2019
ANNUAL REPORT
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In the midst of the current COVID-19 pandemic and of the socio-economic and health tumult we are experiencing as its consequence, it is my pleasure to be able to introduce the 2019 annual report, which comes as a much needed breath of fresh air during this difficult period. Now more than ever, the achievements depicted in the present report provide an unparalleled opportunity to reflect on the scientific excellence of our institute and on the remarkable journey towards translational medicine it has embarked on over the last few years.
As previously anticipated, LIH started setting in motion a string of reforms and restructurings back in 2018, with the aim of reviewing its strategy, processes and budget to make them more effective, synergistic and streamlined towards a common goal. These changes were prompted by the awareness of a rapidly and relentlessly evolving context which we could not and did not want to overlook, but rather exploit and integrate into every aspect of our operations, in order to be able to respond to the high expectations of the public in terms of tangible health benefits stemming from fundamental research. Indeed, the emergence of innovative “e-health” technologies and novel patient-derived disease models holds the potential to fundamentally disrupt the way in which biomedical research has traditionally been carried out. We have been working relentlessly towards implementing substantial changes that would enable us to fully embrace these new opportunities, putting the patient at the centre of our applied research, establishing integrated bed-to-bench-to-bed processes in our projects and thereby accelerating our transition towards a truly translational institute. I am now glad to announce that the year 2019 saw the concretisation of a number of key initiatives in this respect, which have allowed the translational dimension to permeate all areas of LIH’s activities.

A first crucial step was the creation of the dedicated Transversal Translational Medicine (TTM) unit, in collaboration with our long-term partners at the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg and at the Centre Hospitalier de Luxembourg (CHL). Led by one of the luminaries in the field of neurodegenerative diseases, Prof Rejko Krüger, TTM will instil a transversal, translational and collaborative mindset among all relevant stakeholders and develop a pipeline of translational programmes across multiple disease areas, leveraging on the experience gained through the ongoing National Centre for Excellence in Research on Parkinson’s disease (NCER-PD). As proof of its success, NCER-PD saw its financial support renewed by the National Research Fund in 2019 for a second phase.

Another area that has become highly translational and transversal at LIH is cancer research, centred specifically on immune-oncology and tumour resistance to treatment. The Department of Oncology, directed by Prof Simone Niclou as of May 2019, has been strengthening the link between research and clinical practice by establishing joint appointments with a growing number of clinician scientists and leading highly collaborative studies with national and international partners. A glaring example is the Personalised Functional Profiling (PFP) project. This bed-to-bench-to-bed study, launched in May 2019 in partnership with the CHL, the Hôpitaux Robert Schuman (HRS) and the Laboratoire National de Santé (LNS), aims to tailor cancer treatments to the individual characteristics of a patient’s tumour, and constitutes a key stepping stone towards the reinforcement of the reputation of our institute and of our country in general as a centre of excellence in translational oncology. And because true translational research entails a dimension of internationalisation to tangibly improve the health of the population going beyond individual geographical borders, we have also joined forces with the CHL in the context of SPRING, an international clinical trial aiming to test novel therapies on patients suffering from non-small cell lung cancer (NSCLC). This relationship has been further consolidated by the appointment of Dr Guy Berchem, oncologist at CHL and Principal Investigator of the study, as Associated Medical Director at LIH in May 2019.

As mentioned above, we have exploited the enormous disruptive potential of digital technologies and Artificial Intelligence to our favour or, more precisely, to that of our patients. Indeed, the Department of Population Health took several steps to integrate the digital dimension in its public health and epidemiology research activities, starting with the creation of a dedicated “Digital Epidemiology and E-health hub” in June 2019 and the subsequent launch of CoLive Diabetes, the first international digital cohort study on diabetes management and prevention.

A series of organisational changes have also taken place at the level of our renowned platforms, with the aim of further focusing on quality control and standardisation, increasing the added value of our services to the national scientific community and broadening their reach, thus ultimately bringing them at the centre of the translational medicine vision. The new Quantitative Biology Unit (QBU) was thus born in July 2019.

Our ultimate priority is to continue shaping translational research across Europe and beyond. In this respect, LIH and its biobank IBBL joined the consortium of five prestigious and highly competitive European studies, which kicked-off in 2019, and won additional applications for European grants. From supporting the use of digital technologies and Artificial Intelligence in cancer therapy, to the elucidation of the interaction between the immune system and tumours, these projects have reaffirmed our excellent reputation and international visibility as a valued partner for European-funded consortia. This reputation has further been reinforced by the high-quality fundamental research carried out by our researchers, which has resulted in numerous publications in the areas of immunity, oncology, diabetes and public health in prominent international journals.

As ever, I take the opportunity to extend my gratitude to the Ministry of Higher Education and Research, the Ministry of Health and the National Research Fund for their support over the years and for helping us generate continuous benefits for our patients. Finally, I extend my heartfelt thanks to our dedicated and passionate research and administrative staff.
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LIH’s mission is to have a positive 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 at the heart of Europe.
Translational research: implementing the vision
LIH has refined its research strategy to focus more on translational research, placing patients and the population at the centre of its activities. Jointly with its national partners, the institute aims to develop new diagnostic methods, innovative therapies and effective tools to contribute to personalised medicine in Luxembourg and beyond. In June 2019, a first farsighted step adopted to concretise this strategy was the creation of the new, dedicated Transversal Translational Medicine (TTM) Initiative, and the appointment of Prof Rejko Krüger as its Director. This will strengthen collaborations between Luxembourg’s key biomedical research players, healthcare providers and other relevant stakeholders and foster the translation of research results into clinical practice, thus addressing tangible unmet needs and improving health outcomes for patients.

Transversal Translational Medicine at LIH

TTM was established as a joint initiative between three of the main players in Luxembourg’s biomedical ecosystem, namely the Luxembourg Centre for Systems Biomedicine (LCSB) at the University of Luxembourg, the Centre Hospitalier de Luxembourg (CHL) and LIH. Its overarching aim is to instil a transversal, translational and collaborative mindset among researchers, healthcare practitioners and hospitals, allowing them to perform research that transcends the classical boundaries of individual diseases (the ‘transversal’ dimension) and that can be tangibly converted into improved diagnostics, therapies and interventions for patients (the ‘translational’ dimension). To implement this vision, TTM will develop and coordinate a pipeline of translational programmes that span multiple research topics and disease areas, such as oncology and immunity.
These studies will be based on the concept and rationale of the ongoing National Centre for Excellence in Research on Parkinson’s disease (NCER-PD), a translational programme created back in 2015 and funded by the Luxembourg National Research Fund (FNR) (see page 10), and will be supported by specific infrastructures, services and know-how. Indeed, TTM brings together a wealth of expertise, from an experienced team of researchers, to healthcare professionals such as physician scientists, nurses and neuropsychologists, among many other national and international collaborators.

