between the research units at LIH and the platform. Of note, the platform is accessible to external researchers as well. It is planned that we extend our collaborations with other institutions in the future.

Training is also an essential duty of the core facility. To make researchers acquainted with the principles of cytometry and the possibilities it offers, I will regularly hold lectures and individual training sessions. The last years, the platform had been organising Flow Cytometry Days in partnership with cytometry equipment manufacturers. This will be continued.

### ***What makes the National Cytometry Platform so attractive to you?***

I started my career as a scientist and slowly moved to core facility management. The National Cytometry Platform serves a community of researchers trying to understand the complex relationship between human health, the immune system and the environment. This multi-facet approach represents for me a scientific and technological challenge. The close interaction with researchers creates a highly stimulating environment. Moreover, the platform is equipped with innovative instruments-amongst others for mass and imaging flow cytometry-that are rarely present in the same facility. At LIH, I thus found for me a unique occasion to professionally grow and apply my ideas to the field of single cell technology.

### ***What will be your first assignments?***

I mentioned business intelligence before. I aim to integrate it in cytometry data management at LIH as I successfully did in my previous position. The use of business intelligence can further improve the performance and quality of services provided by the National Cytometry Platform.

Business intelligence tools help standardising workflows and harmonising the way multidimensional data is analysed.

*If data is rendered more comparable, it will become possible to use existing data sets from one project to answer a research question from another project.*

Next to providing service to researchers as a platform, I also aim to develop my own research line focusing on enhanced analysis systems for studying the immune system. I am looking forward to bringing new technical advancements to the National Cytometry Platform.

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#### **Biocabulary:**

**Business intelligence** is a term referring to technologies, applications and practices used by enterprises for the collection, integration, analysis and presentation of business information to support better business decision making.

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

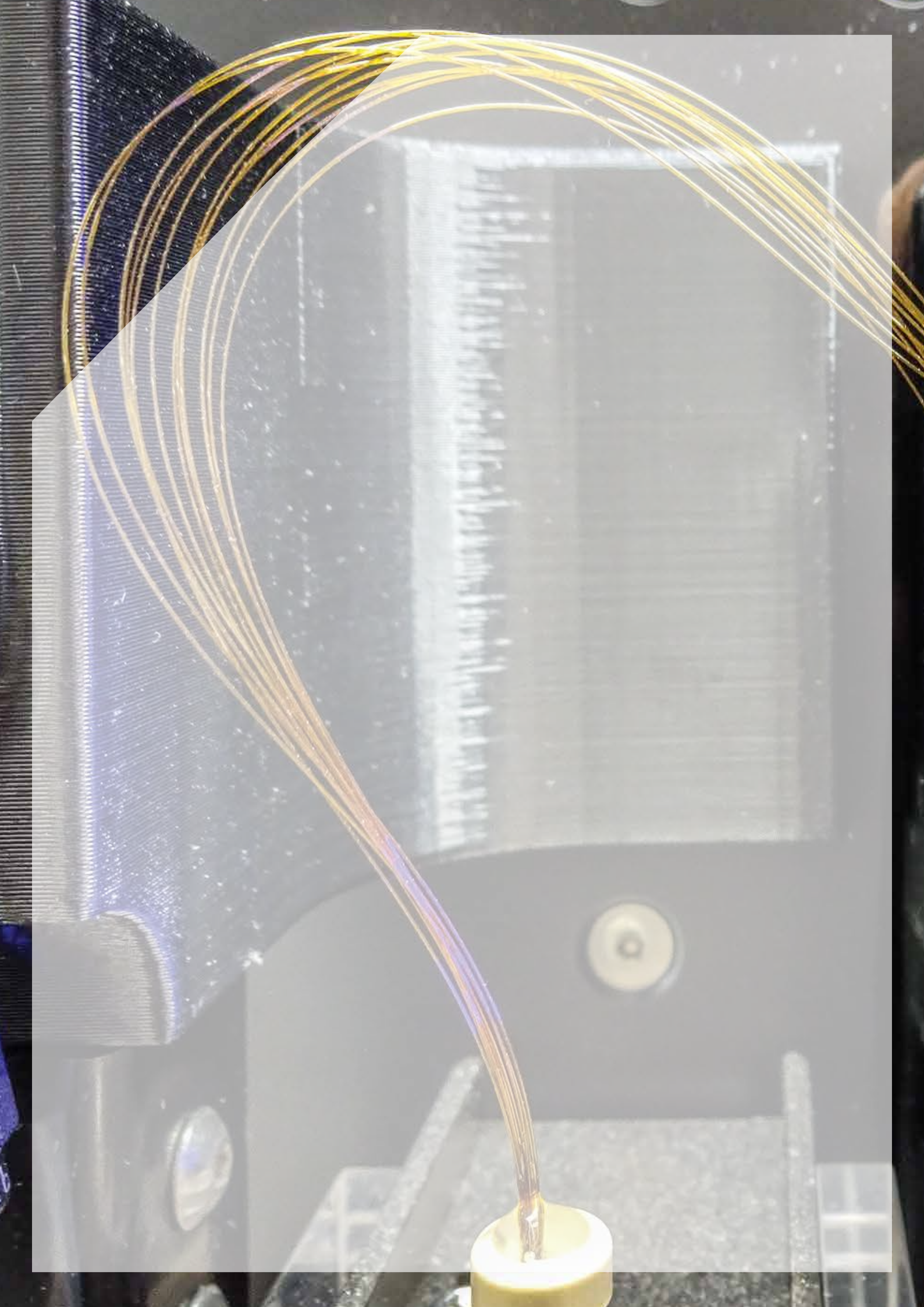
The **fundamental theorem of arithmetic** states that any natural number greater than 1 is either a prime number or can be written as a unique product of prime numbers.

**HIV** or Human Immunodeficiency Virus is a virus of the family of retroviruses. HIV infection leads over time to Acquired Immunodeficiency Syndrome (AIDS), a progressive failure of the immune system that renders the body highly vulnerable to diseases.

A **prime number** is a natural number greater than 1 that cannot be formed by multiplying two smaller natural numbers.

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**DEVELOPMENTS**

35



Prof Gunnar Dittmar



# A SEQUENCING CENTRE FOR LUXEMBOURG

Creation of LuxGen

**To accelerate biomedical research and genetic diagnosis in Luxembourg, LIH and the *Laboratoire national de santé* (LNS) teamed up to create LuxGen, a national sequencing centre.**

After more than a year of intensive negotiations, LIH and LNS signed a collaboration agreement in January to jointly set up the first sequencing platform in Luxembourg. LuxGen shall be equipped with state-of-the-art instruments for Next Generation Sequencing (NGS) and comprise satellite laboratories for the preparation of sequencing libraries in one central location.

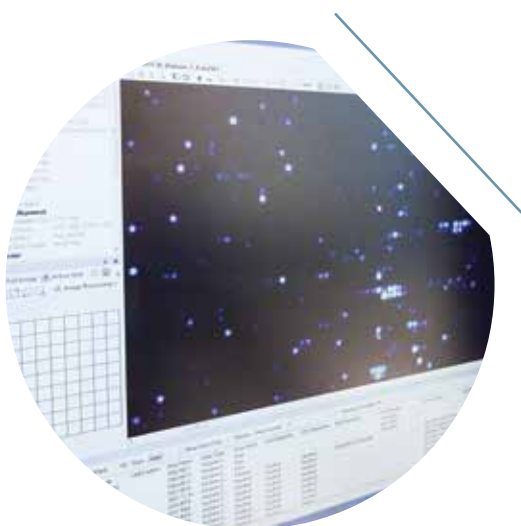


### High-end sequencing

With the creation of LuxGen, a new technological platform will be available for Luxembourg's life sciences research community, enabling deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) sequencing with NGS technology. NGS comprises a set of performant sequencing methods that allow to rapidly read large fractions of genetic information simultaneously and at a reasonable cost. Amongst other applications, the technology can be used to detect genetic abnormalities in human samples leading to disease.

The creation of a common platform for which costs are shared enables the acquisition of new and highly performant equipment. Once the platform is established, it can be used by researchers from both institutions and will subsequently be opened to external users, e.g. from the University of Luxembourg and other research centres. Luxembourg-based scientists will then not need to send samples or conduct sequencing projects abroad anymore. Having a local platform will greatly facilitate their work and is also safer regarding data storage. Moreover, LuxGen shall strengthen the visibility of biomedical research and help to strive ever more for research excellence.

The NGS equipment will be hosted in the rooms of the Department of Genetics in the brand-new building of the LNS in Dudelange. Processing of LIH's research data will be done on the high-performance computing platform of the Proteome and Genome Research Unit.



“LuxGen will allow us to perform high-end sequencing to bring biomedical research to the next level in Luxembourg.”

*Prof Gunnar Dittmar, Co-Head of LuxGen*

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#### Biocabulary:

**Sequencing** means to determine the primary structure of an unbranched biopolymer such as DNA or RNA. It allows to uncover the order/sequence of the basic units called nucleotides of DNA or RNA fragments.

#### Responsibilities:

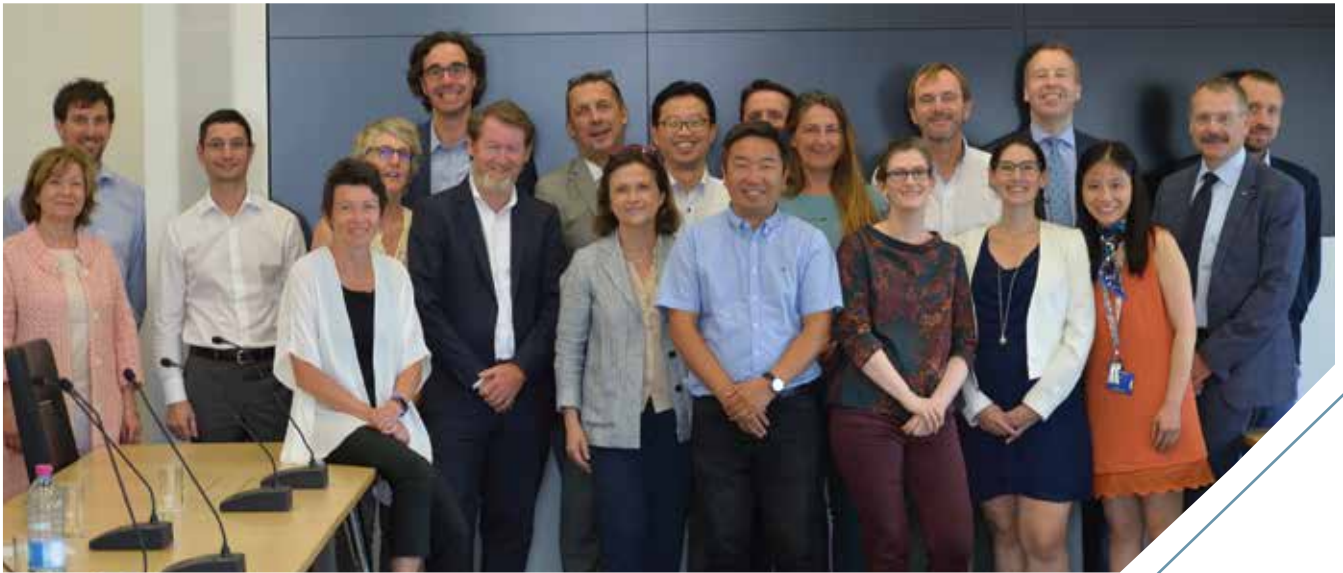
The sequencing centre is led by Prof Gunnar Dittmar, Head of the Proteome and Genome Research Unit at LIH's Department of Oncology and Dr Daniel Stieber from LNS, under the joint responsibility of Prof Ulf Nehrbass, CEO of LIH, and Prof Friedrich Mühlischlegel, Director of LNS.

#### Funding:

The platform is jointly supported by intramural funding from LIH and LNS.

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Meeting of PFP project partners

# TOWARDS TAILOR-MADE CANCER TREATMENT

Launch of the PFP project

**Identify effective tailored treatments for cancer patients. This is the vision of an ambitious multiparty project coordinated by LIH that is in line with the institute's endeavour to generate tangible results in personalised medicine for the benefit of patients.**

Cancer does not develop in the same way in every patient. Just as each individual is unique, his or her cancer and response to treatment is also unique. Drugs that are effective for one patient may not work for another, even if both have the same diagnosis.

The new project aims to set up a platform for personalised functional profiling (PFP) in Luxembourg, an innovative screening method for determining how best to fight cancer in a patient. For this purpose, a culture of tumour cells from a biopsy shall be generated and exposed to a selected panel of approved drugs. Up to 150 compounds could potentially be tested for their efficiency to eliminate cancer cells. In addition, the genetic profile of tumour cells can be elucidated by genomic analysis. This procedure will make it possible to identify within a few weeks only which treatment or combination of treatments could be the most appropriate for a given patient.

Initiated through Prof Ulf Nehrbass, Chief Executive Officer of LIH, the PFP project is carried out jointly with national and international partners from the scientific, medical and pharmaceutical sectors. To ensure the implementation of the project until the end of 2021, feasibility and clinical validation studies of the method are currently underway in collaboration with clinical partners in Luxembourg and abroad.

The clinical partners of the Mannheim Faculty of Medicine of the University of Heidelberg in Germany, and the *Institut Hospitalo-Universitaire de Strasbourg* in France have already obtained promising results for samples of patients with gastro-intestinal cancers. In Luxembourg, the pilot phase continues at the *Hôpitaux Robert Schuman* for gastro-intestinal cancers and will be extended to patients with glioblastoma, a highly aggressive brain cancer, at the *Centre Hospitalier de Luxembourg*.



## CANCER THERAPY

### STANDARD OF CARE THERAPY



The same drug to all population subtypes

### PATIENTS THAT RESPOND TO THERAPY

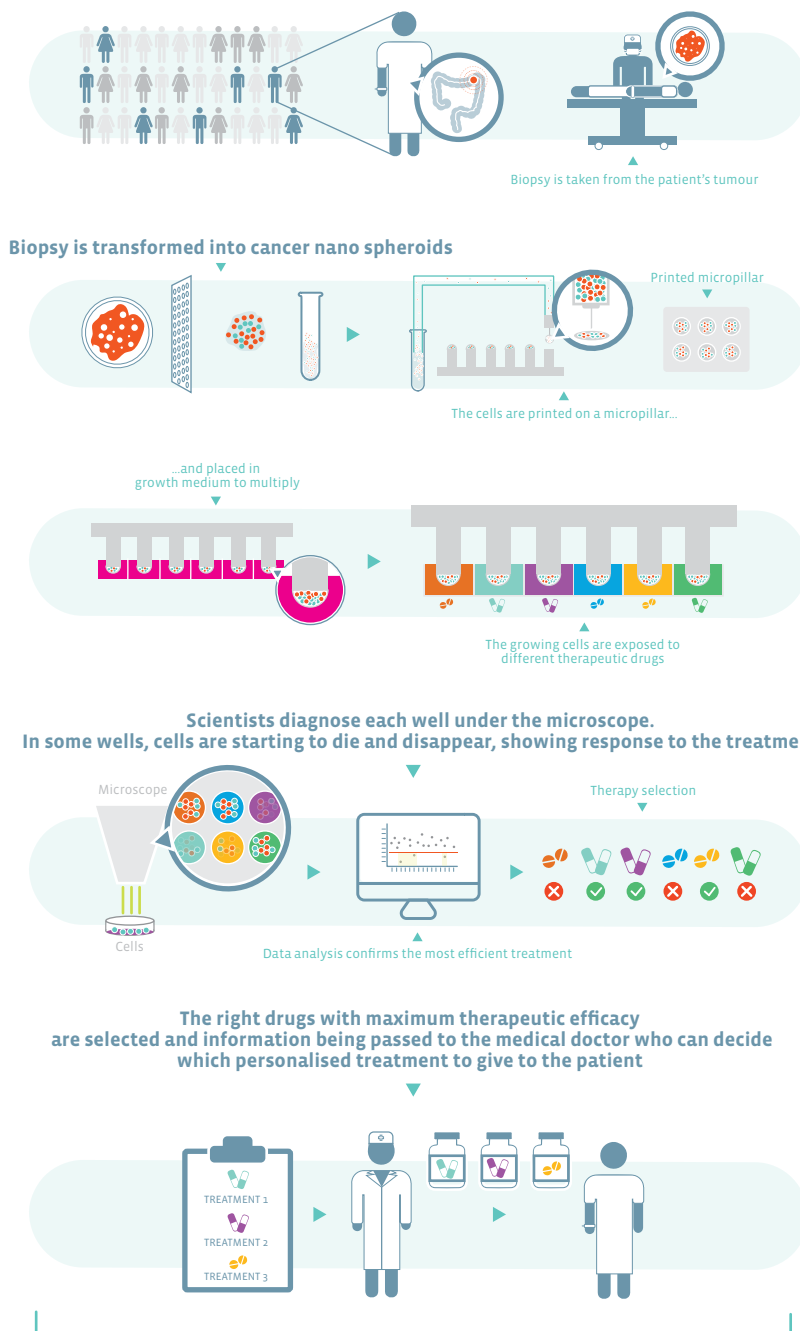


Response to therapy is only partial - there is a need for more targeted care therapy

### The solution

## Personalised Functional Profiling

Identification of the most suitable cancer therapy for individual patients



### IMPACTING ON PEOPLE'S HEALTH!

The PFP project is a translational research undertaking. If successful, it will directly impact on the treatment of cancer patients. Those will be able to benefit from a personalised therapeutic choice based on the profiling results from their biopsy.

### Biocabulary:

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

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

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

### Partners:

The PFP project is conducted in partnership with the *Hôpitaux Robert Schuman*, the *Centre Hospitalier de Luxembourg*, the *Laboratoire national de santé*, the Mannheim Faculty of Medicine of the University of Heidelberg, the *Institut Hospitalo-Universitaire de Strasbourg*, the Fraunhofer Institute for Manufacturing Engineering and Automation and MBD Medical & Bio Decision. A partnership with Norwegian institutions is under discussion.

### Responsibilities:

The project is under the medical direction of Dr Guy Berchem (LIH/Centre Hospitalier de Luxembourg) and under the scientific direction of Dr Yong Jun Kwon (LIH/Ksilink). Dr Xianqing Mao, scientific assistant to the CEO of LIH, is responsible for project management.

### Funding:

The project is supported by intramural funding and co-funded by the clinical partners.



A circular portrait of Dr. Johannes Meiser, a man with dark, wavy hair and a light beard, wearing a maroon t-shirt. The portrait is set against a light background and is partially framed by a white geometric shape on the left side.

*Dr Johannes Meiser*

# A NEW RESEARCH GROUP TO STUDY CANCER METABOLISM

Presenting ATTRACT fellow Dr Johannes Meiser

**On 1<sup>st</sup> September, LIH welcomed Dr Johannes Meiser as new junior group leader. He has been allocated a five-year term ATTRACT starting grant from the Luxembourg National Research Fund to set up his own research line in the area of cancer metabolism.**

*Department of Oncology > NorLux Neuro-Oncology Laboratory > Cancer Metabolism Research Group*

## **A passion for cell metabolism**

During his studies and early career steps, Dr Meiser has always been interested in biochemistry and more specifically in cell metabolism. He completed his PhD in plant molecular physiology in 2011 at the Saarland University, Germany, working on iron metabolism in plants. The German national then joined the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg as a postdoctoral researcher for three years. There, he investigated metabolic alterations in the context of neuro-degeneration and immunity and identified the metabolism of the amino acid serine as an important integration point during metabolic stress conditions. Subsequently, he continued working on serine metabolism in cancer during a postdoctoral stay of more than two years at the Cancer Research UK Beatson Institute in Glasgow, United Kingdom, before joining LIH.



### Investigating formate overflow

When studying metabolism in the context of cancer, it becomes apparent that tumours need to adapt their metabolism to cope with the increased nutrient demands required for growth and metastasis. According to Dr Meiser, not enough is known yet about the metabolic adaptations of cancer cells and how these could be targeted by anti-cancer therapies. Therefore, he decided to further specialise in the field of cancer metabolism.