NCER-PD is TTM’s flagship programme in terms of clinical research, enabling a better understanding of the mechanism of Parkinson’s disease and ultimately leading to its early diagnosis and to the development of highly personalised treatments for patients. In addition to clinical research, the TTM team will also continue carrying out fundamental research to shed light on some of the key biological processes underlying neurodegenerative disorders. Specifically, the group will focus on elucidating the series of chemical reactions occurring at the molecular level which could lead to the onset of neurodegeneration in Parkinson’s disease, as well as the genetic mutations associated with different forms of the disease.

“For laboratory research to be of direct benefit to patients, all key stakeholders must be brought together: researchers, clinicians, patient associations, health authorities and industrial partners.”

Prof Rejko Krüger

A world-renowned leader

The TTM unit will boast an internationally recognised expert in both the clinical and research sides of neurodegenerative diseases as its director. Indeed, in June 2019, Prof Rejko Krüger joined LIH as Director of Transversal Translational Medicine, with his appointment marking the official establishment of TTM. Prof Krüger will lead the TTM group in addition to his concomitant positions as Professor of Neuroscience at the University of Luxembourg and medical doctor specialised in movement disorders and neurodegeneration at the Neurology Department of the Centre Hospitalier de Luxembourg (CHL). Furthermore, he supervises a clinical and experimental research group on Parkinson’s disease at the Luxembourg Centre for Biomedicine Systems (LCSB) at the University of Luxembourg, with the financial support of a PEARL Excellence grant from the FNR. As the coordinator of the NCER-PD programme and Director of TTM, Prof Krüger is in the ideal position to coordinate the implementation of new translational projects generated from the experience of NCER-PD. Moreover, his extensive network and deep knowledge of the Luxembourg biomedical ecosystem will allow him to continue strengthening the ties between all key institutions.

‘For laboratory research to be of direct benefit to patients, all key stakeholders must be brought together: researchers, clinicians, patient associations, health authorities and industrial partners,’ underlines Prof Krüger. ‘The experience gained from NCER-PD, an example of a very successful multi-stakeholder collaboration, will be key in my new role. By using it as a reference model for the implementation of other translational research programmes, the TTM team will bridge the gap between fundamental science and clinical practice, improving the diagnosis and personalised treatment not only of Parkinson’s disease, but of a larger spectrum of chronic conditions through what we call a bed-to-bench-to-bed approach’, he concludes.
Dual success for the National Centre for Excellence in Research on Parkinson’s Disease

Translational programme on Parkinson’s reaches recruitment target and sees its financing renewed

The year 2019 brought a twofold achievement for the National Centre for Excellence in Research on Parkinson’s Disease (NCER-PD), Luxembourg’s flagship translational programme on neurodegeneration. Indeed, in July 2019, the Luxembourg National Research Fund (FNR) committed an additional EUR 6 million to the study, paving the way for its second phase. Subsequently, in December 2019, the NCER-PD team reached its participant recruitment target, having enrolled the planned 1,600 volunteers, patients and healthy controls in the programme.

NCER-PD was established back in 2015 as the first inter-institutional and multidisciplinary research programme of its kind in Luxembourg. It is a collaboration between the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg, LIH and its Integrated BioBank of Luxembourg (IBBL), the Laboratoire National de Santé (LNS) and the Centre Hospitalier de Luxembourg (CHL), financially supported by the FNR. The study leverages on the complementary expertise of the consortium partners to deepen the understanding of the mechanisms underlying Parkinson’s disease (PD), with the aim of improving early-stage diagnosis and developing a personalised treatment according to the individual characteristics of each patient’s disease. The programme is structured in two phases, with Phase I running from June 2015 until November 2019 and Phase II from December 2019 until May 2023.

Patient recruitment target reached!

To achieve its objective, NCER-PD set out to include 800 Parkinson’s patients from Luxembourg and the Greater Region, as well as a control group of 800 healthy individuals by the end of 2019. This is a particularly ambitious goal, given the estimated 1,200 people affected by PD in Luxembourg. Nevertheless, in November 2019, the 800th PD patient was successfully recruited, followed by the 800th healthy control in December 2019. This valuable cohort will generate a large dataset on all disease stages and different forms of Parkinsonism, including early non-motor signs and disease progression data, through annual patient follow-up visits, mobile applications and sensors. The Clinical and Epidemiological Investigation Center (CIEC) at LIH was implicated in both the recruitment process and follow-up visits. “Patient empowerment and involvement proved to
Confirmed financial support for phase II

The first phase of the programme was supported by the FNR through a total commitment of EUR 8.3 million throughout its four-year duration. At the end of the first funding period, the study underwent a successful evaluation by an international jury of experts, obtaining outstanding scores. This resulted in the allocation in July 2019 of an additional EUR 6 million to sustain the second phase, lasting until May 2023. The funding will allow NCER-PD to build on previously obtained findings and evaluate how the observed differences in the composition of the microbial population in the gut between PD patients and healthy subjects can be used as diagnostic biomarkers in clinical practice. Follow-up examinations of the recruited patients and controls will therefore continue on a yearly basis and every four years, respectively, in order to collect the data needed to study disease progression and support the identification of new biomarkers. Furthermore, participants will be divided into sub-cohorts, i.e. sub-groups, based on their genetic characteristics, and specifically on the presence of mutations in the GBA gene. This gene is responsible for the production of glucocerebrosidase, an enzyme involved in the breakdown and recycling of a component of the membrane of dead cells. PD patients harbouring GBA mutations have a higher risk of cognitive decline compared to the ones who do not, and will therefore undergo specific testing and personalised clinical trials on nerve cell cultures derived from their skin samples, in a quest for new therapeutics.

In addition, the renewed FNR financing will support the set-up of an additional cohort, i.e. a new group of participants, focusing on the early signs of PD. Specifically, this cohort will encompass volunteers affected by a sleep disturbance known as REM-Sleep Behaviour Disorder (RBD).