Dr Meiser's research on cancer metabolism has already led to major scientific advances. In previous studies, he observed that cancer cells have very high rates of serine metabolism, exceeding the rates required for growth. This newly discovered phenomenon is characterised by excess production and excretion of the small metabolite formate, a process referred to as formate overflow. Dr Meiser observed that this formate overflow promotes the invasiveness of tumour cells. One of his research goals at LIH will therefore be to investigate the underlying mechanism of how formate promotes cancer invasion. The targeting of this process might be a promising entry point to inhibit tumour progression.

Dr Meiser brings a new set of scientific competences to LIH fostering the development of exciting research projects when combined with the existing know-how. He and his group will be integrated into the NorLux Neuro-Oncology Laboratory that has strong expertise in brain tumour research. Within this research environment, the new junior group leader will be able to study how serine metabolism contributes to tumour progression in the context of glioblastoma, the most frequent and aggressive form of brain cancer.

### New research team

Dr Meiser is supported by the ATTRACT scheme of the Luxembourg National Research Fund. This funding instrument is designed for researchers who are not yet established in Luxembourg and aim to build up an independent research team. Beginning of July, Dr Meiser received the positive decision from the funding agency. With a grant of 1.5 million euros, he will be able to work for five years on a tenure-tracked position and manage a research team composed of two PhD candidates and one post-doctoral researcher.

The promising researcher plans to intensively interact with researchers from LIH and the University of Luxembourg to tackle further research questions. Moreover, he intends to pursue a collaboration with the Helmholtz Institute for Pharmaceutical Research Saarland in Germany to develop compounds that target metabolism.

#### IMPACTING ON PEOPLE'S HEALTH!

The metabolism of cancer cells is distinct of that of healthy cells. Understanding the unique features of the cancer cell metabolism will allow to identify cell mechanisms or components that could serve a drug targets, thus opening avenues for new treatment options.

“ *The ATTRACT funding scheme and the research environment here in Luxembourg are ideal to set up a strong team with a positive long-term perspective.*”

*Dr Johannes Meiser, new group leader*

#### Biocabulary:

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

A **drug target** is a molecule in the body that is intrinsically associated with a particular disease process and could be addressed by a drug.

**Formate** is known as an essential building block for nucleotides and a precursor for methylation reactions.

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

**Serine** is an amino acid that is used in the synthesis of proteins.



*Dr Fabrice Mouche*



# FROM RESEARCH RESULTS TO CONCRETE APPLICATIONS

Support for value creation

*General Management > Business Development Office*

**In 2018, LIH created a Business Development Office (BDO) emerging from its former Research and Knowledge Transfer Office. The BDO supports scientists in the valorisation of their research results, transforming them into concrete applications.**

With its core missions of business development, technology transfer, intellectual property and legal activities, the BDO contributes to lay the foundation for a sustainable entrepreneurial culture encouraging innovation. In 2018, the BDO could report two major developments.



### Appointment of a business developer

With funding from the Knowledge and Innovation Transfer Support Programme of the Luxembourg National Research Fund (FNR), the BDO initiated a project named ProDev. It started in September with the arrival of a new business developer dedicated to establish a high-level business plan on translational research. The business developer will also work on selected projects with market potential. One of these projects, supported by an FNR Pathfinder grant, is about a new neuro-pharmacological modulator developed at the Department of Infection and Immunity that could potentially serve to treat pain.

### National IPR initiative

A number of Luxembourg's research institutions (LIH, Luxembourg Institute of Science and Technology, Luxembourg Institute of Socio-Economic Research, University of Luxembourg, *Laboratoire national de santé*, *Centre Hospitalier de Luxembourg*) with the support of the FNR, agreed to build a shared vision and rally around collaborative research programmes to be internationally competitive.

To go further in building synergies in transversal collaborations, the technology transfer offices of these institutions decided to build a shared framework for intellectual property rights (IPR) and exploitation rights. Coordinated by LIH's BDO, this national IPR initiative shall be translated into a letter of intent to be signed by each institution and an industrial term sheet, serving as a basis to prepare collaboration agreements. Luxembourg institutions plan to market the national initiative.

“ LIH aims to maximise the scientific, economic and societal applications of research, know-how and expertise while nurturing the excellence of research projects.”

*Dr Fabrice Mouche,*  
Head of the Business Development Office

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#### Biocabulary:

A **neuro-pharmacological modulator** is a drug that has an effect on the nervous system.

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

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

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# 10<sup>th</sup> ANNIVERSARY OF IBBL







*Dr Catherine Larue, CEO of IBBL until May 2019*

## MESSAGE FROM CATHERINE LARUE

The year 2018 gave us more than one reason to celebrate. Indeed, it marked not one, but three key milestones for our biobank. It has been a year since the move to our new facilities in Dudelange, six years since I arrived at IBBL and, most importantly, ten years since its establishment. My priority when I first embarked on this mission was to deliver on my promise to the then Ministers of Health and of Higher Education and Research: increasing the visibility of the biobank, both nationally and internationally. A full decade later, I have the pleasure of presenting the major achievements of 2018 that crowned the tenth year of IBBL's existence.

Since the very beginning, all our activities have been revolving around two strategic goals: supporting Luxembourg's biomedical research and establishing then developing international partnerships. At the national level, we are proud to have been actively contributing to numerous national projects in 2018, across a variety of areas, including Parkinson's disease, cancer and population health.

“The last ten years have been an immense satisfaction, a challenge, a pleasure. We have witnessed the transformation of our biobank from an ‘infrastructure project’ to an established and key actor in biomedical research.”



Notably, IBBL extended its commitment to the MyoRPROG study, a proof of concept funded by the National Research Fund (FNR) to validate the new MYO5B colorectal cancer prognostic biomarker discovered by researchers at the University of Luxembourg. Since 2015, IBBL has also been supporting the National Centre of Excellence in Research on Parkinson's Disease (NCER-PD) programme through sample collection, processing and storage activities. In 2018, the study consortium – which includes LIH with IBBL, the Luxembourg Centre for Systems Biomedicine (LCSB), of the University of Luxembourg, the *Centre Hospitalier de Luxembourg* (CHL) and the *Laboratoire national de santé* (LNS) – already obtained ethical authorisation for a novel post-mortem brain donation programme and finalised the study design for a cohort of early-stage PD patients, which will constitute a key part of the second phase of NCER-PD. Moreover, the biobank worked closely with hospitals, the LNS and the Ministry of Health to initiate the Cancer Plan Collection, a project of national importance aiming to expand and standardise sample collection for Luxembourgish cancer researchers.

In parallel, we have been keeping up our efforts to put Luxembourg at the forefront of European biomedical research by pursuing collaborations with international partners. In 2018, IBBL won five competitive European tenders, including the Innovative Medicine Initiatives (IMI) CardiaTeam project in collaboration with the LIH. Through IBBL, Luxembourg's research community is therefore being increasingly represented in European consortia such as Eurostars, IMI, ERA PerMed and Horizon 2020. In June 2018, IBBL also started its biobanking activities for the French National Institute of Health and Medical Research (Inserm) as part of the Constances cohort, with the aim of collecting and storing over two million samples by 2021, as well as assisting Inserm-Transfert in the first steps of the validation of a biomarker for latent tuberculosis. These important achievements have further reinforced IBBL's excellent reputation in Luxembourg and beyond its borders.

One element that characterises our biobank is our focus on quality. IBBL extensively contributed to the development of the new ISO 20387 standard, which was published in August 2018 and which defines the general requirements for biobanks around the world. We have also been actively involved in the development of the ISO 21899 standard for the validation of sample processing methods, which was approved for registration as a Draft International Standard (DIS) in December. In addition, we saw the confirmation of our ISO 17025:2005 accreditation and successfully transitioned to the ISO 9001:2015 norm. In 2018, IBBL's Biorefinery Department concluded several studies to guide researchers in their sample preparation, selection and processing decisions. The team investigated the suitability of alternative fixatives, developed an assay to characterise cold ischemia in tissues and assessed the impact of different nucleic acid extraction techniques and reagents on sample quality.

The last ten years have been an immense satisfaction, a challenge, a pleasure. We have witnessed the transformation of our biobank from an *infrastructure project* to an established and key actor in biomedical research. If we are where we are, we owe it to a very strong support network. I extend my gratitude to the

Ministry of Higher Education and Research for its continuous support over the years, to the Ministry of Economy for contributing to shaping IBBL in its infancy, and to the Ministry of Health for helping us generate added value for our patients and citizens on a daily basis. My acknowledgements also go to our local partners, clinicians and researchers for the stimulating cooperation, and to all donors – patients as well as healthy subjects – that are the driving force behind IBBL. Most importantly, I extend my heartfelt thanks to all our dedicated staff. Without their support, we would not have come this far. Looking ahead, 2019 will be marked by the continuation of our activities to support national projects, particularly during the transition to new phases as with NCER-PD. Moreover, work will be underway on the new European projects, thus ensuring our commitment to biomedical research both in Luxembourg and abroad. Here is to another eventful year!

Dr Catherine Larue  
Former CEO of IBBL







# IBBL TURNS 10 AMONG ITS LUXEMBOURG PARTNERS AND COLLEAGUES!

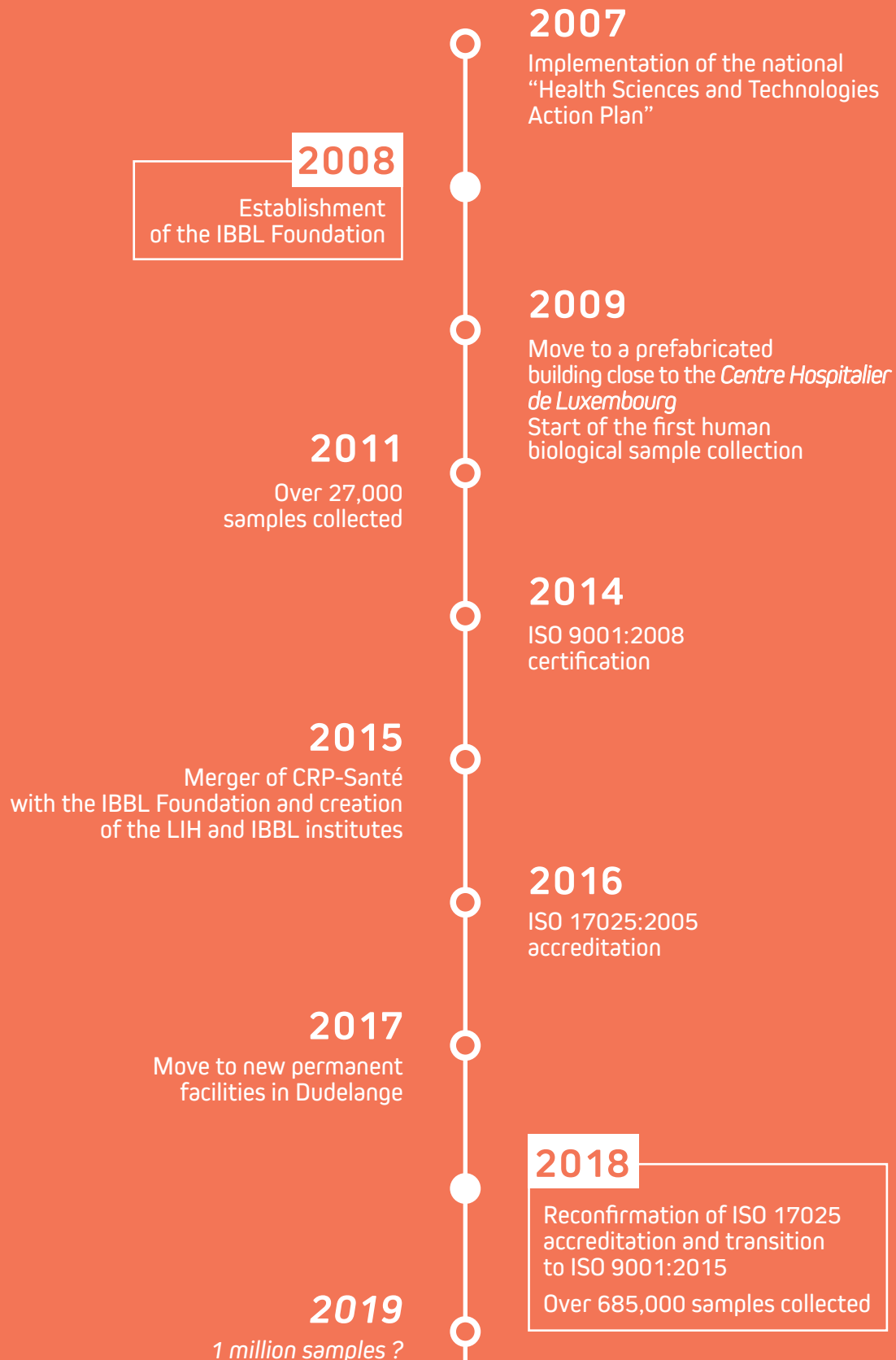
*In the last quarter of 2018, IBBL celebrated the 10<sup>th</sup> anniversary of its creation! Established in 2008 under the National “Health Sciences and Technologies Action Plan”, IBBL has been contributing over the past decade to Luxembourg’s position as an internationally-renowned centre of excellence in the field of biomedical research and personalised medicine. To commemorate the achievements since its foundation and express its gratitude to the stakeholders that have made its success possible, a celebration was organised on 9<sup>th</sup> November 2018 at its premises in Dudelange, bringing together IBBL’s partners, supporters, colleagues and friends from Luxembourg’s leading medical and research institutions in an informal and stimulating setting.*

## **IBBL - Integrated BioBank of Luxembourg: for the benefit of patients**

A biobank is optimally positioned to create a strong link between science and medicine by working closely with hospitals and clinicians on the one hand and researchers on the other. IBBL collects, processes, tests and stores biological samples, including blood, urine, tissue, saliva and stool, from volunteers, both patients and healthy individuals, with their consent. In addition, it collects medical data related to the samples, such as age, gender or diagnosis. These samples and data are then redistributed to scientists for their biomedical research projects. They are instrumental to study the causes and effects of human diseases and develop better prevention measures, diagnostic tests and therapies to improve the health status of patients. IBBL is thus a major player in driving translational research forward.



# 10 YEARS OF IBBL







"10 years ago you planted the first seeds of high-quality research made in Luxembourg. Today, I give you the symbolic result of years of passionate nurturing of such seeds. A small but sturdy tree, well anchored to the ground. Please accept it as a token of our gratitude"

Dr Catherine LARUE  
CEO of IBBL



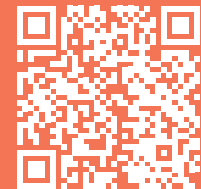
PARKINSON  
(NCER-PD)



[https://youtu.be/lm6rxg1z0\\_w](https://youtu.be/lm6rxg1z0_w)



STAFF



<https://youtu.be/Ilvo0sFlyLo>



"Biological sample collection and storage practices are a real challenge. They evolve constantly and must adapt to both the changing contexts of scientific institutions and to technological innovations. Not only has IBBL been very successful, but it is at the forefront of progress in this area"

Xavier POOS  
MINISTRY OF HEALTH

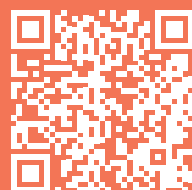


"With the arrival of Catherine Larue, European partnerships in research and innovation really took off. Thank you, Catherine, for having this vision, for following it through, and for creating a highly valued infrastructure for personalised medicine!"

Josiane ENTRINGER  
MINISTRY OF HIGHER EDUCATION  
AND RESEARCH



EORTC



<https://youtu.be/puEvk5XWddw>



CANCER  
(SOCS)



<https://youtu.be/XFB2H6Crb-A>



"I am curious to see how IBBL will look on its 25<sup>th</sup> anniversary... Will research still be done on living samples or will 90% of it be carried out on virtual computer-generated models?"

Dr Gregor BAERTZ  
PRESIDENT OF  
LIH's BOARD OF DIRECTORS



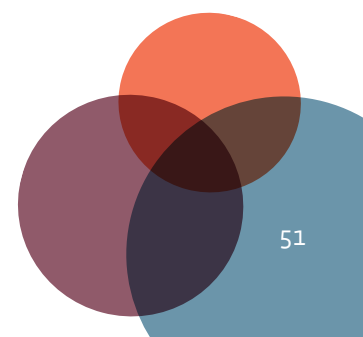


IBBL welcomed very distinguished guests for its anniversary celebration, including representatives from the Ministry of Health and Ministry of Higher Education and Research, the Mayor of Dudelange Mr Biancalana, as well as leading clinicians and researchers from Luxembourg's medical and research landscape.

The event featured a series of video projections which alternated with official speeches from Josiane Entringer from the Ministry of Higher Education and Research, Xavier Poos from the Ministry of Health, Dr Gregor Baertz (president of LIH's Board of Directors) and Dr Ulf Nehrbass (CEO of LIH). Dr Catherine Larue's speech on the importance of the support received from the Luxembourgish government, volunteer donors and IBBL's staff in the biobank's success concluded the first part. As a symbolic gesture, Dr Larue offered Mrs Entringer an olive tree symbolising IBBL's growth from the seeds planted by the Ministries.

A panel session on the evolving role of research infrastructures in personalised medicine animated the second part of the event. The panellists – namely Dr Catherine Larue (IBBL), Erik Steinfelder (BBMRI-ERIC), Prof Laetitia Huiart (LIH), Dr Emilia Tantar (PriceWaterhouse Coopers Luxembourg) and Dr Philippe Aftimos (Institut Jules Bordet) – discussed a variety of topics including Artificial Intelligence, Big Data, biobanking, clinical trials, translational medicine and research platforms.

The event ended with a guided tour of IBBL's cutting-edge laboratories and a cocktail reception, which provided an agreeable setting for participants to exchange on the discussions of the day.







## TEAM LUXEMBOURG AND THE NATIONAL CENTRE OF EXCELLENCE IN RESEARCH ON PARKINSON'S DISEASE

*Estelle Sandt*

IBBL has been contributing to a nation-wide multidisciplinary project on Parkinson's Disease since 2015. In 2018, its unique study design, which is now ready to be applied to other diseases, was published in a renowned international journal. Moreover, the consortium submitted a research proposal for the second phase of the project, obtained ethical authorisation for the setup of a novel post-mortem brain donation programme and finalised the study design for a cohort of early-stage Parkinson's disease patients.





“NCER-PD is essentially redefining the boundaries of science, enabling the application of scientific discoveries to clinical practice, and hence the transition to true translational medicine!”

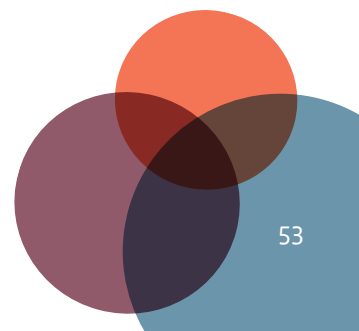
Estelle Sandt, Project Manager

### A multidimensional approach to Parkinson's disease

The complexity and heterogeneity of Parkinson's disease (PD) have led Luxembourg's major biomedical research players to join forces and devise an interdisciplinary action plan that would allow them to improve the early-stage diagnosis of the disease and the stratification of PD patients, which are currently two of the most important scientific and clinical challenges in this area. Thus, the National Centre of Excellence in Research on Parkinson's Disease (NCER-PD) was launched back in 2015 with these aims in mind, with the support of the National Research Fund (FNR). The project is coordinated by the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg and brings together LIH, the *Centre Hospitalier de Luxembourg* (CHL) and, as of 2018, the *Laboratoire national de santé* (LNS). “The strength of our consortium, collectively referred to as *Team Luxembourg*, lies in its multidisciplinary nature, which integrates expertise in systems biomedicine, clinical assessments and research, biomedical IT, biospecimen processing and storage and neuropathology”, states Prof Rejko Krüger, Principal Investigator of the study. NCER-PD is divided in two phases, with Phase I running from June 2015 until November 2019 and Phase II from December 2019 until May 2023. Phase I comprises three main projects, namely the set-up of a PD cohort (known as HELP-PD), systems biology approaches for the identification of biomarker signatures (DIAGNOSIS), and the development of an international resource of PD genetic variants associated with familial and sporadic forms of PD (VARIANT-DB). This multidimensional holistic approach which underpins Phase I – and which encompasses clinical assessments, molecular genetics and biomarker discovery – resulted in a comprehensive model for cohort recruitment, taking into account multiple aspects such as regulatory, ethical and biospecimen biobanking considerations. This unique study design was published in a prestigious international journal in October 2018 and is now ready to be rolled out to other diseases too, thus making NCER-PD an invaluable tool in the implementation of translational medicine.