This disorder, which is characterised by physically acting out dreams during the Rapid Eye Movement (REM) sleep phase, is of particular interest to the NCER-PD research team, as people suffering from it have a higher risk of developing neurodegenerative diseases such as PD. Close monitoring of the cohort will therefore provide insights into the early onset and development of the disease, which will ultimately lead to the identification of novel treatment options.

“Parkinson's disease is a very complex disorder with many symptoms and manifestations. Studying different subgroups of patients, as we have planned for NCER-PD's second phase, will enable us to better understand the underlying mechanisms and open up new therapeutic avenues.” concludes Prof Krüger.
Prof Simone Niclou, what do we mean by translational oncology?

In simple terms, translational oncology encompasses the notion of cancer research being close to patients, addressing real and unmet clinical needs and resulting in a direct positive impact on their care. This is being achieved through the increased adoption of two main tools. Firstly, the use of patient-derived cancer models for pre-clinical research, which replicate and simulate a patient’s cancer, allowing us to understand disease mechanisms and observe therapeutic responses, and is therefore guiding the development and personalised administration of targeted therapies. This will lead to major improvements in drug discovery and validation, ultimately improving patient survival and quality of life. Second, clinical trials driven by researchers provide the ultimate platform to test newly discovered treatments “in real life” on actual patients, thus being a key component of translational oncology research.
What are the key research priorities of the Department of Oncology and, as its newly appointed Director, what actions are you putting in place to implement the translational vision?

Our research is centred on two highly transversal areas, namely immune-oncology and tumour resistance to treatment. We focus mainly on untreatable cancers such as brain tumours and certain types of leukaemia, as well as cancers prone to metastasise, such as breast and gastrointestinal cancers. For tumour escape mechanisms in particular, we also established a dedicated doctoral training programme, CANBIO, in collaboration with the University of Luxembourg and the Laboratoire national de santé (LNS) which is supported by the Luxembourg National Research Fund (FNR) through the PRIDE programme.

In terms of strategic actions, we want to further strengthen the link between research and clinical practice by involving an increasing number of clinician scientists in our department. Indeed, we have longstanding collaborations with the departments of haematology and neurosurgery of the Centre Hospitalier de Luxembourg (CHL), and recently established joint appointments with clinician scientists from the LNS specialised in neuropathology and genetics, so as to give an even stronger transversal dimension to our cancer research. Furthermore, we are currently applying for Horizon 2020 funding under the pharma-driven Innovative medicines Initiative (IMI) programme on Tumour Plasticity, aiming to perform single cell analyses of metastatic cancers. We also continue to refine and improve our work with patient-based models. Most importantly, close cooperation with national and international clinical partners is vital if we want to improve patient care and become a translational research hub. The Personalised Functional Profiling (PFP) project, launched in May 2019 with Dr Guy Berchem as its Principal Investigator, is the perfect example of this.

Can you tell us more about PFP and how it was set up?

The study was initiated in response to the fact that cancers display significant heterogeneity, with the same cancer type bearing different genetic characteristics from individual to individual, but also often from cell to cell in the tumour of the same patient. This diversity implies that cancers respond differently to treatment. Through a novel approach, the study aims to match a patient’s specific tumour profile with the most appropriate and effective treatment, selecting the one to which the tumour reacts better. This will be done by taking a biopsy and generating a three-dimensional culture of cancer cells, which are then exposed to a panel of up to 150 different anticancer drugs available on the market. In addition, the genetic characteristics of tumour cells will be elucidated by genomic analysis. This personalised functional profiling procedure will make it possible to identify within a few weeks which treatment or combination of treatments could be the most appropriate for a given patient, providing oncologists with concrete and personalised therapeutic advice.

What benefits will the study bring to patients and why is it important for LIH?

PFP will contribute to determining the efficacy of a variety of new and established drugs for personalised cancer therapy, which will broaden the portfolio of available treatment options. But it may also already enable personalised cancer therapy for the patients whose tumour samples are analysed in the study. Since the results of the drug testing are shared with the treating physician, patients may see the continuation of the current therapy or, conversely, the switch to a different, more effective one. The project also perfectly matches the translational vision of both DONC and LIH as a whole, being a concrete instance of “bed to bench to bed” study. If successful, we believe it will also act as a model for future projects and contribute to further increasing the visibility and recognition of the institute’s high quality research, both nationally and internationally. Moreover, it reflects the highly collaborative approach of LIH, since it is a partnership with CHL, the Hôpitaux Robert Schuman and the LNS, as well as prestigious international partners from Germany, France and even Korea.

What were the main developments of PFP in 2019 and what is the outlook for 2020?

In 2019, we started by consolidating the relationship with clinical partners and defining roles and responsibilities in view of the start of the pilot phase. The pilot aims to establish an efficient workflow between the hospitals and the laboratories on a small number of patients, and to determine the feasibility and logistics of the approach. We are planning to recruit up to 20 patients, aged 18 and above and suffering from recurring glioblastoma or metastatic gastrointestinal cancer. After successful validation, hopefully in 2020 or 2021, the actual clinical study can start with a larger number of patients and in collaboration with international partners. The pilot will run for approximately two years and will initially focus on glioblastoma, one of the deadliest types of brain cancer, and gastro-intestinal cancer. We have already set up the screening platform at two sites in Luxembourg and established new collaborations with the University of Luxembourg for pre-clinical evaluation of colorectal cancer patient-derived models on the PFP platform.

And finally, are there any other translational oncology projects in the pipeline, Prof Niclou?