### The HELP-PD cohort

IBBL has been particularly involved in setting up Luxembourg's first PD cohort under HELP-PD (Healthy Ageing of the Luxembourgish Population with a focus on Parkinson's Disease). The cohort includes PD patients from Luxembourg and the Greater Region, as well as matched healthy controls. Through annual follow up visits and device-based assessments, a large dataset on all disease stages and forms of Parkinsonism – from early non-motor signs to progression data – is generated, with





the ultimate goal of identifying predictive and progression biomarkers for PD. Indeed, the HELP-PD cohort will be used to validate the diagnostic biomarker signatures developed under DIAGNOSIS. IBBL has been ensuring kit production and delivery to collection centres, as well as logistics, processing and storage of blood, urine and saliva samples. Upon patient consent, cerebrospinal fluid (CSF), stool and skin biopsies are also collected, processed and stored. By end of December 2018, almost 13,000 blood, urine, saliva, stool and CSF samples had been collected from over 600 patients and 600 controls enrolled in the project, and more than 114,000 aliquots and associated data had been generated and stored at IBBL. In addition, IBBL carries out method validations, such as validation of DNA extraction from stool, to ensure that the aliquots derived through its processing methods are fit-for-purpose.

### **Towards a centre of excellence in translational medicine**

Building on the successes of Phase I, *Team Luxembourg* submitted a proposal in late 2018 detailing three projects to be included in Phase II, namely Stratification & Treatment, Biomarkers & Mechanisms and Data & Analytics. These will be the continuation of the three corresponding Phase I projects. Specifically, HELP-PD will provide the basis for Stratification & Treatment, with the goal of establishing a cohort of early-stage PD patients (known as Enriched Risk Cohort for PD – ERiC-PD) to identify at-risk individuals. The ERiC-PD study design and the list of criteria for at-risk individuals were finalised in November 2018. IBBL will be supporting Phase II transversally across all three projects. Aside from continuing the provision of sample collection, logistics, processing and storage services, the biobank will contribute to the set-up of a post-mortem collection of human brains from volunteers, in close cooperation with the LNS, which will support the Stratification & Treatment initiative by allowing the neuropathological validation of the clinical diagnoses made within the study. The post-mortem brain donation programme, which was approved by the National Research Ethics Committee (CNER) in July 2018, is expected to recruit up to 30 subjects annually into each of the target and control groups. Furthermore, under the Biomarkers & Mechanisms project, IBBL will reprogram fibroblast cells from skin biopsies obtained in Phase I into induced pluripotent stem cells (iPSCs), which will subsequently be differentiated into different types of neurons. The patient-specific cellular models thus generated closely reproduce the affected neurons in PD patients and can therefore be used to validate discovered biomarkers and investigate the molecular mechanisms underlying their role in PD. “This is a truly exciting phase of the project”, comments Estelle Sandt, project manager of NCER-PD at IBBL. “Not only will we be extending our activities to the biobanking of human brains, but we will also be taking our expertise in stem cell transformation from *bench to bed* by *converting* skin cells into patient-specific brain cells. NCER-PD is essentially redefining the boundaries of science, enabling the application of scientific discoveries to clinical practice, and hence the transition to true translational medicine”, she concludes.







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#### Biocabulary:

An **aliquot** is a portion of a larger biological sample.

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

A **cohort** is a group of individuals from which samples and data is collected over a period of time.

A **fibroblast** is a cell that is responsible for producing the extracellular matrix and collagen. It is the most common cell type of connective tissue.

**Induced pluripotent stem cells** are cells that can indefinitely self-renew and give rise to every other specialised cell type. They can be generated directly from adult cells.

**Parkinsonism** is any condition that causes a combination of the movement abnormalities seen in Parkinson's disease.

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

**Systems biology** is the computational and mathematical modelling of dynamic systems of biological components (molecules, cells, organisms).

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*Dr Monica Marchese*

## BIOMARKER VALIDATION IN LUXEMBOURG AND BEYOND

In 2018, IBBL - Integrated BioBank of Luxembourg has been accompanying researchers along the path towards biomarker validation, both nationally and internationally. The biobank supported the University of Luxembourg in applying and securing funding for a proof of concept to validate the novel MYO5B biomarker, and assisted Inserm in the first stages of the validation of a biomarker for latent tuberculosis infection.



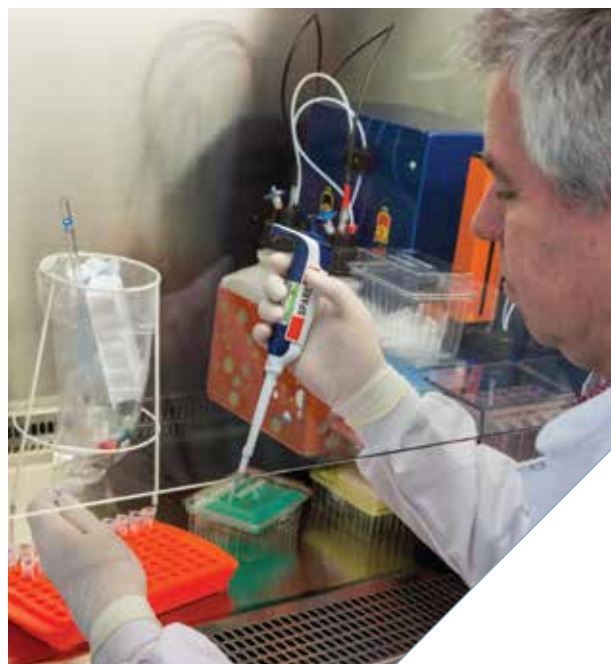
“ We are delighted to be supporting local researchers from the initial steps of the funding application to the actual validation, and to contribute to increasing Luxembourg’s visibility.”

*Dr Monica Marchese, Biomarker Validation Scientist*

IBBL will be responsible for the analytical and clinical verification of the MYO5B biomarker, under the leadership of Biomarker Validation Scientist Dr Monica Marchese and Chief Scientific Officer Dr Fay Betsou. The first step will entail the validation of the methods initially used by Prof Haan and Dr Letellier for the analysis of the expression of MYO5B, as well as an assessment of the pre-analytical factors which could affect the robustness of the biomarker. In the first quarter of 2019, IBBL will start by evaluating two sample types for the extraction of the RNA, namely frozen tissue and formalin-fixed paraffin-embedded (FFPE) tissue, and will compare qPCR with digital PCR (dPCR) to assess whether the latter could provide greater sensitivity. During the clinical verification stage, IBBL will collect 150 new tissue samples from stage II CRC patients to carry out a pilot study and verify the performance of the biomarker in clinical sample sets of limited size. “Translating cancer biomarkers into clinical practice is a significant challenge. We specifically approached IBBL given their proven expertise in biomarker validation and extensive biobank network, which will be invaluable when sourcing new samples from other biobanks for the clinical validation phase”, states Dr Letellier, Principal Investigator of the study. “Securing funding for biomarker validation is often challenging, given the associated degree of uncertainty. Being awarded the FNR grant proves that the discovery and validation of biomarkers are a national priority. We are delighted to be supporting local researchers from the initial steps of the funding application to the actual validation, and to contribute to increasing Luxembourg’s visibility in this domain”, adds Dr Marchese.

### Putting Luxembourg at the forefront

In 2017, Prof Serge Haan and Dr Elisabeth Letellier of the Life Sciences Research Unit (LSRU) at the University of Luxembourg identified protein MYO5B as a novel prognostic biomarker for colorectal cancer (CRC), which could help clinicians assess a patient’s risk of relapse and evaluate the need for chemotherapy following surgery. To validate the marker and develop a prototype kit for preliminary clinical use – a project known as MyoRPROG – the researchers applied for funding for a proof of concept, together with IBBL. April 2018 marked a milestone for the MyoRPROG study. The team was granted of 387,000 euros financing by the National Research Fund (FNR) to develop a companion diagnostic assay based on a quantitative PCR (qPCR) kit that determines the expression of the MYO5B gene, in combination with the closely associated RAB8A gene. The contract between the FNR, IBBL and the University of Luxembourg was signed in the summer of 2018, and work already began at the LSRU in September to confirm that the initial results – the MYO5B protein was originally discovered through immunohistochemistry techniques on tissue samples – could be reproduced by qPCR. Indeed, qPCR is easier to perform, which would facilitate the use of the assay in hospital settings, and provides greater reliability for the purpose of the kit. Moreover, using sequencing data from a publicly available dataset, the team investigated the prognostic potential of different *variants* (isoforms) of the Myo5B gene. This will help design the MyoRPROG assay and define which part of the gene sequence it should detect.







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#### Biocabulary:

An **antigen** is a molecule that is specifically recognised by an antibody.

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

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

**Immunohistochemistry** is a method for detecting antigens in cells of a tissue section by exploiting the principle of antibodies binding specifically to antigens in biological tissues.

**Digital PCR or dPCR** is a biotechnological refinement of conventional polymerase chain reaction (PCR) methods used to directly quantify and amplify nucleic acids. dPCR provides more precise measurements than classical PCR.

**Quantitative PCR or qPCR** is a PCR technique that detects, amplifies and quantifies the amount of RNA in samples, thus giving a measure of gene expression.

**Sequencing** means to determine the primary structure of an unbranched biopolymer such as DNA or RNA. It allows to uncover the order/sequence of the basic units called nucleotides of DNA or RNA fragments.

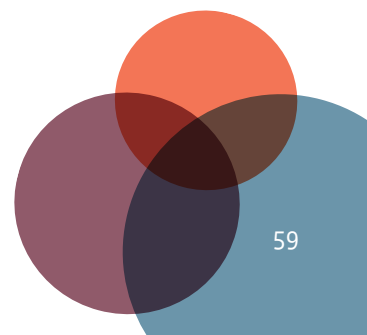
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### The international facet

Dr Marchese has also been assisting the French National Institute of Health and Medical Research (Inserm) in the first stages of the validation of a promising marker for latent tuberculosis infection (LTBI) – an asymptomatic state of persistent immune response to stimulation by the tuberculosis bacterium. The novel diagnostic biomarker, discovered and patented by Inserm Transfert, is based on the increased secretion of a specific cytokine by a certain type of blood cells in LTBI individuals in response to an antigen specific for the quiescent state of the *Mycobacterium tuberculosis*. In 2018, the validation process officially began. “The first step we carried out was the *feasibility and optimisation* phase”, explains Dr Marchese. “Candidate biomarkers often fail in the translation from the *bench to the bed* due to issues related to the reproducibility and validation of the methodology used to discover them in the first place. We therefore sought to reproduce on our platform the exact methods that underpinned the discovery of the biomarker”. Through the *feasibility* step, the IBBL team successfully demonstrated the reproducibility of the protocol on two different sample types and, during the *optimisation* step, optimised it for further application in the everyday laboratory routine. These results were submitted to Inserm Transfert and the decision to proceed to the second phase of the validation was approved. “The next phase will entail the pre-analytical and analytical validation to assess the robustness and integrity of the biomarker and evaluate the fitness for purpose of the analytical method used to discover it”, adds Dr Marchese. “There are currently no accurate tests nor Gold Standards for the diagnosis of LTBI. Although there are assays that are commonly used to diagnose *M. tuberculosis*, these do not discriminate the active from the latent state of the infection. We have shown LTBI individuals to unequivocally respond to a specific antigen, compared to healthy controls and TB subjects. Therefore, if validated, our biomarker could be translated into a novel assay which would allow us to unambiguously distinguish LTBI subjects from patients with active TB and from healthy individuals”, explains Dr Juan Iovanna, Principal Investigator of the study. One third of the world population being estimated to be infected with LTBI, a novel diagnostic assay could help identify and treat asymptomatic carriers and prevent the reactivation of the bacterium, thus controlling the spread of the disease globally.







## SUPPORTING EUROPEAN EPIDEMIOLOGICAL COHORTS: THE CONSTANCES PROJECT

IBBL was selected to be the biobank of the Constances study, a population-based epidemiological cohort funded by the French Government. The pilot phase of the biobanking activities started in June 2018. By the end of the year, more than 74,000 serum, plasma, urine and buffy coat aliquots from over 3,000 volunteers had been generated and stored at IBBL.



“We aimed to understand the individual needs and requirements of each sample collection site and develop workflows adapted to their specificities.”

Estelle Sandt, Project Manager

### Forging new partnerships

In 2017, IBBL was chosen through a European tender to set up a biobank in the context of the Constances study, a partnership between the French National Institute of Health and Medical Research (Inserm), the Versailles Saint Quentin University (UVSQ), the University of Paris, the French National Health Insurance Fund for Salaried Workers (*Caisse nationale de l'assurance maladie des travailleurs salariés* - CNAMTS), the French National Old-Age Insurance Fund (*Caisse nationale d'assurance vieillesse* - Cnav) and the French Ministry of Health.

Constances is a cohort of 200,000 randomly selected French adults aged between 18 and 69, aiming to provide public health and epidemiological information to the research community to support research projects on a broad range of questions. Though a generic cohort, it places particular focus on the occupational and social factors affecting health, as well as chronic diseases and ageing. “The overarching objective of Constances is to establish a large population-based cohort to contribute to epidemiologic research. Just like a telescope, it will not be used to answer a specific question, but rather to help analyse a wide array of scientific problems”, explains Dr Marie Zins, Principal Investigator of the study.

### The Constances biobank

The Constances project also entails the creation of a dedicated biobank to collect and store samples from participating volunteers and subsequently redistribute them to scientists for a variety of biomedical research projects. Ultimately, the biobank will support researchers in elucidating the mechanisms of complex diseases, understanding the role of the interactions between genetic, epigenetic and environmental factors in disease development and in discovering new biomarkers. The underlying workflow relies on the strict collaboration between IBBL and all the partners involved, and specifically the Inserm Constances team, the 21 health clinics (*Centres d'Examens*

*de Santé* - CES) spread across 24 sites and the CNAMTS.

IBBL has been tasked with the collection, transport, processing and storage of samples, guaranteeing their traceability all along the value chain. Following informed consent by the donors, urine and blood samples are collected by the CES using kits provided by IBBL and according to Standard Operating Procedures. The specimens are then transported to IBBL by a specialised company and processed in a completely automated way the day after collection. Following processing and quality control, the serum, plasma and urine aliquots thus generated-26 aliquots are produced for each volunteer-are stored in liquid nitrogen vapour tanks, in a storage area dedicated to Constances. IBBL also provides the CES with the IT infrastructure to record all data associated with the collected samples. “The Constances biobank is a powerful research tool at the disposal of the scientific community that will increase the value of scientific discoveries and facilitate their translation into clinical practice”, adds Dr Zins.

### The pilot phase

June 2018 marked the launch of the pilot phase of the Constances biobank. The pilot sought to evaluate the integration of the operating procedures within the processes of the CES, assess the complete workflow – from patient recruitment to sample storage at IBBL – and verify the overall feasibility of the implementation of the Constances biobank. As part of the pilot, IBBL organised several information sessions to present the biobank to the participating CES and explain the details of the operating procedures, including the use of the IT software. Subsequently, the IBBL and Inserm teams verified the feasibility of the biobank in each CES, ensuring that the required equipment and infrastructure – such as centrifuges compatible with the specific test tubes, fridges to temporarily store collected samples, temperature monitoring systems and barcode scanners – were in place. Collaboration between the two IT





teams was also crucial to install and optimise the software for data collection. “Our goal was to understand the individual needs and requirements of each CES and develop workflows adapted to their specificities”, explains Estelle Sandt, Constances project manager at IBBL. “This way, we could minimise any additional work for the CES and accompany them throughout the set-up phase as smoothly as possible.”

A collection start date was then defined for each CES. Prior to the start date, a three-day training session was delivered to the CES staff by ClinSearch, in cooperation with IBBL. In June 2018, sample collection began at the first pilot CES in Tours, followed by the Bordeaux CES later that month. By the end of 2018, 13 of the 24 sites had started collecting samples, almost 15,000 specimens from over 3,000 volunteers had been received at IBBL and over 74,000 aliquots generated and stored in liquid nitrogen.

### Managing complexity

The project entails a certain degree of complexity, stemming from its duration over three years, the 15,000 collections from the 21 CES spread across 24 sites, and the large number of aliquots to be stored. IBBL’s top priority is therefore to ensure the quality of the samples and data produced through rigorous and efficient processes. To guarantee appropriate temperatures and short delays of 36 hours at most between collection and storage, IBBL has put in place a comprehensive quality monitoring system that is constantly being improved together with the CES and the transport company. These measures will allow the successful collection of about 2.2 million aliquots from 85,000 volunteers until the end of the project in 2021. Looking ahead, operations should be up and running across all CES and the first samples distributed to researchers by end of the first quarter of 2019.

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#### Biocabulary:

An **aliquot** is a portion of a larger biological sample.

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

**Buffy coat** is the fraction of anticoagulated blood that contains most of the white blood cells and platelets obtained following centrifugation of a blood sample.

A **cohort** is a group of individuals from whom samples and data is collected over a period of time.

**Epidemiology** is the study of the distribution and determinants of health-related states or events, and the application of this study to the control of diseases and other health problems.

**Epigenetic factors** are factors that cause modification of gene expression without involving changes to the underlying DNA sequence of genes.

**Plasma** is the liquid, non-cellular fraction of anticoagulated blood obtained with centrifugation of a blood sample.

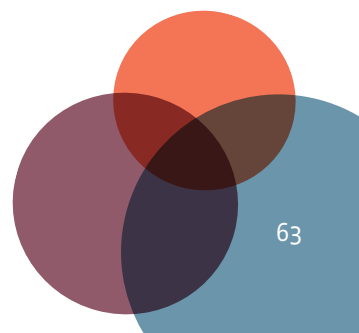
**Serum** is the liquid, non-cellular fraction of clotted blood obtained with centrifugation of a blood sample. In comparison to plasma, serum does not contain clotting factors.

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

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*Dr Sabine Lehmann*

## REDEFINING BIOBANKING QUALITY STANDARDS

2018 was an important year from a quality standpoint, for both IBBL and the biobanking community in general. The international standard ISO 20387 was published, marking an important milestone for biorepositories worldwide, and the international community was invited to formally comment on the draft ISO 21899. In addition, IBBL saw the confirmation of its ISO 17025:2005 accreditation and successfully transitioned to the ISO 9001:2015 norm.





“These quality achievements demonstrate our ability to consistently provide products and services that meet or exceed customer expectations.”

*Dr Sabine Lehmann, Quality Manager*

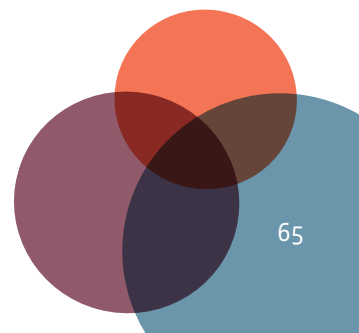
### A new era for biobanks

Unknown or uncontrolled preanalytical variables can compromise a sample's fitness for purpose. Quality assurance related to pre-analytical workflows has therefore been a major area of interest to the international biobanking community. Hundreds of Standard Operating Procedures (SOPs) and guidelines have thus been developed to advance the standardisation of biobanking activities. However, this has sometimes resulted in both an overlap as well as gaps in terms of the requirements set for biorepositories. The need for harmonised international standards entirely dedicated to biobanks was therefore evident.

### ISO 20387: setting biobanking requirements

IBBL's Quality Manager Dr Sabine Lehmann and Chief Scientific Officer Dr Fay Betsou have been working for years on the development of such norms, in close cooperation with international experts under the ISO technical committee TC 276 *Biotechnology*. The year 2018 marked an important milestone not only for IBBL, but for the biorepository community as a whole. Indeed, the International Standard ISO 20387:2018 (Biotechnology - Biobanking - General requirements for biobanking) was published in August 2018. The norm applies to all organisations performing biobanking activities, including biobanking of human, animal, plant and microorganism resources for research purposes. It clearly defines the structural, resource, process and Quality Management System (QMS) requirements enabling biobanks to demonstrate the competence of their staff, the quality of their operations and their ability to provide biological material and associated data of appropriate quality for Research & Development, ultimately promoting confidence in biobanking. “As project co-leader, the approval of the new ISO 20387 standard is both a personal satisfaction, as well as a success for the entire biobanking world”, states Dr Lehmann. “The benefits of the norm are multiple. It will bring about a much needed improvement in the access to and quality of biological material and associated data, as well as unifying policies and procedures for biobanks and supporting the exchange of biological resources. Not to mention the expected reductions in the costs related to the lack of reproducibility of scientific studies: approximately 28 billion US Dollars per year is estimated to be spent on irreproducible preclinical research”, she explains.

In October, the use of ISO 20387 as a standalone standard for the accreditation of biobanks was endorsed by the International Laboratory Accreditation Cooperation (ILAC).





This will drive the development and implementation of accreditation schemes by national accreditation bodies, with the first biobanks being expected to be accredited in 2019. In the meantime, the work of the ISO technical committee is ongoing, as an *Implementation Guide* is being developed to support the harmonised interpretation of the requirements defined in the standard across the biobanking and accreditation community. This document is set to be published in 2019 as an ISO *Technical Report* (ISO/TR 22758).

### ISO 21899: validating processing methods

Because good news come in pairs, in December the Working Group 2 of the ISO technical committee approved ISO 21899 for registration as a Draft International Standard (DIS). This means that the draft document – the work on which Dr Lehmann and Dr Betsou have been leading from the start – will proceed to the next step of the development process, being released to the international community for commenting in early 2019. “This is a significant achievement for us members of the technical committee! The draft standard will soon be shared with the broader community to benefit from their improvements and suggestions”, comments Dr Betsou. “If the ensuing rounds of ballots are successful, ISO 21899 will be published as a complementary standard to ISO 20387, setting out the general requirements for the validation and verification of processing methods in biobanks”, she explains.

### Reinforcing IBBL’s QMS

The year 2018 was characterised by a collective effort to continue consolidating IBBL’s QMS, particularly in light of the move to the new premises in Dudelange in November 2017. Indeed, already in March 2018, IBBL went through and successfully passed the reaccreditation audit for ISO 17025:2005, which resulted in the confirmation of its accreditation in May. “Although we had voluntarily suspended our ISO 17025 accreditation due to the move, we immediately took the opportunity to reconfirm the rigour and strength of our QMS and be audited shortly after”, states Dr Lehmann. The accreditation specifies the general requirements for the competence of testing and calibration laboratories and covers eight different methods. The reaccreditation was followed by another successful audit, which allowed IBBL to become certified according to the latest version of the ISO 9001 norm (ISO 9001:2015), specifying the requirements of Quality Management Systems. “These quality achievements demonstrate our ability to consistently provide products and services that meet or exceed customer expectations”, adds Dr Lehmann. “The passion, competence and commitment of our staff have been a decisive element in the positive outcomes of the audits and are the key to our reputation as a quality-driven and client-oriented organisation”, she concludes.

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#### Biocabulary:

**Pre-analytical workflows** consist of the collection, processing and storage of biospecimens.

**Biorepository** is another term for biobank.

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*Dr William Mathieson*

## MAKING CLINICAL SAMPLES FIT FOR RESEARCH

Clinical biospecimens are the most frequently used sample-type for research purposes, but are often of poor quality given their susceptibility to uncontrolled and unrecorded preanalytical variables. In 2018, IBBL's Biorefinery Department, led by Dr Fay Betsou, concluded several studies to guide researchers in their sample preparation, selection and processing decisions. Dr William Mathieson and his colleagues investigated the suitability of a non-formalin fixative, developed an assay to characterise cold ischemia in tissues and assessed the impact of automated DNA extraction and SpeedVac concentration on extracted nucleic acids.



“Our goal is to continuously expand the value that tissue banks can offer. By providing researchers with biospecimens of known quality, and by understanding what drives poor quality, tissue banks play a crucial role in curing disease.”

*Dr William Mathieson, Biorefinery Scientist*

### Sample preparation: identifying the best fixative

Before a tissue sample can be used for diagnosis or research, it needs to be preserved and be made amenable to analyses such as immunohistochemistry and molecular biology, either by fixation or stabilisation. Most tissue biospecimens are fixed using formalin then embedded in paraffin, resulting in a formalin-fixed paraffin-embedded (FFPE) tissue block. Despite the many advantages of this method, nucleic acids extracted from FFPE tissue blocks are fragmented and chemically modified. The PAXgene tissue fixative was therefore developed as an alternative to formalin. However, it was not known how resistant PAXgene-fixed paraffin-embedded (PFPE) tissue blocks are to storage. The IBBL research team, together with Imperial College London and the Wales Cancer Bank, tackled this question by comparing the integrity of RNA and microRNA (miRNA) extracted from PFPE blocks immediately after fixation with that extracted from the same blocks seven years later. They found that RNA degraded in the PFPE blocks during storage but the miRNA was much more stable. However, no degradation occurred during the seven-year period when RNA was extracted from the PFPE blocks immediately upon collection and stored at -80 °C. “Our work supports researchers in choosing the most suitable fixative according to the type of downstream analyses to be carried out, and on the specific logistics of sample collection and processing”, explains Dr Mathieson. “The degradation during long-term storage of tissues as PFPE blocks makes them unsuitable for some molecular biology analyses, so it is advisable to collect enough material to have both a fresh-frozen tissue block and an FFPE block. However, PFPE fixation is a viable alternative when it is not possible to freeze the tissue (for example

collections at a remote location) or when the sample is too small to obtain both a frozen and an FFPE block”, he adds.

### Choosing the right sample: the Cold Ischemia Score

Cold ischemic (CI) time, is a preanalytical variable that has been shown to influence gene and protein expression and stability: the longer the CI time, the greater the risk of repercussions on sample quality. Since CI times are not usually recorded upon collection, researchers do not know the extent to which their results will be affected by it. To identify the tissue blocks that have been subjected to long CI times, IBBL scientists collaborated with the US National Cancer Institute and the Van Andel Institute to devise a reliable assay based on a gene expression pattern. They extracted RNA from 40 colon, kidney and ovary cancer FFPE blocks with different CI times, then measured the expression levels of 23 genes to identify those that are particularly stable or unstable in response to cold ischemia.

The expression of three genes, namely PRKACA, FOS, and EGR1, was found to be upregulated due to CI. Using a gene (POLR2A) whose expression remains unvaried as a baseline, the combination of the three genes gives a Cold Ischemia (CI) Score that distinguishes samples with CI times shorter than 3 hours from those with 12 hours, with 62% sensitivity and 84% specificity. “The CI Score is easy to validate, practical and accessible to laboratories, enabling researchers to retrospectively qualify legacy collections of FFPE tissue samples with undocumented preanalytics and select the samples that are fit for the purpose of their research”, states Dr Mathieson.





## Nucleic acid extraction: selecting suitable techniques

-DNA extracted from FFPE tissue blocks is increasingly being used for applications such as next generation sequencing to determine patients' therapeutic treatment. Automated robots that simultaneously extract DNA from multiple samples are commonly used by high-throughput laboratories such as IBBL. However, many still rely on manual extractions. To assess whether DNA quality is compromised by the choice of particular manual or automated extractions, the IBBL team, collaborating with Imperial College London, extracted DNA from 42 FFPE tissue blocks using two automated platforms and a manual method. Results show that both integrity and yield were slightly higher in the manual extractions, while automated techniques allowed for slightly better reproducibility and required much less intervention by technicians. "The extraction methods have different strengths and weaknesses. The choice of which to use therefore depends on the specific requirements of the users. However, our findings are particularly relevant to smaller laboratories which cannot necessarily invest in expensive automated technologies, since we confirm the high reliability and quality of manual extractions", explains Dr Mathieson.

Following extraction from FFPE, DNA and RNA are often too dilute to be further analysed, and are concentrated usually by applying vacuum centrifugal concentration (SpeedVac). IBBL researchers assessed the impact of this technique by concentrating the nucleic acids extracted from FFPE tissues with SpeedVac at different times and temperatures and measuring the changes in quantity, purity and integrity. The study showed that SpeedVac has no negative effects on the DNA and RNA. In addition to reassuring researchers in their choice of concentration procedure, these findings can be used by biobanks seeking ISO 20387 accreditation to validate their processing methods. "Our goal is to continuously expand the value that tissue banks can offer. By providing researchers with biospecimens of known quality, and by understanding what drives poor quality, tissue banks play a crucial role in curing disease", Dr Mathieson concludes.

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### Biocabulary:

**Cold ischemia** refers to the cooling of a tissue when it is removed from the body and not supplied with blood anymore.

**Cold ischemic time** is the time between tissue collection and fixation, during which the tissue is deprived of oxygen and is below body temperature.

**Fixation** is the preservation of biological tissues from decay.

A **fixative** is a substance used for tissue fixation. The most commonly used fixative is formalin, also called formaldehyde.

**MicroRNA** or **miRNA** are small noncoding ribonucleic acids involved in the regulation of gene expression.

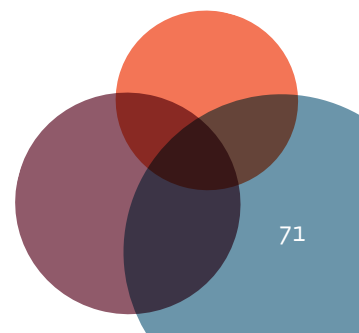
**Next generation sequencing** refers to a set of modern high-throughput sequencing methods.

**Sequencing** means to determine the primary structure of an unbranched biopolymer such as DNA or RNA. It allows to uncover the order/sequence of the basic units called nucleotides of DNA or RNA fragments.

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# PARTNERS & CLIENTS

## Legend

- Collection Partner
- Industrial Partner
- Research Collaborator
- Client

### FRANCE

- Tumorothèque CHU Amiens
- CARDIATEAM consortium
- RNAssist
- Inserm
- Inserm Transfert
- Sorbonne University/Inserm research teams at Institute of Cardiometabolism And Nutrition (ICAN)

### UNITED KINGDOM

- Imperial College London
- Wales Cancer Bank
- Northern Ireland Biobank
- LITMUS consortium

### BELGIUM

- Antwerp University Hospital
- CANCER-ID consortium
- IMMUCan consortium
- Breast International Group
- EORTC (European Organisation for Research and Treatment of Cancer)
- Trinean

### SPAIN

- Biobanco del Sistema Público de Andalucía
- Pulmonary Biobank Consortium Hospital

### CANADA

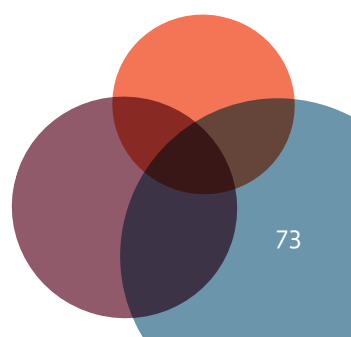
- DNA - Genotek
- International Society for Biological and Environmental Repositories (ISBER)

### UNITED STATES

- Beaumont Biobank
- Chan Soon-Shiong Institute of Molecular Medicine
- Basque Engineering and Science
- Vitalant Research Institute
- National Institute of Standards and Technology (NIST)
- National Cancer Institute (NCI)
- Texas Children's Hospital
- BD (Becton Dickinson)
- LABVANTAGE
- CryoXtract
- WaferGen Biosystems (Takara)
- Precision for Medicine



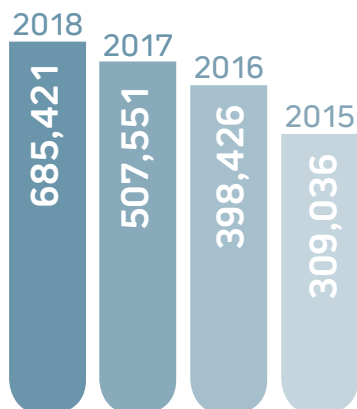




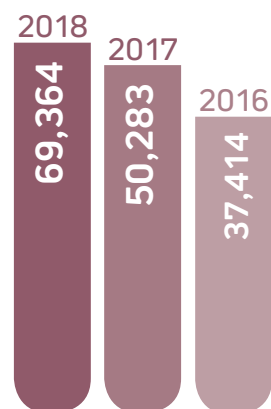


# COLLECTION STATISTICS\*

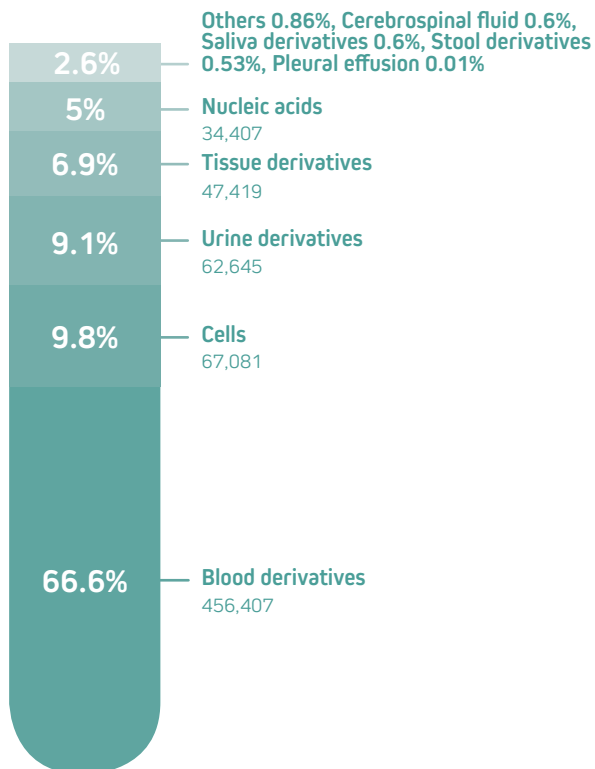
## TOTAL SAMPLES COLLECTED



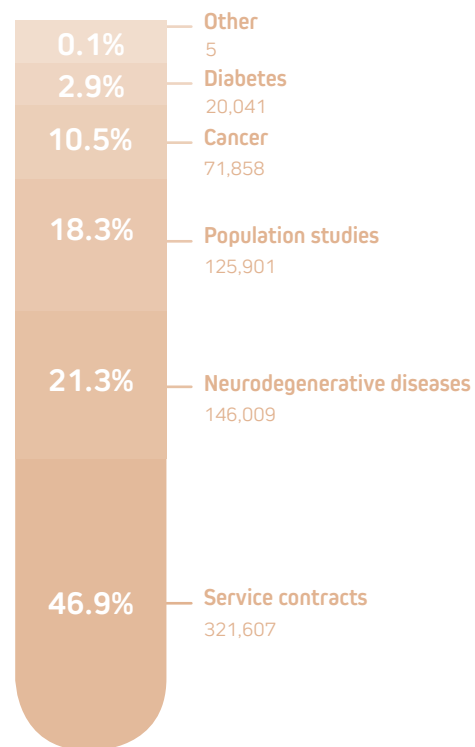
## DISTRIBUTED



## SAMPLES BY TYPE



## SAMPLES BY PROGRAMME



\*The methodology for the calculation of sample collection and distribution statistics has been revised relative to previous years.





**NEWLY  
FUNDED  
PROJECTS**

75



# TACKLING DISEASE MECHANISM AND TREATMENT

Three FNR CORE projects funded

Three proposals submitted by LIH for financial support by the central funding instrument CORE of the Luxembourg National Research Fund (FNR) were successfully retained. The projects that shall start in 2019 will give new insights into disease mechanisms to pave the way for new therapeutic strategies.

Zoom on the three successful applications:

## // cROsfire 2.0

The cROsfire 2.0 project will focus on immunometabolism in the context of multiple sclerosis. For this neurodegenerative autoimmune disease, the current treatment options are not efficient or present too many adverse effects. It is known that an accurate regulation of the cell metabolism is crucial for the maintenance of normal cell function and that the metabolism is altered in the disease state. A promising treatment approach could therefore be to interfere with altered metabolic cell signalling. In this project, metabolic profiling of immune cells will be conducted with the aim to identify cell- or disease-specific metabolic features representing potential therapeutic targets.

The project will be conducted in collaboration with German partners at the *Technische Universität Braunschweig*, the Helmholtz Centre for Infection Research and the Medical Faculty of the University of Mannheim together with the University of Heidelberg and is also supported by the *Deutsche Forschungsgemeinschaft*.



“A better understanding of the immunometabolism in disease will be an important step for the development of targeted therapeutic strategies.”

Prof Dirk Brenner, FNR ATTRACT fellow and Principal Investigator, Experimental and Molecular Immunology Research Group, Department of Infection and Immunity



“The ultimate goal of this research is to enhance existing therapies using the newly-gained knowledge on the mucobiome.”

Prof Mahesh Desai, Principal Investigator, Eco-Immunology and Microbiome Research Group, Department of Infection and Immunity

## // Muco-IBD

Muco-IBD will investigate the role of mucobiomes in the pathogenesis of inflammatory bowel disease (IBD). The term IBD refers to a group of disorders of the gastrointestinal tract for which the pathogenesis mechanisms are poorly understood. Mucobiomes are communities of colonic mucus-degrading bacteria whose activities are regulated by dietary fibre. For this project, culture collections of mucobiomes from patients will be established and studied in mouse models\*. The research team aims to identify the underlying immune pathways related to mucus deterioration and to understand mucobiome alterations that occur during the commonly employed therapies to treat IBD. Next-generation prebiotic fibres may be beneficial to modulate the mucobiome and improve current therapies.

The project involves collaborations with the *Centre Hospitalier de Luxembourg*, the University of Michigan Medical School, United States, the Johns Hopkins University, United States, and the Gothenburg University, Sweden.



## // COMBATIC

Immune checkpoint blockade (ICB)-based immunotherapy is a revolutionary treatment against cancer. However, the ground-breaking success of ICB has been seriously challenged by clinical observations showing that only a small fraction of patients obtain durable and sustained clinical benefit from this therapy. COMBATIC is a translational research project aiming to increase the clinical benefit of ICB and extend its use to the large number of non-responder cancer patients. Through its both clinically oriented and basic research aspects, the project relies on the development of innovative combination approaches to switch “cold” immune desert tumours - not eligible to ICB - to “hot” immune inflamed tumours - eligible to ICB - able to drive anti-tumour effector immune cells to the tumour bed. The translational aspect of the COMBATIC project relies on the establishment of the proof of concept to set up clinical trials using innovative combination immunotherapy for the benefit of cancer patients.

In addition to the FNR CORE funding, the project also received financial support from *Fondation Cancer*, the Luxembourg Cancer Foundation.



**“ We aim to improve the clinical benefit of immune checkpoint blockade-based cancer immunotherapy by designing innovative combination approaches to switch cold into hot tumours. ”**

*Dr Bassam Janji, Deputy Head,  
Laboratory of Experimental Cancer Research,  
Department of Oncology*

### Biocabulary:

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

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

**Immune checkpoint** are molecules on the surface of certain immune cells that regulate the immune system. Cancer cells can find ways to use these checkpoints to avoid being attacked. The blockade of immune checkpoints by specific inhibitors is a therapeutic strategy.

**Immunometabolism** is a recently emerged research field studying the metabolism of immune cells.

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

**Prebiotics** are non-digestible fibre compounds that promote the growth of beneficial microorganisms in the gut.

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

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

\*National and European animal experimentation and animal welfare guidelines are strictly applied for all LIH research projects involving *in vivo* experiments.





Handing of a cheque on 28<sup>th</sup> February in the premises of Fondation Cancer. From left to right: Lucienne Thommes (Director of the Cancer Foundation), Dr Ulf Nehrbaß (CEO of LIH), Prof Simone Niclou (Head of the NorLux Neuro-Oncology Laboratory, Department of Oncology) and Dr Carlo Bock (President of the Cancer Foundation)

# HOW DO TUMOUR CELLS INVADE BRAIN TISSUE?

## Fondation Cancer funding

Department of Oncology > NorLux Neuro-Oncology Laboratory > Glioma Biology Research Group

**Fondation Cancer, the Luxembourg Cancer Foundation supports a new research project that aims at unravelling the mechanisms underlying cancer cell invasion in glioma and at proposing new therapeutic strategies to block tumour progression.**

Gliomas or glioblastomas are malignant brain tumours that can occur at any age and for which the standard cancer treatment is often not sufficient. The tumour can affect different brain regions and causes large lesions. It has the ability to penetrate deeply into brain tissue. Its invasive nature prevents complete surgical resection. Current treatments mainly target dividing tumour cells, but to be truly effective, they should be combined with therapies blocking the invasive process. To develop such strategies it is important to better understand the underlying molecular mechanisms of tumour invasiveness.