In line with the National Cancer Plan, we are working in close cooperation with several national clinical and research partners on setting up a Centre of Excellence in Translational Oncology, which would integrate cancer research and patient care. The idea is to create an infrastructure and a seamless workflow that integrates fundamental and translational research with clinical care, allowing patients to have access to innovative treatments through clinical trials. We particularly count on the support of national funding agencies, since I believe this concept to be a priority for cancer patients in Luxembourg.
Strengthening national synergies to support translational medicine internationally

The SPRING clinical trial

Translational research encompasses the notion of internationalisation, relying on shared global expertise to go beyond geographical borders and tangibly improve health outcomes for patients worldwide. Having appreciated this, LIH has been working towards further reinforcing national collaborations with leading healthcare providers, in view of contributing to shaping the next generation of international clinical care. Specifically, LIH joined forces with the Centre Hospitalier de Luxembourg (CHL) in the context of SPRING, an international clinical trial aiming to test novel therapies on patients suffering from non-small cell lung cancer (NSCLC). In addition, Dr Guy Berchem, oncologist at CHL and Principal Investigator of the study, was appointed Associated Medical Director at LIH in May 2019.
First international Phase I clinical trial for Luxembourg hospital

The cancer centre “Kriibszentrum” at the Centre Hospitalier de Luxembourg (CHL), the Clinical and Epidemiological Investigation Centre (CIEC) at LIH’s Department of Population Health (DoPH) and the Integrated Biobank of Luxembourg (IBBL) are part of an international Phase I clinical trial, aiming to evaluate the efficacy and benefits of a combination of three novel targeted drugs – a so-called tri-therapy – on patients with advanced and/or metastatic NSCLC. Specifically, Phase I of the Survival Prolongation by Rational Innovative Genomics (SPRING) clinical research project seeks to assess the tolerability of the tri-therapy and identify its optimal doses, which will subsequently be administered to patients during the second phase of the trial to evaluate the effectiveness. The three drugs include avelumab, an antibody that acts as an immune checkpoint inhibitor to stimulate immune cells to fight cancer cells; axitinib, a tyrosine kinase inhibitor that blocks the abnormal formation of blood vessels and reduces tumour progression and metastases; and palbociclib, an inhibitor of kinases that interferes with cellular growth, thus slowing down the proliferation of cancer cells. During Phase I, which ran from the end of 2017 until the end of 2019, this tri-therapy was first tested on 15 patients at different dosages, following a specific dose-escalation scheme. By December 2019, the optimal dose had successfully been determined and will be administered to a group of at least 100 patients to be recruited during Phase II, which will run from the third quarter of 2020 for a period of 3.5 years.

In order to launch the study, considerable preparatory work was needed to assess its feasibility at the CHL site in Luxembourg and to fulfill all clinical and regulatory requirements. It is particularly at this stage that the support of LIH’s Clinical and Epidemiological Investigation Centre was essential. Indeed, CIEC has a long-term experience in assisting clinical trials, both in Luxembourg and abroad. “It is important to guarantee to the CHL patients who have agreed to be included in the study that all the necessary precautions have been taken regarding their safety”, underlines Prof Laetitia Huiart, Director of LIH’s Department of Population Health. Thus, CIEC was responsible for submitting the initial regulatory and ethical authorisation requests to the Ministry of Health and the National Research Ethics Committee (CNER) and, subsequently, for participating in patient recruitment, which was completed by the end of 2019. Moreover, regular patient visits took place until March 2019 during the first phase of the trial. These were carried out by CIEC’s experienced clinical research nurses, who performed tasks such as measuring key parameters, collecting patient biological samples and associated data, performing blood tests, administering the prescribed treatments and recording any side-effects, in close cooperation with medical doctors. The collected data was then used to assess the interactions and tolerability of the tri-therapy. CIEC also played an important role in the logistics of Phase I, liaising with service providers such as laboratories and pharmacies, recording the observed parameters and clinical data in an electronic log and maintaining regular contacts with the study coordinators. During Phase II, CIEC will continue to participate in patient recruitment and routine visits, as well as providing administrative support such as regulatory authorisation submissions and amendments.

In parallel, IBBL has been responsible for the preparation of formalin-fixed paraffin-embedded (FFPE) blocks of both healthy and cancerous tissues obtained from patient biopsies, in view of transcriptomic and genomic analyses performed by other consortium partners.

Indeed, throughout Phase I and Phase II, SPRING will carry out thorough biomolecular tests on the tumours of each patient, including DNA sequencing and the analysis of the expression of different types of RNA, so as to identify relevant genetic abnormalities between healthy and cancerous tissue biopsies. This will enable the consortium to assess the clinical utility of the SIMS algorithm (Simplified Intervventional Mapping System), developed during a previous clinical trial, as a tool to predict a patient’s response to the tri-therapy and therefore to accompany its prescription, based on the identified genetic anomalies.
In order to improve existing cancer treatments and propose new ones, there must be a close interaction between biomedical research and the clinical world."

Dr Guy Berchem
Digital technologies and Artificial Intelligence are disrupting traditional biomedical research and healthcare, increasingly enabling the translation of research results into clinical practice and bringing about concrete health benefits for patients. Having anticipated this, the Department of Population Health (DoPH) took several steps to integrate the digital dimension in its public health and epidemiology research activities, from the creation of a dedicated “Digital Epidemiology and E-health hub” in June 2019 to the launch of CoLive Diabetes, the first international digital cohort study on diabetes. Prof Laetitia Huiart (LH), Director of DoPH, and Dr Guy Fagherazzi (GF), Research Leader of the “Digital Epidemiology and E-health hub”, explain how this transversal research axis is being developed at LIH.

**Prof Huiart, what role are digital technologies playing in supporting translational medicine?**

**LH:** In essence, digital technologies are having an impact on three main aspects that are crucial for translational medicine: data collection, data analysis and health interventions. Connected devices — such as smartphones, tablets but also wearable devices like sensors — are making it possible to collect unprecedented amounts and types of real-life patient data. Once collected, this large quantity of information, ranging from health parameters to lifestyle, needs to be analysed and integrated with other ‘omics’, biological and clinical data in order to better characterise the disease in each individual patient. Artificial Intelligence and Big Data enable us to deal with these large datasets and extract meaningful information. The combination of biomedical data and real-world data and its analysis, known as Deep Digital Phenotyping, provides us with a deeper and holistic understanding of chronic diseases in all their facets, which will in turn facilitate their prevention, treatment and management.
What actions are being put in place at LIH to develop digital epidemiology and e-health?

LH: We had identified digital health as being one of our research priorities back in 2018. We therefore decided to organise a dedicated lecture series on “e-health”, funded by the FNR, which would give us the opportunity to invite a selection of leading external international experts and exchange with them on this topic. The first lecture in the series took place in December 2018, and was followed by another eleven seminars until November 2019. These interactions, and particularly the fruitful discussions with our first invited speaker Dr Guy Fagherazzi, proved to be instrumental in helping us shape our vision and put in place concrete measures. So much so, that we ended up creating a strategic “Digital Epidemiology and E-health hub” within DoPH, with Dr Fagherazzi joining us in June 2019 as its Research Leader. Moreover, we are recruiting five interns specialising in digital health, who will assist several research groups within DoPH in strengthening their e-health expertise and building their digital capacity. This will allow all groups to integrate digital technologies in their research and therefore be involved in the creation of new solutions for public health. And then there is the CoLive Diabetes study, of course.