The project is led by postdoctoral researcher Dr Anne Schuster, whose work is supported by the Cancer Foundation since 2014. It is based on promising results from previous research. A major discovery by the research team had been the identification of a gene involved in the invasive behaviour of glioma cells. The knowledge on this gene can help to further unravel the molecular signalling that takes place inside cells to drive tumour invasion. In a next step, databases shall be analysed that contain a wide range of already commercialised drugs known to affect specific signalling pathways to identify a treatment potentially effective against tumour invasion.

### IMPACTING ON PEOPLE'S HEALTH!

Promising drug candidates identified in this project could be tested in preclinical studies and later in clinical trials to evaluate whether they can be approved for patients. Thus, new applications could be found for existing drugs to be used in combination with radio- and chemotherapy to significantly improve disease outcome.

### Biocabulary:

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

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





# SURMOUNTING DRUG RESISTANCE IN LUNG CANCER

Lions Club Luxembourg funding

*Department of Oncology > Proteome and Genome Research Unit*

**A research project aiming at identifying therapeutic strategies to overcome the problem of drug resistance in lung cancer treatment was granted funding by Action Lions Vaincre le Cancer of the Lions Clubs Luxembourg.**

Despite important technological and biomedical breakthroughs, lung cancer is still a leading cause of death in the world. The activation of enzymes named epidermal growth factor receptor (EGFR) tyrosine kinases has been associated with the progression of lung cancer. In the past, therapies targeting EGFR tyrosine kinases using specific inhibitors showed remarkable effect against Non-Small Cell Lung cancer (NSCLC) bearing EGFR-activating mutations. Nevertheless, the emergence of resistance to these agents seems inevitable, and is often related to a particular mutation in the enzymes. To overcome drug resistance, third-generation EGFR inhibitors have already been developed, but resistance to these new inhibitors has also already been reported.

The supported project involves state-of-the-art high-throughput technologies that will allow to better understand the molecular basis of resistance to third-generation EGFR tyrosine kinase inhibitors, which is essential to develop therapeutic strategies to overcome drug resistance in lung cancer.

The grant has been attributed to researcher Dr Victoria El Khoury and Prof Rolf Bjerkvig, former Director of the Department of Oncology. This project complements the work initiated in the frame of the Partnership for Personalised Medicine (PPM) programme whose main goal is to contribute to the advancement of personalised medicine in lung cancer.

## **IMPACTING ON PEOPLE'S HEALTH!**

This research purposes to find new therapeutic targets and combination treatments with third-generation EGFR tyrosine kinase inhibitors to reverse or circumvent drug resistance and to identify the subset of lung cancer patients who could benefit the most from these treatments.

### **Biocabulary:**

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

**Epidermal growth factor** is a protein produced by many cells in the body and by some types of tumours. It allows cells to grow and differentiate.

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

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

A **receptor** is a protein on the cell surface that can bind a ligand. The binding produces a signal in the cell activating or inhibiting cellular processes.

A **tyrosine kinase** is an enzyme that transfers phosphate groups to proteins. This changes the state of the proteins e.g. activating them.





Prof Simone Niclou (left) and Dr Sabrina Fritah (right) receiving a cheque at a reception held at the Kinepolis cinema on 6<sup>th</sup> June by Rotary Club Luxembourg.

# REVERTING MUTATIONS IN BRAIN CANCER

## Rotary Club Luxembourg funding

Department of Oncology > NorLux Neuro-Oncology Laboratory > Glioma Biology Research Group

**For the sixth time, the Rotary Club Luxembourg gave financial support for brain research in the framework of its initiative *Espoir-en-tête* that collects donations by organising movie sessions in cinemas. A research project on reverting cancer driver mutations in brain cancer was supported.**

The planned research work will investigate the therapeutic potential of targeting driver mutations in gliomas, severe brain tumours that are difficult to treat due to their cellular heterogeneity. A few driver mutations in genes involved in epigenetic regulation have been identified in adult and paediatric gliomas. These mutations lead to profound molecular changes that can further increase the tumour's heterogeneity. Therefore, the repairing of driver mutations is thought to be a promising approach in anticancer gene therapy.

Over the past years, the research unit headed by Prof Simone Niclou has been developing specific glioma models, an expertise that makes it one of the leaders in the field of glioma research. Recently, the team also got experience in using CRISPR/Cas9 genome editing technology.

The present project led by Dr Fritah aims to use this revolutionising technique to correct point mutations in the glioma models. Subsequently, the researchers plan to monitor the impact of reverting these mutations on genome stability and tumour heterogeneity using high-throughput DNA sequencing. The funding will enable the acquirement of a new instrument for DNA visualisation and cover costs for deep sequencing of glioma specimens from patients.

### IMPACTING ON PEOPLE'S HEALTH!

This project will shed light on the impact of cancer driver gene editing on tumour epigenetic plasticity and pave the way for further developing the explored therapeutic strategy, so that it may be applied to patients in the future.

#### Biocabulary:

**CRISPR/Cas9** is a recent method in molecular biology to precisely cut and edit DNA allowing to add, remove or alter genes.

**DNA sequencing** means to determine the primary structure of DNA fragments to uncover the order/sequence of the basic units called nucleotides.

A **driver mutation** is a mutation within a gene that confers a selective growth advantage to cells, thus promoting cancer progression.

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

In **gene therapy**, DNA is introduced into a patient to treat a disease.

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

A **point mutation** is a mutation where a single nucleotide base is changed, inserted or deleted.

**Tumour heterogeneity** means that different tumour cells in the same tumour can display distinct characteristics, showing for example differences in morphology, gene expression, metabolism, motility, proliferation or metastatic potential.



A photograph of two students in white lab coats using VR headsets. The student in the foreground is looking towards the camera while holding the VR headset. The student in the background is seen from the side, also using a VR headset. The image has a blue tint and a semi-transparent blue overlay at the bottom.

# COMMUNICATING SCIENCE

81



# THEMATIC LECTURE SERIES FOR THE RESEARCH COMMUNITY

Promoting scientific exchange

In 2018, four annual lecture series on specific scientific topics related to LIH's research activities were organised by the institute and a new one was launched at the end of the year. The programmes contained many names of internationally renowned speakers who especially came to Luxembourg to share their latest research findings.

LIH's lecture series are aimed at addressing current hot research topics and promote scientific exchange and networking.

## // Cancer Research

The third edition of the lecture series in *Cancer Research* ran from mid-2017 to mid-2018 with eleven events. Each lecture was followed by a "Meet & Eat" session during which a restricted group of early-stage researchers could meet the speakers to ask questions about their research, techniques or career. The programme of this lecture series was jointly set up by LIH's Department of Oncology and the Life Sciences Research Unit of the University of Luxembourg. This lecture series will be continued in 2019.



Lectures series Cancer Research: Prof Patrizia Agostinis from the University of Leuven, Belgium, shared findings about cancer immunotherapy on 26<sup>th</sup> April

## // Infection and Immunity

The fifth edition of the lecture series in *Infection and Immunity* ran from February 2018 to January 2019. The programme comprised ten lectures by international speakers working in different fields related to immunology were invited by the Department of Infection and Immunity. Each lecture was followed by a "Meet & Eat" session around a light lunch to allow early-stage researchers to informally exchange with the speakers. A new programme for 2019 is set up.

Lecture series Infection and Immunity: Prof Klaus Warnatz from the University of Freiburg, Germany, talked about "Autoimmunity in Immunodeficiency" on 14<sup>th</sup> June



## // Biomedical research - from discovery to patients

The lecture series entitled *Biomedical research - from discovery to patients* started in May 2017 and was successfully completed in June 2018 after 12 events in total. This very popular lecture series, to which local and international speakers participated, focused on the actors and major challenges of biomedical research and innovation through testimonials from researchers-entrepreneurs. The programme was set up by LIH's Business Development Office. More about this lecture series on page 84.



## // Translational bioinformatics and systems biomedicine

The lecture series named *Translational bioinformatics and systems biomedicine* had a first programme running from mid-2017 to mid-2018 with nine lectures followed by “Meet the speaker” sessions. Due to its success, it continued with a second edition comprising ten lectures held between June 2018 and March 2019. For both editions, the scientific organising committee included researchers from the Departments of Oncology and Infection and Immunity at LIH, and the Life Sciences Research Unit and the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg.



Lecture series *Translational bioinformatics and systems biomedicine*: Prof Jessica Tenenbaum from the Duke University School of Medicine, Durham, United States, presented “*Translational Bioinformatics in the precision medicine era*” on 1<sup>st</sup> February

## // Improving patient & population health through innovative e-health interventions

A brand new lecture series is organised by the Department of Population Health since December 2018. It shall run throughout the year 2019 and include 12 lectures. Labelled *Improving patient & population health through innovative e-health interventions*, it focuses on digital technologies that support and advance health services, epidemiology and public health research. The programme is set up with the contribution of different national partners. More about this lecture series on page 86.

### Biocabulary:

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

**Epidemiology** is the study of the distribution and determinants of health-related states or events, and the application of this study to the control of diseases and other health problems.

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

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

### Funding:

All lecture series are funded by the Luxembourg National Research Fund. The lecture series *Cancer Research, Infection and Immunity, Translational bioinformatics and systems biomedicine* and *Improving patient & population health through innovative e-health interventions* benefit from RESCOM grants, whereas the lecture series *Biomedical Research - from discovery to patients* is supported by a KITS grant.





From left to right: Prof Markus Ollert, Sandrine Lavallé, Anne Weydert and Prof Rejko Krüger

# ZOOM ON THE BIOMEDICAL RESEARCH LECTURE SERIES

Highpoints of a stimulating programme

The lecture series *Biomedical research - from discovery to patients* organised by LIH's Business Development Office was divided into two main parts: Part A termed *Research results at the centre of the therapeutic revolution* presented how results from academic research can be transferred into clinical applications and explained the general process behind that transfer. Part B provided scientists with key tools to define, mature and implement their applied research projects.

The lecture series allowed for highly interesting discussions with researchers-entrepreneurs and healthcare communities engaged in clinical research about the pathways by which scientific discoveries lead to benefits for the patients. The sessions also gave the opportunity to exchange opinions regarding open innovation models or the expectations of parties in public-private partnerships.

The information received during this inspiring lecture series shall support the establishment of new patient-centric projects which represent the ideal scenario of research valorisation.

The lectures series composed of 12 events had two special lectures in 2018 to which more than one speaker was invited. Those events are presented in more detail in the following sections.

“ *Personalised medicine means giving the right medication at the right dosage and at the right time to each patient.*”

*Prof Rejko Krüger, Luxembourg Centre for Systems Biomedicine, University of Luxembourg, speaker in the lecture series Biomedical research - from discovery to patients*



### First featured topic: Research for and with the patient

A true highpoint of the lecture series was the seminar held on 27<sup>th</sup> April, chaired by Prof Markus Ollert, Director of the Department of Infection and Immunity. It focused on the connection between researchers, clinicians, patients associations and patients that is essential to drive innovation in research and to develop tailor-made treatments.

On that occasion, Prof Rejko Krüger, Professor for Neuroscience at the University of Luxembourg, FNR PEARL Chair and member of the National Centre of Excellence in Research on Parkinson's Disease (NCER-PD), presented the current research efforts around Parkinson's disease in Luxembourg. NCER-PD aims for earlier disease diagnosis and personalised treatments for the neurodegenerative disorder. With some examples he showed that the knowledge on a specific gene involved in Parkinson's disease can help for the development of an effective treatment. He also outlined the importance of consulting patients and patient associations to allow them to contribute to the research programme with their input and finished by presenting ParkinsonNet Luxembourg, a recently launched network that connects the professionals involved in the treatment of Parkinson's disease patients to foster patient-centred care.

EUPATI, the National Platform created in Luxembourg in 2014 was on the agenda of the second part of the seminar. It was presented by Sandrine Lavallé, Scientific Collaborator at the Department of Population Health, and Anne Weydert, a patient involved in the association. EUPATI, standing for European Patients' Academy on Therapeutic Innovation, is a European association that aims to promote patient empowerment by letting patients, patient organisations, advocacy leaders and the lay public become effective advisors in medical research, namely in clinical trials. The association provides extensive training material to educate patients in order to enable them to enter into fruitful discussions with the research world. Both speakers emphasised on the patients' expectations for biomedical research and referred to the specific context in Luxembourg. Mrs Weydert also shared her personal experience and concerns as a patient with a neurological disease and how she benefitted from EUPATI training sessions.

“ Consulting patients for research design would avoid conducting science that is too far from the people's needs.”

*Sandrine Lavallé, Epidemiology and Public Health Research Unit, Department of Population Health, speaker in the lecture series Biomedical research - from discovery to patients*

### Second featured topic: Support for biomedical entrepreneurship

The closing lecture of the programme chaired by Prof Markus Ollert, Director of the Department of Infection and Immunity, was also a highlight: four speakers were invited on 29<sup>th</sup> June to present the support that is given to researchers in Luxembourg to develop entrepreneurial projects in the field of biomedicine.

Dr Françoise Liners from the Ministry of Economy introduced what entrepreneurship is about, how it is influenced by the ecosystem and what it takes to be an entrepreneur. She stressed that the key characteristics of an entrepreneur are the readiness to take risks and the ability to convince people about ideas.

Various tools have been presented to researchers who might be tempted by entrepreneurship:

- > the JUMP Programme, which supports the transfer of research results to the market (by Dr Andreea Monnat from the Luxembourg National Research Fund),
- > the “Fit 4 Start” programme for start-ups, which provides tailor-made advisory services to researchers with innovative ideas (by Stefan Berend from Luxinnovation),
- > new structures to bridge funding gaps in innovation: LuXseed for seed capital, and Capsula, a future Luxembourg-based spin-off incubator (by Prof Eric Tschirhart from the University of Luxembourg).

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#### Biocabulary:

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

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

#### Funding:

The lecture series *Biomedical Research - from discovery to patients* was supported by a grant from the Knowledge & Innovation Transfer Support Programme (KITS) of the Luxembourg National Research Fund.

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Inaugural lecture on 17<sup>th</sup> December  
by Dr Guy Fagherazzi from the Centre  
of Research in Epidemiology and  
Population Health in Villejuif, France

# LAUNCH OF A NEW LECTURE SERIES ON E-HEALTH

Presenting innovative tools for population health

LIH's Department of Population Health coordinates a new lecture series named *Improving patient & population health through innovative e-health interventions*. Within the series, 12 lectures by outstanding speakers are planned to take place at the *Centre Hospitalier de Luxembourg*, followed by more informal "Meet the speaker" sessions with light lunch in LIH's premises.

E-health has received growing interest and attention in public health research as an upsurge in both the availability and use of e-health tools has been observed. Due to high prevalence rates in chronic diseases, clinical public health research increasingly focuses on innovative e-health with regards to patients' and population's health maintenance, prevention, improvement and surveillance. In addition, innovative e-health interventions represent a unique opportunity to address challenges in healthcare delivery and disease management.

The new lecture series initiated under the lead of Prof Laetitia Huiart, Director of the Department of Population Health, features transdisciplinary research dedicated to the usability of innovative e-health interventions.



## Successful opening

An inaugural lecture was held on 17<sup>th</sup> December by Dr Guy Fagherazzi, senior scientist in digital epidemiology from the Centre of Research in Epidemiology and Population Health in Villejuif, France. He gave an inspirational talk on how population health could be improved in the age of digital and artificial intelligence.

Dr Fagherazzi discussed the evolution of the field of epidemiology and presented some key research initiatives combining innovative sources of information such as social media or connected devices with more traditional epidemiological and clinical data. He featured amongst others a study on diabetes conducted with Twitter users. The data generated online by an individual-which can be called the “digitosome”-provides indeed new possibilities for public health studies and interventions. He also illustrated how Artificial Intelligence methods can be leveraged in the context of population health research.

The speaker expressed an advice to the public: to rethink the way epidemiology and public health is practised and to be open to conduct research at the interface of epidemiology and other disciplines to make science advance more efficiently.



LECTURE SERIES 2018/2019

**IMPROVING PATIENT & POPULATION HEALTH THROUGH INNOVATIVE e-HEALTH INTERVENTIONS**

**17**

DEC 2018

Monday

**LECTURE**

CHL - Centre  
4, rue Ernest Barblé  
L-1520 Luxembourg  
Room: Amphitheatre

**11.30-12.30pm**

**MEET THE SPEAKER\***

Light snacks provided  
LH, 2A-B, rue Thomas Edison  
L-1425 Strassen  
Room: Curio/Pastour (2<sup>nd</sup> floor)

**12.45-2.00pm**

**LUXEMBOURG INSTITUTE OF HEALTH**  
RESEARCH AND INNOVATION

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\*Registration is mandatory to meet the speaker by sending an email to [tania.zamboni@ilh.lu](mailto:tania.zamboni@ilh.lu)

**e-Health & e-Epidemiology: how to improve population health in the age of digital and artificial intelligence?**

**ABSTRACT**

e-Health is a constantly evolving field referring to the organization and delivery of health services and information using the Internet and related technologies such as smartphone apps, connected devices but also social media. Data generated online by an individual - which can be summarized under the concept of “**digitosome**” - constitutes, by the quantity and the variety of information it represents, a great potential to 1) deeply modify the way we practice epidemiology and public health and 2) improve population health. While epidemiology, as practiced today, will still continue to be practiced in the future, there is also a need to rethink how to optimally integrate these data to tackle current medical research challenges.

During this conference, Guy Fagherazzi will discuss the evolution of the field of epidemiology, present some key research initiatives combining innovative sources of information such as social media or connected devices with more traditional epidemiological and clinical data and will also illustrate how Artificial Intelligence methods can be leveraged in the context of population health research to help developing the future of public health studies and interventions.



**SPEAKER**

**Dr Guy Fagherazzi**  
Senior research scientist in digital epidemiology,  
Center of Research in Epidemiology  
and Population Health in Villejuif, France

**HOST:**  
LH

**INVITED BY:**  
Prof Laetitia HUJART  
Department of Population Health

[www.jih.lu](http://www.jih.lu)

**Supported by:**



**Partners:**






## Biocabulary:

**E-health** converges modern digital technology with health monitoring and healthcare.

**Epidemiology** is the study of the distribution and determinants of health-related states or events, and the application of this study to the control of diseases and other health problems.

## Funding:

The lecture series received support from the Luxembourg National Research Fund through the RESCOM funding scheme dedicated to seminars and conferences with an international dimension.

## Partners:

The lecture programme is set up with the contribution of the University of Luxembourg, the Luxembourg Institute of Socio-Economic Research, the Luxembourg Institute of Science and Technology, the *Centre Hospitalier du Luxembourg*, the *Centre Hospitalier Emile Mayrich* and the company Information Technology for Translational Medicine.





# THE LAY PUBLIC ENGAGED TO A SCIENTIFIC MISSION

## LIH Science Quest

*General Management > Communication Unit*

From 23<sup>rd</sup> to 25<sup>th</sup> February, LIH held a large science-promoting event, the first of its kind in Luxembourg. Aiming at presenting the institute's biomedical research activities to high school classes and the broad public in an unconventional and entertaining way, the participants of the LIH Science Quest were plunged into an unexpected setup that put them into the shoes of a research team.

On the first day, the Science Quest was inaugurated and visited by Lydia Mutsch, Minister of Health, and Marc Hansen, Delegate Minister for Higher Education and Research who both showed great enthusiasm about the concept. This first day was reserved to high school classes, whereas the other two days were open to all public.

### Team challenge

An exceptional two-hour programme, inspired from adventure and escape games, awaited the more than 50 teams during the three days. The game's scenario? A team of researchers from LIH was close to a crucial discovery, but then it suddenly disappeared! From there, one choice only was left for the participants: to put themselves in the shoes of the scientists and take over their research project!

By solving enigmas and experiencing fun physical, cerebral and virtual challenges, the teams passed through different rooms kept in semi-darkness to complete their important mission: identify the efficient cancer treatment that the lost research group had been close to discovering.



## Stunning activities

In each room, a scientific concept was explained in a simplified way by a short video. The teams, guided in their mission by a “real” LIH scientist or staff member, had to collect and win money during the game to finance their mission and try to be as fast as possible to complete each challenge. Each room harboured an unexpected activity: the participants could jump into a giant ball pool to find the right treatment for a specific cancer type, prove their mathematical skills and dexterity to determine the optimal treatment dose, pilot drones to transport biological samples, help the immune system spot resistant cancer cells, perform pipetting experiments to screen for drugs and finally efficiency kill cancer cells in the body in a virtual reality game.

More than 300 people participated in the LIH Science Quest and gave a very positive feedback to the organisers. A second edition of the event with a different thematic focus may therefore be organised in 2020.



**“ This is the largest event ever organised by LIH to promote its research activities and science in general to the lay public.”**

*Juliette Pertuy, Communication Manager and project leader for the LIH Science Quest*



*Opening of the LIH Science Quest. From left to right: Prof Ulf Nehrbaas (CEO of LIH), Xavier Poos (Ministry of Health and member of LIH's Board of Directors), Lydia Mutsch (Minister of Health), Marc Hansen (Delegate Minister for Higher Education and Research), Dr Catherine Larue (CEO of IBBL) and Jean-Paul Bertemes (Luxembourg National Research Fund).*



### Funding:

The event was subsidised by the Luxembourg National Research Fund through the PSP funding scheme that supports initiatives for science promotion to the public.

### Partners:

LIH's Communication Unit organised the event in partnership with the Marketing and Communication Unit of IBBL – Integrated BioBank of Luxembourg. The Ministry of Health was present with a stand to promote healthy nutrition and life style.





# MAX, THE TINY MICROBE WHO WANTS TO BE A SUPER HERO

Publication of a children's book

General Management > Communication Unit

**LIH has the mission to promote science and research to the lay public, in particular to the younger generation. Why not start to catch interest already in those of very young age?**

The Communication Unit edited a storybook suitable for children from four years onwards. The topic is related to one of LIH's research axes: investigating the role of the human gut microbiota, the population of microbes in the intestine.

Written in an easy language and extensively illustrated with appealing images, the book tells the tale of a friendly gut microbe named Max. The funny and trilling story does not only entertain children, it also transmits knowledge on the functioning of the human body and educative messages related to recent results in microbiology research.

The hardcover book of 24 pages, currently available in two languages, can be ordered by sending an e-mail to **[communication@lih.lu](mailto:communication@lih.lu)** to be used for educational purposes in nursery or primary schools.



## Reference:

*Max - le tout petit microbe qui voulait devenir un super héros* (French), *Max - De butzeg klengje Mikrob dee gär e Superheld wier* (Luxembourgish)  
 Authors: Laura Star and Juliette Pertuy, Illustrator: Yves d'Agostino, Translation: Dr Malou Fraiture



### Book preview:

Max, is small...VERY SMALL. So tiny that you cannot see him with the naked eye! Max lives in the gut of Lea, a little girl. With his friends Julie and Marius and billions of other tiny microbes, he helps to keep Lea healthy every day.

Max is rather unhappy to be such a seamless microbe. *"I'm fed up with being a microbe! Nobody likes us. Humans just think we are all naughty and dangerous!"* He does not feel inspired to follow the example of his father, the chief police officer who controls and regulates transit of digested food in the gut. Instead he wants to become a SUPER HERO!

One day, Lea does not pay attention when preparing food for a barbecue with her parents. She should have listened to her dad who told her to wash her hands. Too late! An invasion of evil companions has started.

This is the chance for Max to prove to the world that he can be a SUPER HERO! However, will he and his microbe friends be able to fight the invading Salmonella bacteria and prevent Lea from getting ill?

"Let's launch the offensive!" shouts Max.



**“ With this book we popularise complex scientific notions and touch a very young audience, thanks to a catching story tale, nice illustrations and cute characters.”**

*Laura Star, Communication officer and main author of the book*









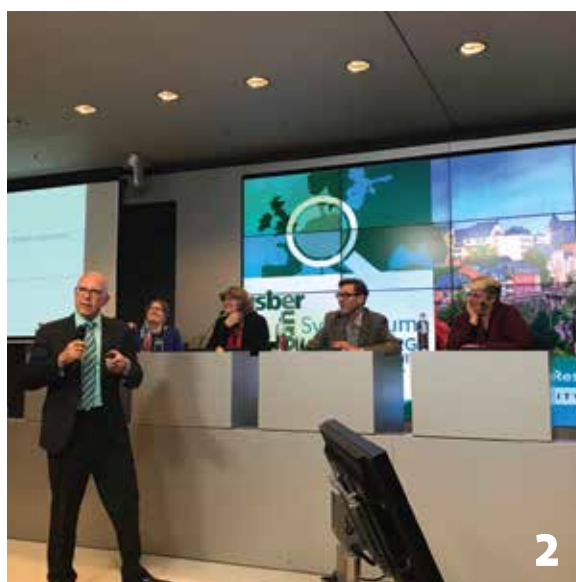


# HIGHLIGHTS CALENDAR 2018

News, events, awards and nominations

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1

## Multiannual framework agreement signed

On 25<sup>th</sup> January, a new framework agreement between LIH and the Luxembourg Government was set up for the period 2018-2021. The Government allocates 149.9 million euros to LIH, which corresponds to a 26% increase compared to the past four-year period. The agreement was signed by Marc Hansen, Minister Delegate for Higher Education and Research, Lydia Mutsch, Minister of Health, Dr Gregor Baertz, President of LIH's Board of Directors, Dr Ulf Nehrbass, CEO of LIH, and Dr Catherine Larue, CEO of IBBL - Integrated BioBank of Luxembourg. Among the key performance indicators stated in the agreement are the quality of the scientific production as well as the ability to translate research excellence towards applications.

*Photo: Signature of the 2018-2021 framework agreement. Back - from left to right: Dr Gregor Baertz (President of LIH's Board of Directors), Gaston Schmit (Ministry of Higher Education and Research), Robert Kerger (Ministry of Higher Education and Research). Front - from left to right: Dr Ulf Nehrbass (CEO of LIH), Lydia Mutsch (Minister of Health), Marc Hansen (Minister Delegate for Higher Education and Research), Dr Catherine Larue, CEO of IBBL.*

2

## Biospecimen Research Symposium held in Luxembourg

The International Society for Biological and Environmental Repositories (ISBER) and IBBL - Integrated BioBank of Luxembourg welcomed biospecimen research experts to Luxembourg on 27<sup>th</sup> and 28<sup>th</sup> February for the first-ever Biospecimen Research Symposium in Europe. Throughout the symposium, international biospecimen research experts presented and discussed recent findings and developments in the field for all major types of specimens, such as human fluid or tissue. The event was supported by the Luxembourg National Research Fund.

3

## Fulbright scholarship for a research stay in the United States

In March, Mathis Wolter, PhD candidate in the Eco-Immunology and Microbiome Research Group at LIH's Department of Infection and Immunity, was awarded a prestigious scholarship by the Fulbright Scholar Programme of the United States of America, co-funded by the Luxembourg National Research Fund. The scholarship enables him to spend four months in a laboratory at the University of Michigan Medical School with which the research group has a tight collaboration. This research stay is part of his PhD project in which he investigates the complex interplay between gut microbes, the gut mucus layer and dietary fibre.

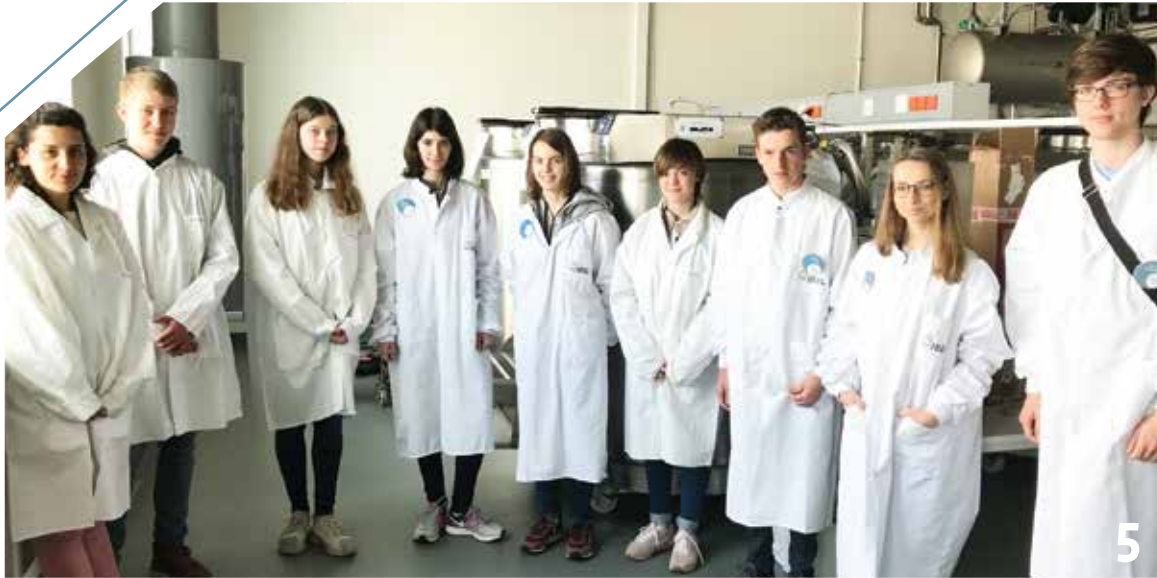
4

## LIH participated to the state visit in France

From 19<sup>th</sup> to 21<sup>st</sup> March, President Emmanuel Macron invited Their Royal Highnesses Grand Duke and Grand Duchess of Luxembourg to France for a state visit. Next to the Luxembourg Prime Minister and members of the Government, over 200 officials accompanied the Grand Ducal couple. Three representatives from LIH were part of the Luxembourg biomedical research delegation: Prof Laetitia Huiart, Director of the Department of Population Health, Dr Manon Gantenbein, Head of the Clinical and Epidemiological Investigation Centre, and Dr Catherine Larue, CEO of IBBL - Integrated BioBank of Luxembourg. They had the opportunity to meet the executives of major French research organisations and alliances such as Inserm, Aviesan or Medicen and discuss about possible collaborations to strengthen population health and clinical research in Luxembourg.

*Photo: Visit of Luxembourg biomedical research delegation at Inserm in Paris, France*







5

## Science Club visited the biobank

To present its activities to the young generation, IBBL - Integrated BioBank of Luxembourg welcomed a group of teenagers, members of the Luxembourg Science Club, for a guided tour of its new facilities in Dudelange on 12<sup>th</sup> April. The Science Club, coordinated by the National Museum of Natural History, is open to young people between 11 and 18 years interested in science and technology.

6

## New GOTS presidency

The German-Austrian-Swiss Society for Orthopaedic Sports Medicine (Gesellschaft für Orthopädisch-Traumatologische Sportmedizin, GOTS) designated Prof Romain Seil as its new president. The GOTS committee unanimously elected him for a period of two years at the annual GOTS congress held from 24<sup>th</sup> to 26<sup>th</sup> May at the University of Hamburg, Germany, and gathering 900 experts in sports medicine. Prof Seil is an orthopaedic surgeon at the *Centre Hospitalier de Luxembourg* leading the Department *Appareil Locomoteur*. He is also co-founder of the Sports Medicine Research Laboratory within LIH's Department of Population Health.

7

## Medal from the Japanese Bifidus Foundation

Prof Mahesh Desai, Principal Investigator of the Eco-Immunology and Microbiome research group at LIH's Department of Infection and Immunity, was honoured with the Dr Tissier's medal at the 22<sup>nd</sup> annual meeting of the Japanese Bifidus Foundation held on 31<sup>st</sup> May and 1<sup>st</sup> June in Tokyo, Japan. Prof Desai was invited to hold a plenary lecture for an audience of hundreds of researchers. Subsequently he was handed the Dr Tissier's medal for his excellent contributions to the field of intestinal microbiology. The medal is designed in remembrance of Dr Henri Tissier, a French paediatrician who had been the first to observe *Bifidobacteria* from the human gut.





8



9

ISO  
9001:2015  
CERTIFIED

10



11



©MAEE

12



8

## Pillow fight against Parkinson's disease

On 9<sup>th</sup> June, a Giant Public Pillow Fight took place in Luxembourg City in front of the Grand Ducal Palace. The aim of this symbolic event was to raise awareness about Parkinson's disease and the research activities of the National Centre of Excellence in Research on Parkinson's Disease (NCER-PD), a multiparty research programme supported by the Luxembourg National Research Fund. Hundreds of visitors joined the fun event and could visit stands from different organisations informing about Parkinson's disease and research in Luxembourg. This second edition of the Giant Public Pillow Fight was co-organised by NCER-PD, the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg and LIH.

10

## Successful transition to ISO 9001:2015 certification

LIH was able to successfully renew its ISO 9001 certification for its previously certified administrative and research services following an external audit of its quality management system on 21<sup>st</sup> and 22<sup>nd</sup> June. Importantly, the transition to ISO 9001:2015, the latest version of the norm, was achieved. The ISO 9001 standard sets out the criteria of a good quality management system, ensuring processes that foster continuous improvement in services. Such a system is valuable for a research institution as a governance tool as it allows for effective performance measurement, contributes to bottom line improvements and helps to manage risks.

12

## Advancing sexually transmitted diseases treatment in Africa

On 28<sup>th</sup> June, the Minister of Cooperation and Humanitarian Action, Mr Romain Schneider, signed an agreement with LIH and other partners for a new operational research and capacity-building programme named CARES. The ambitious project that shall run from 2018 to 2022 aims at improving the health status of the population in West Africa regarding sexually transmitted diseases. Its main objective is the qualitative management, in the Ziguinchor region of Senegal and Guinea-Bissau, of infections with Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Human Papillomavirus (HPV), the latter being involved in the development of cervical cancer. CARES will facilitate the access to diagnosis and treatment of infected people, thereby reducing mortality in the targeted regions.

*Photo: Signing ceremony for the CARES project. Project leader Dr Carole Devaux (Head of LIH's Infectious Diseases Research Unit, Department of Infection and Immunity) is standing in the first row with Minister Romain Schneider on her right and Prof Markus Ollert (Director of LIH's Department of Infection and Immunity) on her left.*

9

## Award nomination at the European Communication Summit

At the European Communication Summit held from 13<sup>th</sup> to 14<sup>th</sup> June in Berlin, Germany, LIH's Communication Unit got the second position for the Young Communicator Award, when presenting the innovative concept of the LIH Science Quest 2018. Communication Manager Juliette Pertuy gave a pitch to an audience of professionals in communication coming from all over Europe. Inspired from escape and adventure games, the LIH Science Quest is an innovative science-promoting event, the first of its kind in Luxembourg bringing the lay public in touch with biomedical research.

11

## Inspiring encounters at the Lindau Nobel Laureate Meeting

Davide Franchina, PhD candidate in the Experimental and Molecular Immunology Research Group at LIH's Department of Infection and Immunity, had the opportunity from 24<sup>th</sup> to 29<sup>th</sup> June to be among the 600 young researchers from all over the world who had been selected to attend the 68<sup>th</sup> edition of the Nobel Laureate Meeting in Lindau, Germany. The 2018 meeting was dedicated to the field of physiology and medicine and hosted 39 Nobel laureates. The doctoral candidate was able to exchange with many of them and get input for his research project that aims at investigating how cellular stress interferes with the immune response.







13

## Rotary Europe 4 Europe visit

On 24<sup>th</sup> July, IBBL - Integrated BioBank of Luxembourg welcomed 22 students from all over Europe for a guided visit of its new facilities under the Rotary's Europe 4 Europe cultural awareness exchange programme. The visit focused on IBBL's operations, from the traditional biobanking services of sample storage and collection, to sample processing and biospecimen research activities.

14

## World Hepatitis Day

On 28<sup>th</sup> July, at the occasion of the World Hepatitis Day, the Ministry of Health, together with the Luxembourg Red Cross, LIH and the *Centre Hospitalier de Luxembourg* held an awareness campaign on hepatitis. A booth was placed at the main train station in Luxembourg City where people could get information on the viral disease and take a travel through the human body with a virtual reality device. Rapid hepatitis screening was offered in the DIMPS van (Mobile Intervention Device for the Promotion of Sexual Health). In addition, LIH published a campaign on its Facebook page to present the different national actors involved in hepatitis prevention and diagnostics in Luxembourg.

## AUGUST

15

## LIH at position 15 of international ranking of research institutions

*Times Higher Education*, known for providing the World University Rankings, a performance analysis of universities worldwide, published a ranking of independent research institutions and hospitals. LIH appeared on position 15 in the list, along with top research institutions such as the Howard Huges Medical Institute and the Cold Spring Harbor Laboratory in the United States or the European Molecular Biology Laboratory in Germany. When considering only European institutions, the institute outperformed the largest part, ranking on position 7. The classification is based on the field-weighted citation index of the institutions' publications from 2013 to 2017. This high positioning underlines the originality, quality and competitiveness of LIH's research developed over the last few years.

## SEPTEMBER

16

## Best publication award by German Stem Cell Network

At the 6<sup>th</sup> annual meeting of the German Stem Cell Network held in Heidelberg, Germany from 19<sup>th</sup> to 21<sup>st</sup> September, a publication co-authored by Dr Gunnar Dittmar, Head of the Proteome and Genome Research at LIH's Department of Oncology, was selected as the "Publication of the Year 2018". The article titled *Senescence-associated reprogramming promotes cancer stemness* appeared in the prestigious journal *Nature* in 2017. It is a ground-breaking study that provides new mechanistic insights into the plasticity of cancer cells and could have an impact on cancer therapies.

17

## RIKEN-IMS visit to Luxembourg's biomedical research centres

A delegation from the renowned Japanese RIKEN Centre for Integrative Medical Sciences (RIKEN-IMS) visited Luxembourg from 24<sup>th</sup> to 26<sup>th</sup> September to meet Government representatives and the directors of the local biomedical research institutions. LIH and the Luxembourg Centre for Systems Biomedicine at the University of Luxembourg have been intensively collaborating with RIKEN-IMS for the past few years in the field of immunology, microbiome and inflammatory diseases. The three-day visit aimed at further strengthening these ties. It included a symposium to present the joint research projects, tours of the local biomedical research facilities including LIH's Department of Infection and Immunity, and a workshop to exchange on the possible establishment of an outpost laboratory of RIKEN-IMS in Luxembourg.





THE LUXEMBOURG  
INSTITUTE OF HEALTH PRESENTS :  
THE TÉTONS TATTOO SHOP  
& LES FRANJYNES  
ON TOUR POUR  
OCTOBRE ROSE 2018



  
**18 octobre**  
**The Office**  
// 29 Boulevard de la Grande-  
Duchesse Charlotte //  
L-1331 Luxembourg

**21**



18

## Kick-off of a COST Action initiated by LIH

A new COST Action named CardioRNA was successfully launched with a kick-off meeting on 3<sup>rd</sup> October in Brussels, Belgium. The European Cooperation in Science and Technology (COST) is a funding organisation that supports the creation of international research networks, called COST Actions. CardioRNA specifically aims at accelerating transcriptomics research in cardiovascular disease and furthering the translation of experimental data into practical applications for diagnostics and therapies. Dr Yvan Devaux, Head of the Cardiovascular Research Unit at LIH's Department of Population Health, is the Scientific Chair of the Action.

19

## Best poster award at EACR Conference on Cancer Metabolism

Andrés Cano Galiano, PhD candidate at the NorLux Neuro-Oncology Laboratory in LIH's Department of Oncology, was awarded a prize for his research poster at the international conference "Mechanisms to Therapies: Innovations in Cancer Metabolism" organised by the European Association of Cancer Research (EACR). The conference held from 9<sup>th</sup> to 11<sup>th</sup> October in Bilbao, Spain, gathered top experts in the field of oncology to discuss the current knowledge on metabolic alterations in tumours and how those can be exploited to treat cancer. The award was sponsored by *Cancer at Nature Research* of the Nature Publishing Group.