Dr Fagherazzi, can you tell us more about CoLive Diabetes and how it was set up?

GF: CoLive Diabetes is the flagship project of the transversal “Digital Epidemiology and E-health hub”. It is an international digital cohort, i.e. a group of patients with the same disease who share their health and lifestyle data through digital technologies, which aims to improve the management of diabetes, the prevention of related complications and ultimately the quality of life of patients. Namely, the study will recruit up to 50,000 volunteers with type 1 and type 2 diabetes worldwide, who will share with us different types of information through a smartphone application conceived by the IT team at DoPH, and who will be followed up over a period of ten years. The CoLive application will allow participants to capture data related to their lifestyle and their physical and psychological well-being. This includes geolocation data, social media usage, selfies and voice recordings. Voice recordings in particular will enable us to identify and study specific signatures in their voices – so-called vocal biomarkers – that can be associated with emotions and psychological factors such as fear, anger, stress, anxiety or even an episode of hypoglycaemia. Collected data are of course treated confidentially and cannot be traced back to an individual person. All this information will then be integrated with medical data from connected medical devices, such as connected continuous glucose monitors, enabling us to understand how their interaction influences the evolution of the disease and to ultimately alleviate its burden.

What benefits will the study bring to patients?

GF: By analysing these large datasets through Artificial Intelligence techniques, we will first of all obtain the deep digital phenotypes of each participant, i.e. the complete characterisation of all the observable clinical and non-clinical features associated with a patient’s individual disease. This will allow us to match each new patient with a so-called “digital twin” — another patient with the same set of traits and disease progression trend. This should enable healthcare professionals to predict the course of diabetes more accurately, anticipate potential complications and intervene at an early stage, resulting in an individual long-term prognosis and improved patient outcomes. Soon, the CoLive Diabetes model will also be applied to other chronic diseases, thus extending its benefits to a broader population of chronically ill patients. The notions of deep digital phenotype and digital twin developed under CoLive Diabetes will support the transition from strictly observational studies like CoLive itself, to interventional approaches such as “Just in Time Adaptive Interventions” (JITAIs). JITAIs is an intervention design aiming to provide the right type and amount of care, at the right time, by adapting it to the patient’s specific context and real-life routine. Once the habits of participants have been defined through CoLive, volunteers will then be invited to take part in JITAIs, which are the embodiment of the personalised treatment concept.

What were the main developments of CoLive Diabetes in 2019 and what is the outlook for 2020?

GF: In 2019 we began by setting the scientific, ethical and technological basis for the project. Indeed, we finalised the scientific protocol, set up an international scientific advisory board and started the ethical procedures with the National Research Ethics Committee (CNER). We also designed the first version of the smartphone application in strict consultation with people with diabetes and thought of additional ways to keep including them throughout the project set-up and deployment. Patient buy-in is truly key for the success of the study. For 2020, we plan to obtain ethical clearing and organise focus groups with patients from Luxembourg to finalise the mobile application and the protocol. This will ensure we are ready to launch our patient recruitment campaign already in 2020.

And finally, are there any other translational projects on digital health in the pipeline, Prof Huiart?

LH: Yes indeed! One of our doctoral candidates, Catherine Goetzinger, is currently leveraging on digital technologies to develop a “connected” pill organiser to improve treatment adherence in women with breast cancer. Moreover, we have recently applied for funding under the FNR PRIDE programme for a project in collaboration with the Luxembourg Institute of Socio-Economic Research (LISER), the University of Luxembourg and the Luxembourg Institute of Science and Technology (LIST). The funding should allow us to support several PhD projects that aim to explore how to use digital technologies to characterise the environmental factors that affect cardiometabolism and mental health in the general population. The year 2020 will therefore see a further consolidation of our transversal digital epidemiology research activities.
LIH boasts a broad set of skills, technologies and expertise to assist fellow scientists in setting up and designing their projects, carrying out laboratory-based experiments using state-of-the-art equipment and performing a variety of analyses on the generated data. These services are offered through several platforms, each dedicated to a particular technology addressing a specific research need. In 2019, a series of changes were made to the organisation of such platforms, with the aim of maximising their impact and added-value, and ultimately bringing them at the centre of the translational medicine vision.

A wealth of research support services

LIH has channeled its know-how and cutting-edge laboratory infrastructure into six distinct platforms, which are shared resource facilities that pool together specific sets of competences and equipment with the goal of supplying well-organised, structured and concerted research support to scientists, assisting them throughout the entire lifespan of their project. This support spans from data analysis and bioinformatics, to imaging solutions and the provision of “omic” information.
Proteomics Platform
The platform shares its expertise in the analysis of the complete set of proteins in the human cell – known as “proteome” – by giving LIH researchers access to high-resolution mass spectrometry technologies, enabling them to carry out a variety of projects, such as the validation of cancer biomarkers.

Reverse Phase Protein Array (RPPA) Platform
The platform provides scientists with accurate and quantitative information on the amounts and specific characteristics of proteins present in tissues or cell samples, and can be used to identify novel therapeutic targets or study response to drugs.

LuxGen Platform
A joint undertaking of the LIH and the Laboratoire National de Santé (LNS), it offers scientists from both institutes access to high-quality next-generation sequencing (NGS) of DNA and RNA samples, as well as other technologies, allowing them to rapidly “read” large sets of genetic information simultaneously. This technology can be used for instance to detect genetic abnormalities and understand how they lead to disease.

Bioinformatics Platform
“Omics” data originating from genomics and proteomics techniques can subsequently be analysed by the Bioinformatics Platform through a series of advanced approaches, including machine learning and statistics.

The National Cytometry Platform
Projects studying complex cellular interactions often rely on specific methods that enable the analysis at the level of individual cells. The National Cytometry Platform at LIH allows scientists to benefit from the latest cytometry technology to measure a wide spectrum of cellular characteristics, from size, counts, shape and structure, to the presence or absence of proteins of interest on the surface of a cell.

In vivo Imaging Platform (IIP)
Once experimental findings have taken place in a test tube outside of a living organism (i.e. in vitro), they need to be validated in vivo by using models that mimic the context and conditions of the human body. The IIP puts a series of equipment – from Magnetic Resonance Imaging (MRI) to Positron emission tomography–computed tomography (PET/CT scans) – at the service of researchers, allowing them to visualise the physical changes taking place inside the model organisms and validate their findings, such as promising new drugs or treatments, before they are considered for clinical trials.