20

## Nomination to the EANO Executive Board

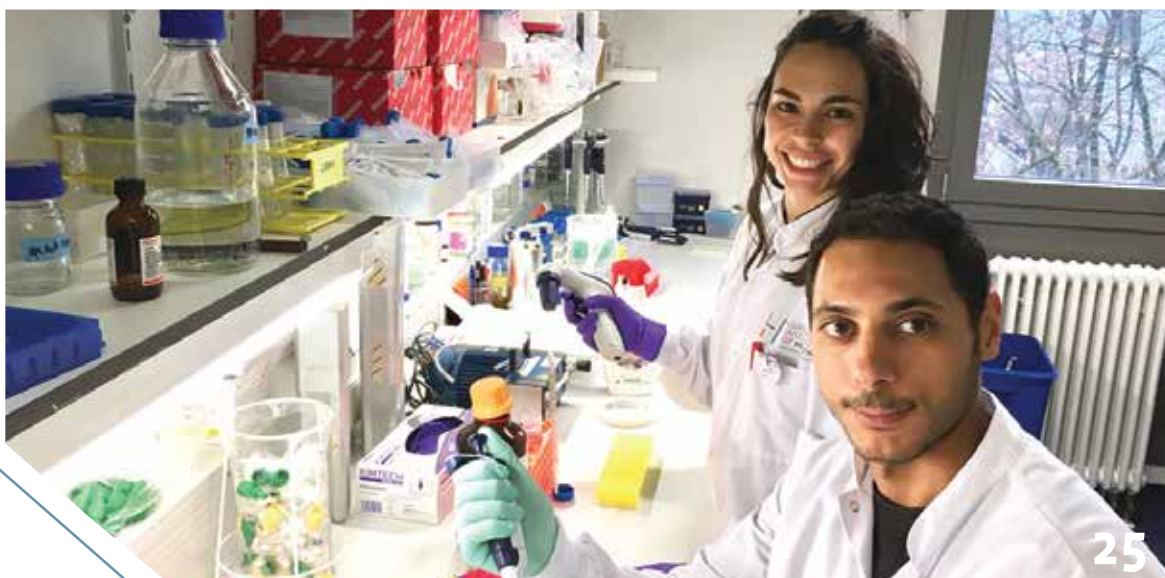
On 15<sup>th</sup> October, Prof Simone Niclou was elected to join the Executive Board of the European Association of Neuro-Oncology (EANO) for a period of two years. EANO is Europe's multidisciplinary neuro-oncology organisation embodying all medical and scientific disciplines involved in the prevention, diagnosis and treatment of tumours of the central nervous system. Prof Niclou has been a member of EANO for many years. As Head of the NorLux Neuro-Oncology Laboratory within LIH's Department of Oncology, she is an expert in neuro-oncology focusing her research on the biology of brain tumours.

21

## *Téton Tattoo Shop* and *Franjynes* on tour for Pink October

October is the month to raise awareness on breast cancer. On 18<sup>th</sup> October, LIH invited for an encounter with two women from France who took initiatives that help cancer patients to live on despite their disease. Alexia Cassar, formerly researcher in oncology, presented her tattoo studio *Téton Tattoo Shop* dedicated to nipple reconstruction after breast cancer surgery. Julie Meunier showed an alternative to wigs for patients who lose their hair during chemotherapy. *Franjynes* sells patented hair fringes of different styles that can be worn with a turban.







22

## Two awards for doctoral candidates at the PhD Days

The 2018 edition of the PhD Days organised by the Doctoral School in Science and Engineering of the University of Luxembourg attracted roughly 100 doctoral candidates to the *Maison du Savoir* in Esch-sur-Alzette on 18<sup>th</sup> and 19<sup>th</sup> October. This year, the event included five keynote lectures, 14 talks by PhD candidates and four poster sessions. Marina Wierz, PhD candidate at the Department of Oncology, received the first prize for her excellent oral presentation on her recent findings on leukaemia. The prize for the best research poster, subsidised by the Luxembourg National Research Fund, was awarded to Yolanda Pires Afonso from the Department of Oncology who presented her PhD project related to brain cancer.

*Photo: Yolanda Pires (left) and Marina Wierz (right) were awarded for their excellent presentations at the PhD Days 2018.*

23

## Successful Medical Research Day

On 24<sup>th</sup> October, the fourth edition of the Medical Research Day was held at the *Centre Hospitalier de Luxembourg* to open the world of medical research to the young generation. The event was organised by the hospital jointly with LIH and the Luxembourg Centre for Systems Biomedicine of the University of Luxembourg. Over 300 high school students attended and participated in parallel information sessions and workshops to learn about current projects and challenges in medical research. The young people also had the opportunity to test their knowledge in a quiz moderated by Luxembourg's "Mister Science".

24

## Science Award 2018 by the Signal Transduction Society

The Signal Transduction Society (STS), an active society devoted to the scientific exchange around cellular signalling, honoured Prof Dirk Brenner with the "Science Award 2018". The prize, awarded during the 22<sup>nd</sup> international STS Meeting on 7<sup>th</sup> November in Weimar, Germany, is a recognition for Prof Brenner's excellent research work on the metabolism of immune cells. The researcher joined LIH in 2015 to set up his own team, the Experimental and Molecular Immunology Research Group at the Department of Infection and Immunity, supported by an ATTRACT Consolidator grant from the Luxembourg National Research Fund.

25

## Pelican grants for two young researchers

PhD candidates Yolanda Pires Afonso and Mohamad Sarmini are two of the successful applicants for the "Pelican Grant 2018" given by the foundation *Fondation du Pélican de Mie et Pierre Hippert-Faber* that is under the aegis of the *Fondation de Luxembourg*. This grant can cover expenses related to training such as travel and accommodation costs for conferences, courses or short-term research stays abroad. This financial support is beneficial for their professional development and their PhD projects in brain cancer biology carried out in the NorLux Neuro-Oncology Laboratory at LIH's Department of Oncology.

26

## Fellowship for Interdisciplinary Life Sciences from the Joachim Herz Stiftung

Dr Katharina Baum, postdoctoral researcher in the Bioinformatics and Modelling research group at LIH's Department of Oncology, was granted an add-on fellowship for Interdisciplinary Life Sciences by the German foundation *Joachim Herz Stiftung*. This competitive grant allows her to cover training, conference and research fees as well as travel costs related to visits to Singapore in the frame of her research project in bioinformatics funded by a bilateral AFR grant from the Luxembourg National Research Fund.





27



28



30





27

## The biobank turned 10

On 9<sup>th</sup> November, IBBL - Integrated BioBank of Luxembourg celebrated the 10<sup>th</sup> anniversary of its creation. On this occasion, a formal celebration was organised in its premises in Dudelange, bringing together all key stakeholders of Luxembourg's medical and research landscape and providing a stimulating setting for debating on the future of national research infrastructures and personalised medicine. Established in 2008 under the National "Health Sciences and Technologies Action Plan", IBBL has been contributing over the past decade to Luxembourg's positioning as an internationally renowned centre of excellence in biobanking at the service of biomedical research.

28

## Newcomers gathered at the National PhD Welcome Day 2018

On 22<sup>nd</sup> November, the third edition of the National PhD Welcome Day united over 100 doctoral candidates from all disciplines who recently started their PhD in Luxembourg. This year, the focus of the event was on science communication. The young researchers got useful input on how to reach out to the lay public and to share scientific findings to tailored audiences. The National PhD Welcome Day 2018 was organised under the lead of the Luxembourg Institute of Socio-Economic Research in partnership with all national stakeholders in doctoral training.

29

## International table tennis congress

The first international table tennis congress in Luxembourg was held on 23<sup>rd</sup> and 24<sup>th</sup> November with 75 attendees from 14 countries. Under the slogan "Linking Practice and Science", it featured a series of international experts from table tennis practice and science who provided state-of-the-art information on this highly complex and demanding sport. Aspects related to performance and health took centre stage for a target audience of trainers, coaches, medical staff members, players and scientists of the field. This event for which LIH was one of the four co-organisers marked the highlight of the annual Sports Medicine Colloquium series of the Luxembourg Academy of Sports Medicine, Physiotherapy and Science.

30

## Connecting the public with science at the Researchers' Days

At the 2018 edition of the Researchers' Days on 30<sup>th</sup> November and 1<sup>st</sup> December, which attracted around 6,500 visitors, LIH was present with three hands-on workshops to display its activities to the lay public in a straightforward and fun way. The workshop "Outbreak detectives at work" put people in the shoes of microbiologists working in a disease outbreak situation. In another workshop, visitors dealt with "broken hearts". As "heart engineers", they had to make a simple device work as a pump with one-way valves, imitating the functioning of a heart. IBBL - Integrated BioBank of Luxembourg presented the stunning workshop "Frozen to the bone" to explain how biological samples are stored. The Researchers' Days are organised every two years by the Luxembourg National Research Fund.

31

## Raising awareness on AIDS in high schools

An awareness day on Acquired Immune Deficiency Syndrome (AIDS) was organised for high school classes at *Forum Geesseknäppchen* in Luxembourg City on 30<sup>th</sup> November. During different workshops, experts informed the pupils about disease prevention, diagnosis and treatment. The event was co-organised by *HIV Berodung* of the Luxembourg Red Cross, the Preventive Medicine Division of the Ministry of Health, the Infectious Diseases Unit of the *Centre Hospitalier du Luxembourg*, the non-governmental organisation Stop Aids Now/Access and LIH.





## Prise en charge des cancers du poumon au Luxembourg 2013–2014

Résultats issus du Registre National du Cancer



### Rapport scientifique





32

### Affiliated professorship at the University of Luxembourg

From 1<sup>st</sup> December, Prof Laetitia Huiart, Director of LIH's Department of Population Health, holds an affiliated professorship with the Faculty of Science, Technology and Communication of the University of Luxembourg. This appointment for a three-year term aims at further strengthening the cooperation between the country's university and the biomedical research institution.

33

### Postdoctoral researchers reflecting on career options

From 4<sup>th</sup> to 7<sup>th</sup> December took place the fourth edition of the Cross-border Postdoctoriales in Luxembourg City, a career orientation workshop of four days for postdoctoral researchers from Luxembourg, France and Germany. Organised by *Association Bernard Grégory* and the Franco-German University, in partnership with the Luxembourg National Research Fund and the main public research institutions in Luxembourg, it gathered 18 selected participants. The workshop allowed the attendees to reflect on their professional goals, learn about the job market in the Greater Region, meet recruiters and network with PhD holders from different fields.

34

### First report on lung cancer care in Luxembourg

The National Cancer Registry (RNC) has published its first report in December assessing the quality of care provided to lung cancer patients in the country. For several years, Luxembourg has been developing concrete actions within the framework of the National Cancer Plan to improve the quality of care provided to cancer patients. In this context, the RNC has been specifically developed to allow for quality assessment. The published report, composed of a scientific and a technical document, compiles results from RNC data collected between 2013 and 2014. It presents the main characteristics of lung cancer patients in Luxembourg and draws up a list of 24 quality of care indicators to evaluate diagnosis and treatment.

*Image: Cover page of scientific report*







35

## Winning team in Health Data Challenge

Dr Petr Nazarov and Tony Kaoma from the Bioinformatics and Modelling research group at LIH's Department of Oncology won a health data analysis challenge organised by the Data Institute of the University Grenoble Alpes, France. The challenge was given to nine interdisciplinary teams of three to four members with participants from France, Germany, Luxembourg, the Netherlands, Russia and United States. It was about finding appropriate statistical methods for genomics data analysis that allow quantifying tumour heterogeneity in samples from cancer patients.

*Photo: Tony Kaoma (left) and Dr Petr Nazarov (middle) with their team colleague Fabien Bergman*

36

## Annual Personalised Medicine Consortium retreat

On 10<sup>th</sup> December, Luxembourg's researchers and clinicians gathered at the eighth edition of the annual retreat of the Personalised Medicine Consortium (PMC). The event was an opportunity to exchange knowledge, provide updates on the progress of ongoing projects in personalised medicine and announce the awardees of the 2018 PMC Pump Prime Fund. Dr Feng He, heading the Immune Systems Biology Research Group at LIH's Department of Infection and Immunity was one of the awardees for a new collaborative project on Parkinson's disease.

*Photo: Dr Feng He, awardee of the PMC Pump Prime Fund*

37

## Appointment of new CFAO

Marc Grabowski was recruited as new Chief Financial and Administrative Officer (CFAO) of LIH to start in January 2019. He replaces Karl-Heinz Dick who held the position of CFAO of LIH and previously of IBBL - Integrated BioBank of Luxembourg for more than five years. Mr Grabowski holds Master's degrees in International Finance and Business Administration. He started his career as auditor, before moving to the finance sector where he held various positions of increasing responsibility, including as Chief Financial Officer and Chief Executive Officer.









# **INSTITUTIONAL ORGANISATION AND FIGURES**

113





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

## BOARDS

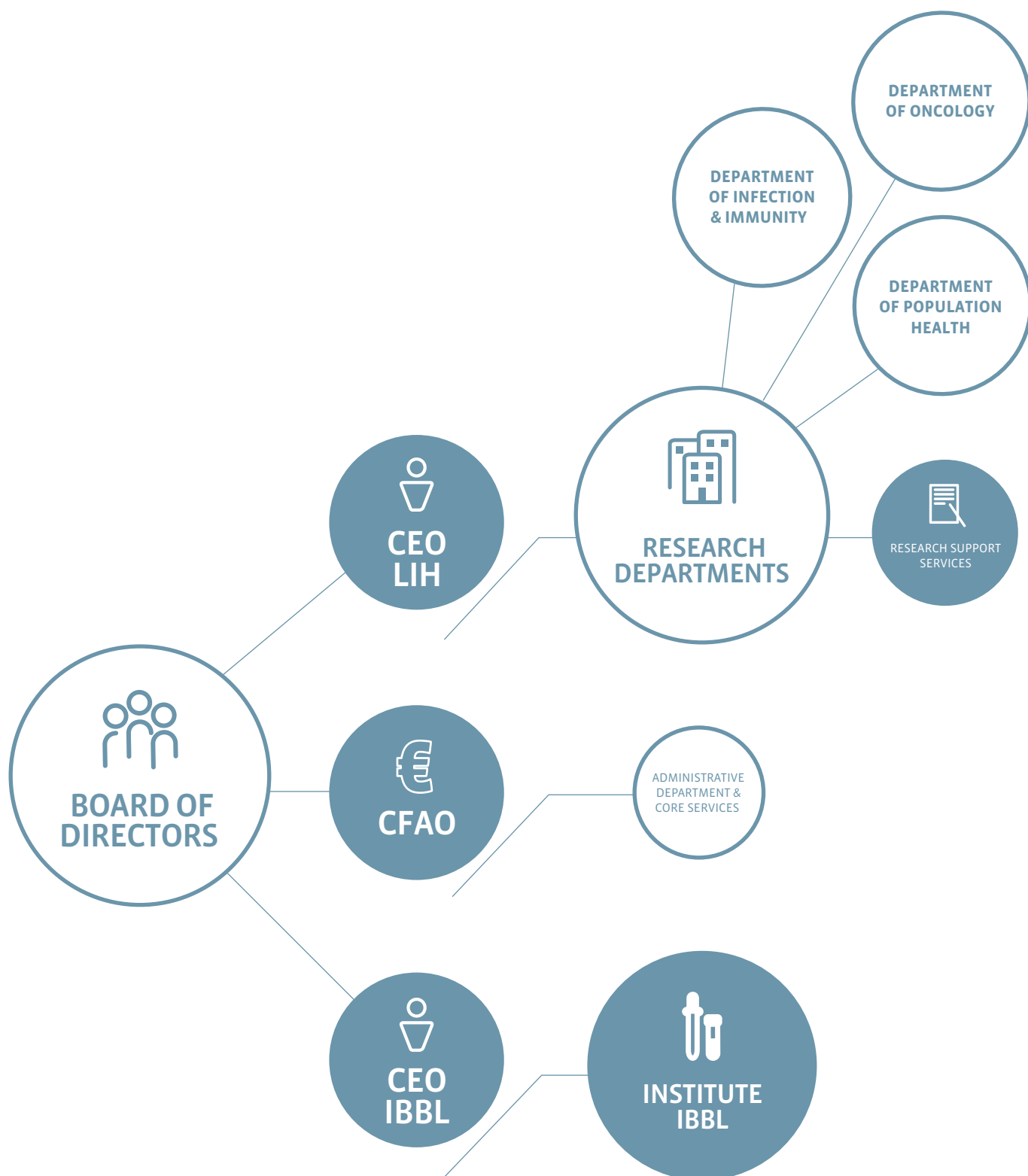
The **Board of Directors** is nominated by the Government and is composed of nine external members of different professional backgrounds. Its mission is to oversee the activities at LIH. It is responsible for the general organisation, for defining internal rules, for budget control, for framework contracts 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 **Coordinating Council** is a consultative body composed of internal representatives of the researchers, the personal delegation and the research and innovation support personnel. It issues advisory opinions to the Board of Directors regarding research policy, development and innovation and can advise on the content of the 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.







# KEY FACTS\*

2018



**3**

RESEARCH  
DEPARTMENTS



**1**

BIOBANK



**271**

PUBLICATIONS



**204**

SCIENTISTS



**3**

PATENT  
APPLICATIONS



**13.2** €  
MIO

THIRD-PARTY  
INCOME

\*figures as of 31<sup>st</sup> December 2018





**13**

PhD  
DEFENCES



**33**

NATIONALITIES



**383**

EMPLOYEES



**>300**

AGREEMENTS  
SIGNED



**23**

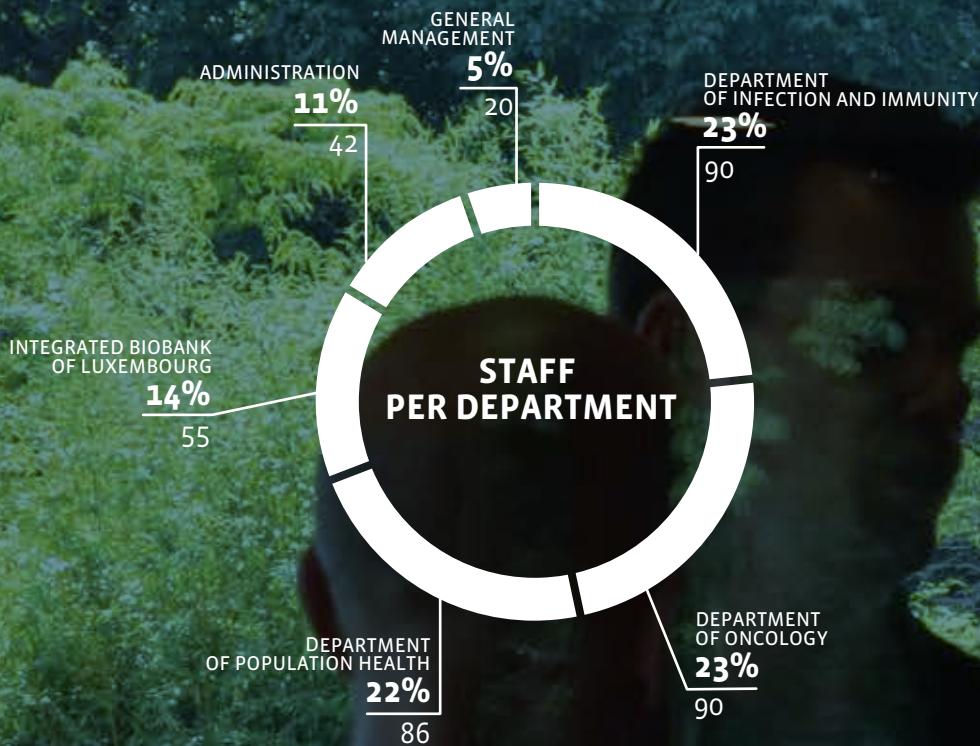
NEW PUBLIC-PRIVATE  
PARTNERSHIPS



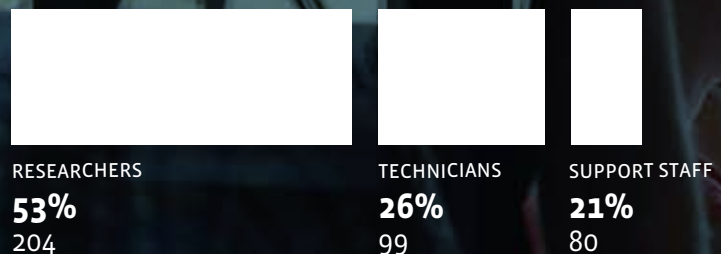
**>370**

ONGOING  
PROJECTS





## STAFF BY FUNCTION

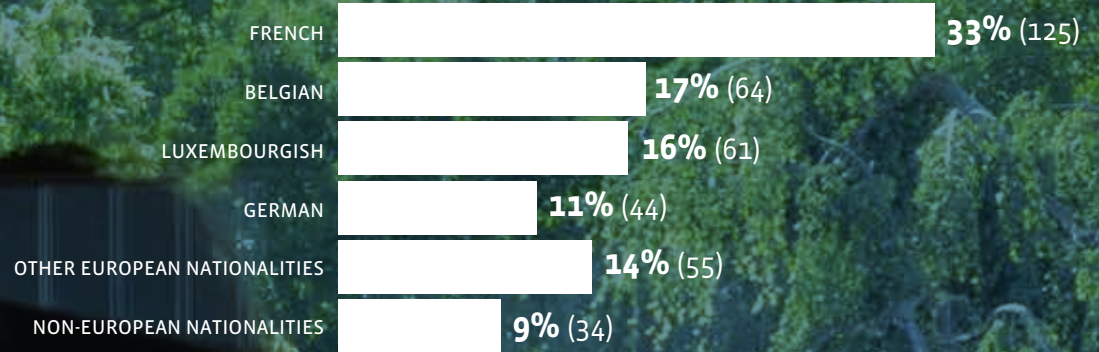


# HUMAN RESOURCES

(31<sup>st</sup> December 2018)