Strengthening platform reach and streamlining services
Given their pivotal function, platforms should be accessible to a broad scientific audience, so as to maximise the impact of their high-quality services. With this in mind, the decision was taken to separate them from their respective departments and reorganise them into a new, distinct unit — the Quantitative Biology Unit (QBU). Prof Gunnar Dittmar led the operations behind the structuring and creation of the new unit. After a year of organisational work in July 2019, three new platforms (Proteomics, RPPA and Bioinformatics) were created from the former Proteome and Genome research laboratory, headed by Prof Gunnar Dittmar, and combined with the other existing LIH platforms. All these were subsequently spun off from their respective departments, with the aim of making their use and availability more balanced across the entire institute. Thus, the Proteomics, In vivo imaging, Bioinformatics and Reverse Phase Protein Array platforms were separated from the Department of Oncology (DONC), while the National Cytometry Platform was made independent from the Department of Infection and Immunity (DII). The new QBU was therefore set up. The platforms of the QBU are also associated with five technology-oriented research groups, allowing the rapid transfer of new technologies to the platforms. This new structure will ensure that the services provided are standardised and streamlined across all platforms, and that information exchanged between them is interoperable and compatible, in view of maintaining a high level of quality. The QBU is led on an annual rotating basis by Prof Gunnar Dittmar, Head of QBU in 2019, and by Dr Antonio Cosma, Head of QBU for 2020.

“Our vision is to put LIH platforms at the disposal of the entire European biomedical sector, by being involved in European-funded consortia as a valued and recognised supplier of research and support services.”
Dr Antonio Cosma

“‘The changes in the way platforms are organised will have a two-fold impact. First of all, they will allow us to focus on quality control and standardisation even further, ultimately increasing the added value of our services to the national scientific community and broadening their reach. Secondly, our vision is to put LIH platforms at the disposal of the entire European biomedical sector, by being involved in European-funded consortia as a valued and recognised supplier of research and support services’, explains Dr Cosma.

“We have already started submitting applications in this respect, and I am looking forward to the numerous opportunities ahead of us”, he concludes.
Key 2019 translational research milestones and achievements

May 2019:
› Appointment of Prof Simone Niclou as Director of the Department of Oncology
› Launch of the Personalised Functional Profiling (PFP) clinical feasibility study
› Appointment of Dr Guy Berchem as Associated Medical Director

June 2019:
› Creation of the “Digital Epidemiology and E-health hub”
› Appointment of Dr Guy Fagherazzi as Research Leader of the “Digital Epidemiology and E-health hub”
› Creation of Transversal Translational Medicine (TTM) unit at LIH and appointment of Prof Rejko Krüger as its Director

July 2019:
› Phase II of the National Centre for Excellence in Research on Parkinson’s Disease (NCER-PD) financed by the Luxembourg National Research Fund (FNR)
› Creation of the Quantitative Biology Unit (QBU) with Dr Gunnar Dittmar as Head for 2019

November 2019:
› Launch of the “CoLive Diabetes” international digital cohort
› 800th Parkinson’s disease patient successfully recruited under NCER-PD
› End of NCER-PD Phase I

December 2019:
› 800th healthy control recruited under NCER-PD
› Start of NCER-PD Phase II
› End of SPRING clinical trial Phase I
International excellence
A valued partner for European consortia

In line with the vision of putting their expertise at the service of the global biomedical research community to shape translational medicine in Europe and beyond, LIH and IBBL constantly seek new opportunities to participate in European-funded projects. The year 2019 further confirmed the recognition of the added-value of the two institutes at the international level. Indeed, LIH and IBBL joined the consortium of five prestigious and highly competitive European studies, which kicked-off in 2019, and won additional applications for two European grants. These contracts span a variety of priority areas for LIH and IBBL, including the use of digital technologies and Artificial Intelligence to improve cancer therapies, the elucidation of the interaction between the immune system and tumours, as well as the characterisation of the correlation between diabetes and cardiovascular disease. Participation in these projects consolidates LIH and IBBL collaborations with leading international partners and further contributes to strengthening the visibility of the institutes, and of Luxembourg’s biomedical research ecosystem in general, as an international centre of excellence in translational and transversal medicine.

PEVOdata: immunotherapy, epigenetics and data analysis to fight squamous cell carcinomas

Through its biobank IBBL, LIH joined the consortium of PEVOdata, a three-year precision medicine project co-funded by the European Commission’s ERA Net ERA PerMed instrument. The study, which kicked off in June 2019 and is managed by Dr Kristin Kornerup at IBBL, leverages on immunotherapy, epigenetics and data analysis to identify new therapeutic strategies in patients with recurrent and/or metastatic squamous cell carcinomas (SCCs). SCCs are among the most frequent solid cancers in humans, representing a major cause of death worldwide. They can originate from various locations in the body, such as the head and neck, cervix, lung, anus, vagina and penis. Despite their similar molecular features, SCCs are very heterogeneous and often display drug resistance mechanisms, with many patients not responding to treatment. Therapeutic approaches based on a combination of different drugs are therefore urgently needed. PEVOdata will evaluate an innovative treatment strategy relying on the combination of immunotherapy – specifically the Pembrolizumab antibody – and of Vorinostat, an ‘epidrug’ acting on the epigenetic modifications of genes, i.e. modifications that do not involve changes in the DNA sequence. To this end, patients from several centres in France and Italy will be included in the PEVO²° ‘basket trial’¹⁸ to assess the antitumor activity of the Pembrolizumab-Vorinostat combination in subjects with late stage SCC of the head and neck, cervix, lung, anus, vulva and penis. Clinical, genetic and molecular data will be collected in order to better understand the mechanisms of response or resistance to this combination, and molecular analyses will be performed on samples collected during patient treatment and follow-up.