## STAFF BY NATIONALITY



## STAFF BY GENDER



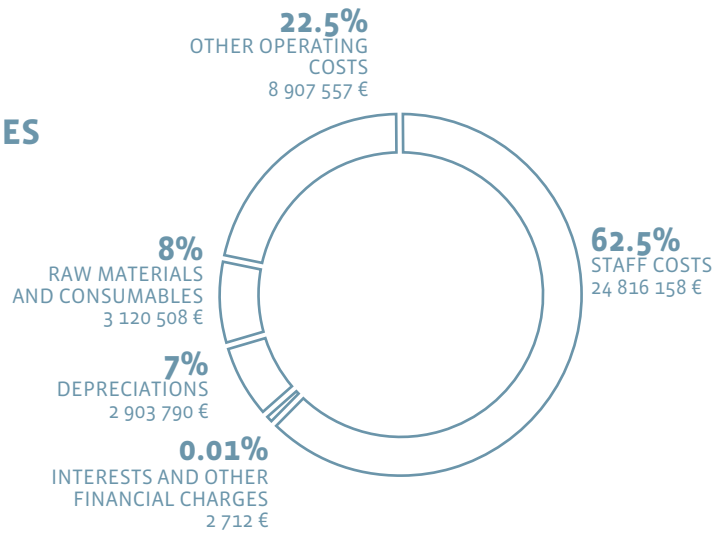
## STAFF BY WORK CONTRACT TYPES



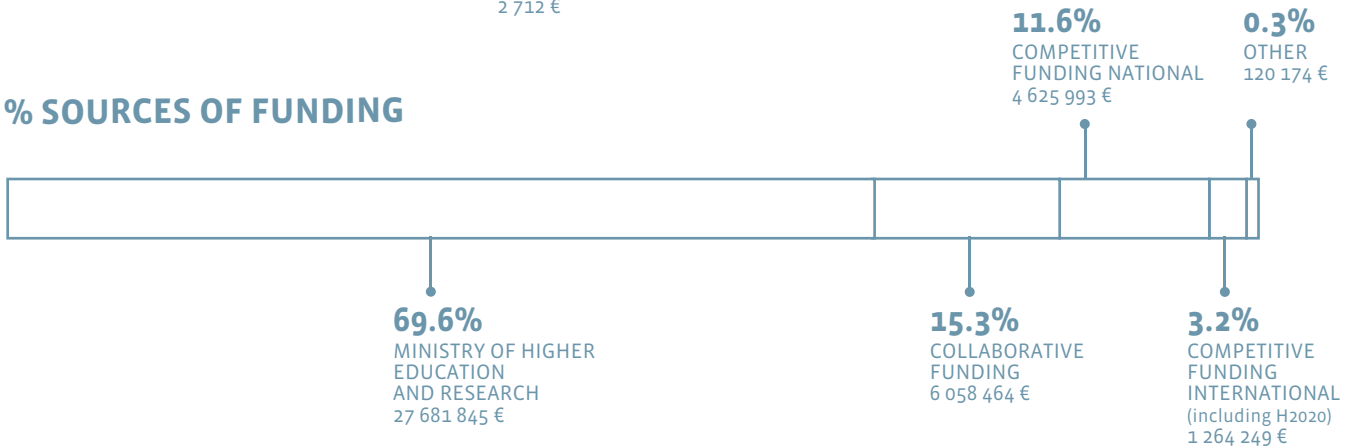


LIH

## % COST CATEGORIES

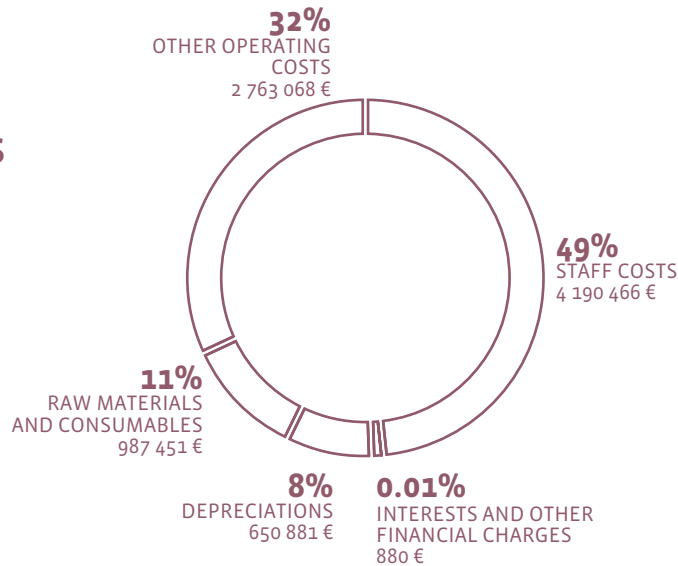


## % SOURCES OF FUNDING

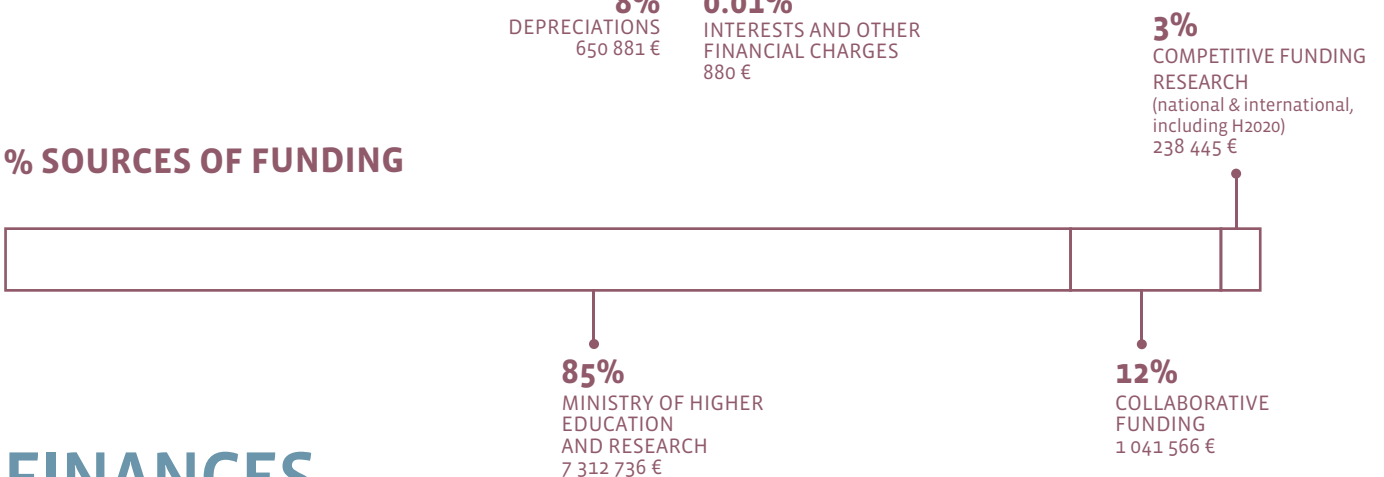


IBBL

## % COST CATEGORIES



## % SOURCES OF FUNDING



# FINANCES

## STATUTORY EXPENSES



**PROFIT AND LOSS ACCOUNT (EUR)****2018**  
01.01 - 31.12.18**2017**  
01.01 - 31.12.17**A. CHARGES**

1. Use of merchandise, raw materials and consumable materials	4.107.959.111	4.343.167.73
2. Other expenses	11.670.624	10.103.869
3. Staff costs	29.006.624	28.384.706
4. Value adjustment on intangible and tangible fixed assets	3.554.670	3.336.832
5. Interests and other financial charges	3.592	8.131
6. Profit for the financial year	0	0
<b>TOTAL CHARGES</b>	<b>48.343.471</b>	<b>46.176.706</b>

**B. INCOME**

1. Net turnover	1.724.477	1.757.498
2. Subsidies	45.529.604	43.868.440
3. Other income	1.011.435	78.568
4. Interests and other financial income	25.710	29.622
5. Loss for the financial year	52.244	442.578
<b>TOTAL INCOME</b>	<b>48.343.471</b>	<b>46.176.706</b>

# FINANCES

## PROFIT AND LOSS ACCOUNT

(31<sup>st</sup> December 2018)



ASSETS (EUR)	2018 01.01 - 31.12.18	2017 01.01 - 31.12.17
<b>FIXED ASSETS</b>		
Intangible fixed assets	739.359	829.365
Tangible fixed assets	8.012.126	8.122.938
Financial fixed assets	4.849	425.585
<b>TOTAL FIXED ASSETS</b>	<b>8.756.334</b>	<b>9.377.888</b>
<b>CURRENT ASSETS</b>		
<b>Debtors</b>		
<b>1. Trade debtors</b>	<b>1.294.302</b>	<b>1.077.438</b>
a. Becoming due and payable within one year	1.257.758	1.058.894
b. Becoming due and payable after more than one year	18.544	18.544
<b>2. Other debtors</b>	<b>2.767.222</b>	<b>6.976.361</b>
a. Becoming due and payable within one year	2.767.222	6.976.361
Cash at bank and in hand	<b>27.688.452</b>	<b>24.760.483</b>
<b>TOTAL CURRENT ASSETS</b>	<b>31.749.976</b>	<b>32.814.282</b>
<b>Prepayments</b>	<b>791.273</b>	<b>656.857</b>
<b>TOTAL ASSETS</b>	<b>41.297.583</b>	<b>42.849.027</b>

# FINANCES

## BALANCE SHEET

(31<sup>st</sup> December 2018)



**LIABILITIES (EUR)****2018**  
01.01 - 31.12.18**2017**  
01.01 - 31.12.17**CAPITAL AND RESERVES**

Financial wealth	4.099.157	4.099.157
Reserves	1.486.881	1.486.881
Profit or loss brought forward	8.051.788	8.494.366
Profit or loss for the financial year	-52.244	-442.578
Capital investment subsidies	9.632.094	9.886.546
<b>TOTAL CAPITAL AND RESERVES</b>	<b>23.217.676</b>	<b>23.524.372</b>
<b>Available reserve for projects</b>	<b>12.713.774</b>	<b>14.260.441</b>
<b>Provisions</b>	<b>1.271.426</b>	<b>1.661.304</b>

**NON-SUBORDINATED DEBTS**

<b>1. Trade creditors</b>	<b>3.073.941</b>	<b>2.406.668</b>
a. Becoming due and payable within one year	3.052.980	2.385.707
b. Becoming due and payable after more than one year	20.961	20.961
<b>2. Tax and social security debts</b>	<b>960.976</b>	<b>945.406</b>
a. Tax debts	5.040	4.837
b. Social security debts	955.936	940.569
<b>3. Other creditors</b>	<b>59.401</b>	<b>45.875</b>
a. Becoming due and payable within one year	59.401	45.875
<b>TOTAL AVAILABLE RESERVE FOR PROJECTS, PROVISIONS AND CREDITORS</b>	<b>18.079.518</b>	<b>19.319.694</b>
<b>Deferred income</b>	<b>389</b>	<b>4.961</b>
<b>TOTAL CAPITAL, RESERVES AND LIABILITIES</b>	<b>41.297.583</b>	<b>42.849.027</b>









**PUBLICATIONS**

**125**



# DEPARTMENT OF INFECTION AND IMMUNITY

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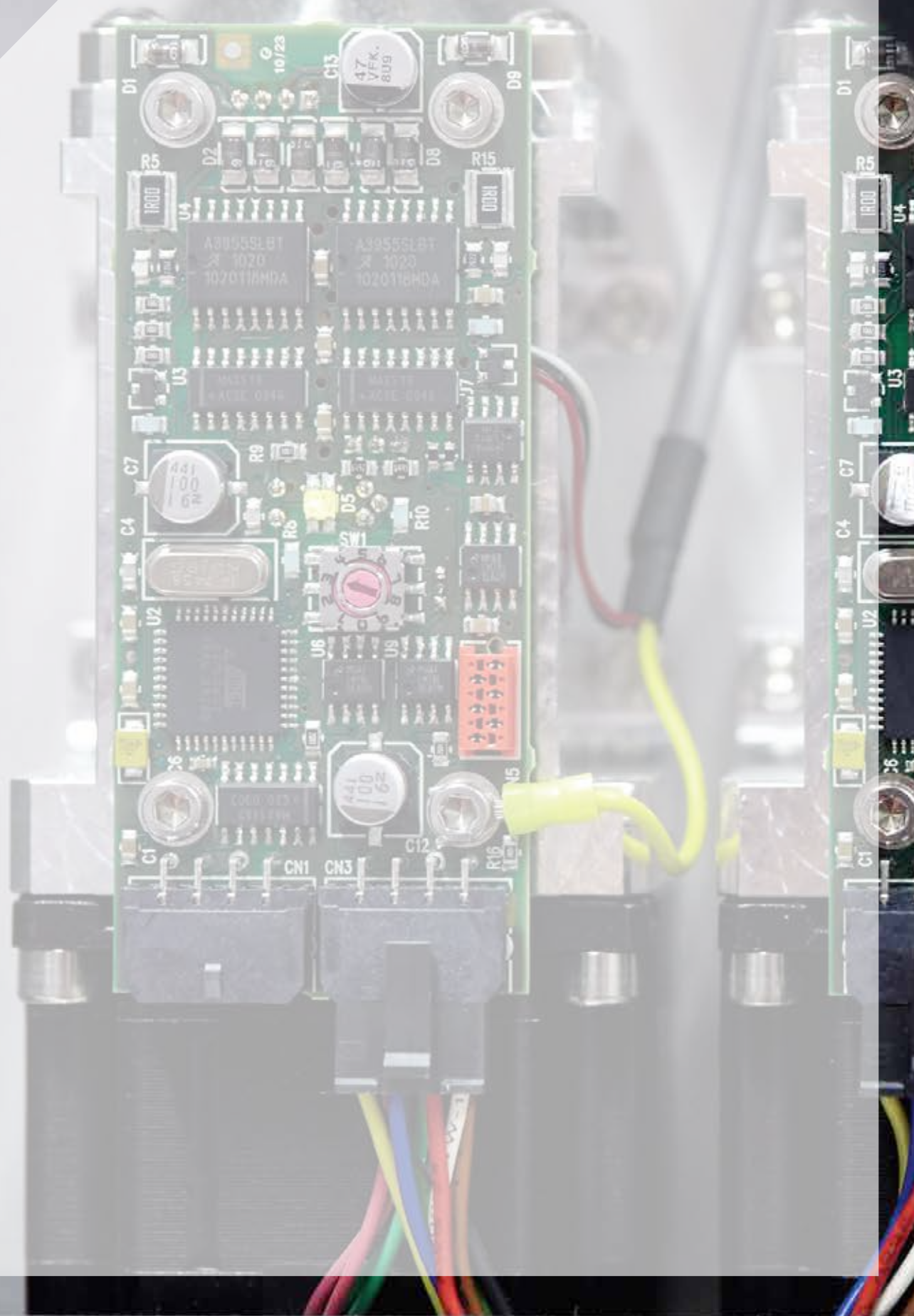
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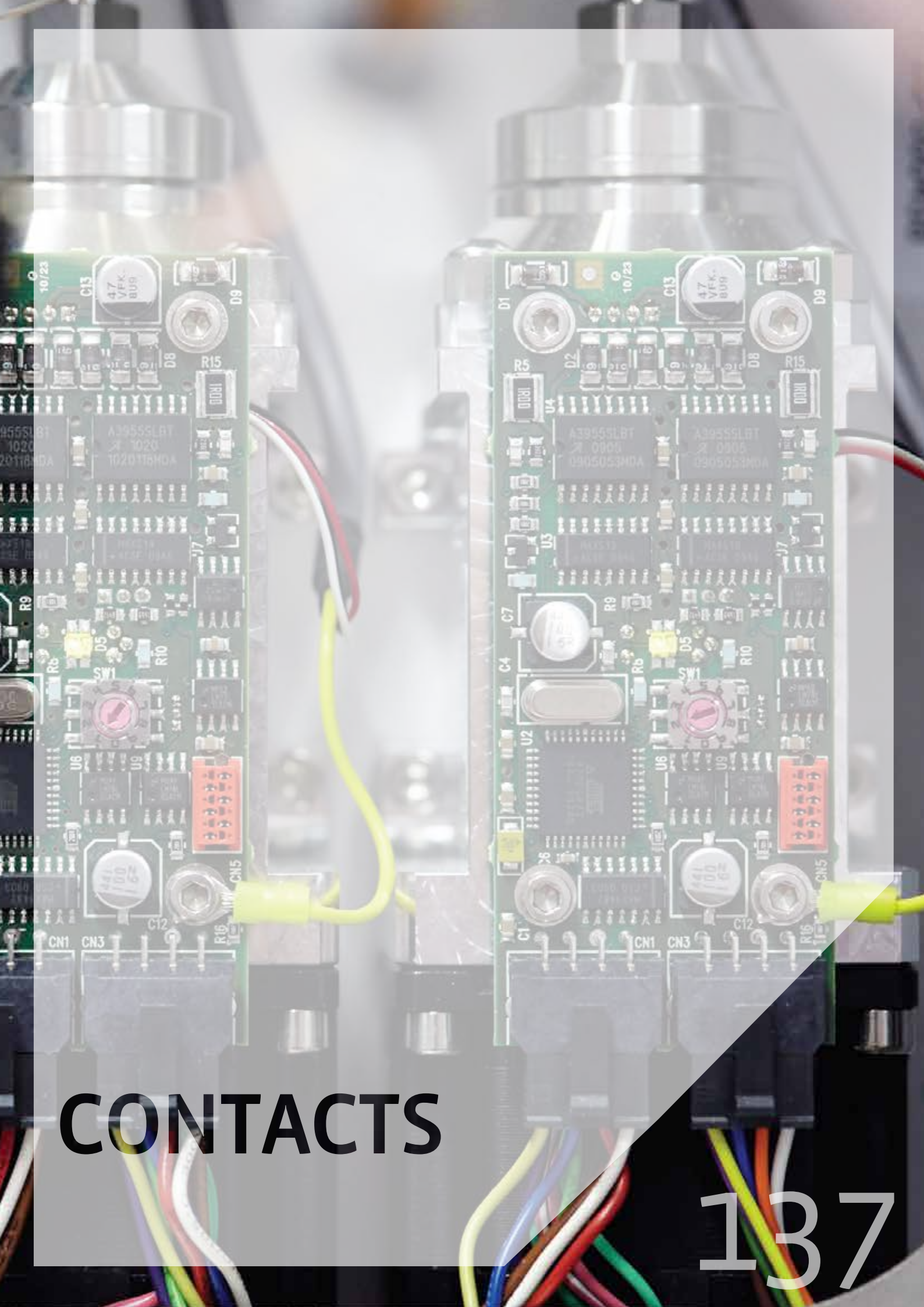
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