¹ A new type of clinical trial aiming to test a drug on patients presenting the same specific genomic alteration.
Activating the immune system to unleash an attack on cancer cells is the principle behind Immune Checkpoint Inhibitors, a type of immunotherapy which has shown promising results for the treatment of some cancers. However, the lack of biomarkers to screen patients that might respond to the treatment and of rationales for combining Immune Checkpoint Inhibitors with conventional therapies constitute a barrier to the efficacy of existing immunotherapies and to the development of new ones. In March 2019, LIH and IBBL joined the consortium of IMMUcan (Integrated IMMUnoprofiling of large adaptive CANcer patient cohorts), a study financed by the European Commission through the Innovative Medicine Initiative 2 (IMI-2) programme. The project will characterise the molecular and cellular characteristics of the tumour and its microenvironment from up to 3,000 cancer patients. Once integrated with clinical information, this comprehensive data will provide a thorough insight into the mechanisms by which the immune system interacts with the tumour, ultimately clarifying the impact of current therapeutic interventions and improving their efficacy. IMMUcan focuses specifically on colorectal, lung, head and neck, breast, gastric and renal cancers. Under the coordination of project manager Suzanne Delfortrie, IBBL acts as the central biobank of the project, being responsible for the processing, quality control and storage of all biological samples collected as part of the study, including tumour tissue, blood, stool and saliva. These biospecimens will be used to identify potential predictive biomarkers to evaluate patient response to immunotherapy. The consortium is led by EORTC (European Organisation for Research and Treatment of Cancer) and Merck, and includes a total of 28 partners between academia, industry and patient associations.
Up to 50% of antibiotics are thought to be prescribed unnecessarily in Europe, therefore exacerbating the phenomenon of anti-microbial resistance (AMR). Increasing the use of diagnostic tests could help address this growing issue by ensuring that antibiotics are administered only when appropriate. However, the wider use of diagnostic tests in healthcare is currently hampered by a lack of insight into their medical, technological and economical value. In this context, LIH and IBBL joined the consortium of VALUE-Dx in April 2019, with the goal of contributing to the generation of evidence on the medical, economic and public health value of diagnostics in tackling AMR. The four-year project, co-funded by the European Commission under the Innovative Medicines Initiative (IMI), will specifically focus on acute respiratory tract infections acquired in community care settings, as they are the most frequent cause of medical consultation and inappropriate antibiotic use. The purpose of the study is to transform medical practice to achieve more personalised, evidence-based antibiotic prescription and use through the widespread adoption of clinical and cost-effective innovative diagnostic strategies. As part of the project, IBBL is involved in the development of a business plan for the creation and maintenance of a biobank of clinical specimens, bacterial strains and DNA, under the coordination of project manager Dr Kristin Kornerup. The outcomes of VALUE-Dx could subsequently apply to other common infections such as urinary tract infections, bloodstream infections and hospital-acquired respiratory tract infections. The project consortium, coordinated by the University of Antwerp, includes 26 partners from academia, industry and other organisations.
Looking forward: two newly-won prestigious projects

In order to keep contributing significantly to biomedical research at the European level in the longer term, LIH and IBBL have been applying for additional EU-funded opportunities throughout 2019. In the second half of the year, the institutes were further rewarded, having successfully won applications for two new projects and thus officially being part of the newly-formed consortia. Specifically, the two studies in the pipeline include REVERT and EATRIS-Plus. The former aims to leverage on artificial intelligence to identify a predictive algorithm to be used in the treatment of patients with advanced colorectal cancer, while the latter will facilitate access to the capacities and services needed to support the translation of biomedical discoveries into novel therapies and medical interventions. The LIH-IBBL team will contribute to the projects through their expertise in quality assurance, biomarker validation and proficiency testing. Both REVERT and EATRIS-Plus are funded under the European Commission’s Horizon 2020 programme and are set to kick-off in the first quarter of 2020.

CARDIATEAM and CardioRNA: delving into the “heart” of translational research

In 2019, LIH and IBBL participated in two European-funded translational projects focusing on cardiovascular diseases. The first project, CARDIATEAM, was launched in March 2019 with the goal of elucidating the correlation between Type 2 Diabetes (T2DM) and heart failure. Specifically, the five-year study will determine whether T2DM represents a central factor contributing to the onset and progression of a specific type of cardiomyopathy, known as “diabetic cardiomyopathy” (DCM), and assess whether DCM is unique and distinct from the other forms of heart failure. The study will therefore identify new biomarkers that can serve as indicators for the disorder, as well as at finding innovative therapeutic targets. This will ultimately enable an early and more precise diagnosis and treatment of DCM. LIH’s Cardiovascular Research Unit, led by Dr Yvan Devaux, is involved in the interpretation of a large set of ‘transcriptomics’ data — i.e. data on the characteristics and quantities of the pool of RNA molecules in the cell — generated from the analysis of patient blood samples. As the central biobank of the project, and under the coordination of Dr Kristin Kornerup, IBBL is responsible for the collection, storage and redistribution of blood samples to relevant analytical centres, as well as for DNA extraction and quality control tests, ensuring that samples are fit for the purpose of further analyses. CARDIATEAM boasts a multidisciplinary consortium of 21 partners from nine EU countries and is co-funded by the European Commission under the Innovative Medicines Initiative (IMI). In parallel, Dr Devaux has been chairing the CardioRNA COST Action CA17129, a collaborative pan-European network of multidisciplinary researchers, clinicians and industrial partners aiming to accelerate the understanding of the functions and interactions of the different cellular RNAs in the origination and development of cardiovascular disease (CVD). Ultimately, CardioRNA will promote the translation of experimental data into usable applications to improve personalised medicine in this field. The project is funded through COST (European Cooperation in Science and Technology), the longest-running European framework supporting trans-national cooperation among researchers, engineers, and scholars across Europe.
Modulating blood flow to reach the target

Prof Tak Mak – renowned for cloning the human T cell receptor and for his pioneering genetic manipulation experiments in vivo – together with his team and collaboration partners, published a new study providing the first proof-of-function findings for T cell-derived acetylcholine in antiviral immunity. Acetylcholine produced by T cells during viral infection was found to be essential to trigger vasodilation, allowing the immune cells to leave the blood stream and migrate towards virus-infected cells in tissues.

LIH researcher Prof Dirk Brenner contributed to a scientific breakthrough, which brought forward a new mechanism by which immune system T cells fight off viral infections through the production of acetylcholine, a neurotransmitter in the brain. This novel ground-breaking finding from the laboratory of Prof Tak Mak at the Princess Margaret Cancer Centre in Toronto, Canada, was published in the prestigious journal Science in February 2019.

Controlling antiviral immune responses with acetylcholine
Contribution to a Science publication
Department of Infection and Immunity > Experimental & Molecular Immunology
“The study solves a puzzle scientists have pondered for more than a century”, says Prof Mak. He explains the main discovery in simple terms. “In the brain, acetylcholine functions as a neurotransmitter that controls learning and memory. Although we knew from a previous study that T cells were also able to synthesise acetylcholine during infection, the biological role of this immune-derived neurotransmitter in the immune response remained a mystery. Our current research shows that T cells producing this classical brain chemical are able to leave the blood circulation – in a process known as extravasation – and penetrate the infected tissues to fight the pathogens”.

“It is truly astonishing to have identified this dual function in a neurotransmitter. When secreted by T cells, acetylcholine essentially dilates blood vessels and slows down the bloodstream locally at the sites of infection”, adds Prof Dirk Brenner, Head of Experimental & Molecular Immunology at LIH’s Department of Infection and Immunity, who participated in the study.

**Acetylcholine and interleukin-21: a winning team against viral intruders...**

The discovery was made when the team genetically engineered mice lacking the enzyme acetylcholine transferase in T cells, making them unable to produce acetylcholine. The researchers observed reduced vasodilation, impaired migration of antiviral T cells into infected tissues and, ultimately, a compromised control of chronic viral infections by the immune cells of these mutant animals. The study therefore gives absolute genetic proof that acetylcholine plays a key role in regulating the proper functioning of the immune system. Specifically, its production by T cells is induced by the presence of cytokine interleukin-21 (IL-21), a small protein that stimulates and activates immune system cells in response to pathogens, and which is therefore equally crucial in mediating antiviral immunity.

...and against cancer cells

Not only is efficient migration of T cells into tissues critical for clearing viral infections, but it is also fundamental for mounting immune responses against cancers. Indeed, IL-21 and consequently acetylcholine, enhance the ability of immune system lymphocytes to infiltrate and kill tumour cells, and are therefore of particular interest for cancer immunotherapy. In fact, tumours are often surrounded by immune cells that cannot break through their defences, possibly due to the fact that they do not produce sufficient amounts of acetylcholine. In this respect, therapeutic strategies that increase immune neurotransmitter production and stimulate immune cell entry into cancerous tissues may be beneficial.

**Acetylcholine and autoimmunity**

On the other hand, an excessive T cell activity underscores several autoimmune diseases such as rheumatoid arthritis or multiple sclerosis, resulting in an attack on self tissues. In these cases, a reduction in neurotransmitter secretion may subdue the self-destructive action of immune cells invading joints or the central nervous system.

“By elucidating the role of acetylcholine in determining the efficacy of immune responses, we have essentially discovered an entirely new lens through which to look at a variety of immune-related diseases, from viral infections to cancer and autoimmune disorders”, concludes Prof Brenner.

The next research goal of Prof Mak’s team will be to identify and target the key receptors that facilitate the interactions between immune cells and diseased organs.

The study, first-authored by Dr Maureen Cox, was published in February 2019 in the prestigious journal Science, with the full title “Choline acetyltransferase-expressing T cells are required to control chronic viral infection”. The work was mainly funded by a grant from the Canadian Institutes of Health Research to Prof Mak, a Cancer Research Institute Irvington Postdoctoral Fellowship to Dr Cox, and by The Princess Margaret Cancer Foundation. Prof Dirk Brenner is funded through an ATTRACT Consolidator grant by the Luxembourg National Research Fund (FNR).

“By elucidating the role of acetylcholine in determining the efficacy of immune responses, we have essentially discovered an entirely new lens through which to look at a variety of immune-related diseases, from viral infections to cancer and autoimmune disorders.”

**Prof Dirk Brenner**
Dr Ala’a Alkerwi from LIH Department of Population Health contributed to a global public health study on obesity, which was published in Nature in May 2019. By analysing trends in body-mass index (BMI) evolution over thirty years, the research revealed that BMI is rising faster in rural compared to urban areas, with this phenomenon being the main driver of the global obesity epidemic. The study was conducted in the framework of the Non-Communicable Diseases Risk Factor Collaboration (NCD-RisC) and coordinated by the World Health Organization (WHO) Collaborating Centre on Non-Communicable Disease Surveillance and Epidemiology at Imperial College London.

Body-mass index (BMI) — an index based on height and weight that describes a person as being underweight or overweight — has increased progressively across most countries, in parallel with a rise in the proportion of the population living in cities. This has led to the common view that urbanisation is one of the most important drivers of the global rise in obesity, due to the fat-rich diets and more sedentary lifestyles associated with urban living. Nevertheless, only few studies have looked at the changes in BMI over long timespans and across a large number of countries, and specifically in cities versus rural areas.
Explaining the rise in global obesity

To address this gap, the research analysed the height and weight data of more than 112 million adults across urban and rural areas in 200 countries and territories between 1985 and 2017, in order to calculate national, regional and global trends in BMI evolution. The researchers found that, over the last three decades, BMI rose globally from 22.6 kg/m² to 24.7 kg/m² in women, and from 22.2 kg/m² to 24.4 kg/m² in men. Specifically, more than half of the global rise in mean BMI and more than 80% in some low- and middle-income countries was due to the increase in BMI in rural areas. Indeed, the average BMI in rural areas has increased by 2.1 kg/m² in both women and men, whereas in cities the rise was 1.3 kg/m² and 1.6 kg/m² in women and men, respectively. This proves the fact that the observed worldwide increase in BMI over the last 33 years has been mainly driven by the rising BMI in rural areas, thus disproving the theory that urbanisation has been fuelling the global obesity epidemic.

Urbanisation of rural life: narrowing the BMI gap

These trends have led to striking changes in the geography of BMI over the three decades. In 1985, urban men and women in over three quarters of the countries had a higher BMI than their rural counterparts. Over time, the gap between urban and rural BMI in many of these countries shrank or even reversed. According to the authors, BMI was previously lower in rural areas of low- and middle-income countries compared to cities, due to a combination of both higher energy expenditure by rural residents linked to hard labour, as well as lower incomes limiting food consumption. With agriculture becoming progressively mechanised, less physically demanding jobs becoming more common in rural areas over time and incomes increasing, spending on food and caloric intake rose disproportionately more in rural areas than in urban settlements, while energy expenditure declined. Moreover, the intake of processed carbohydrates and cheaper foods may have grown excessively in rural areas. These factors, often referred to as ‘urbanisation of rural life’, could explain the larger increase in rural BMI observed by the authors.

Similarly, in high-income countries, the study reported a persistently higher rural BMI compared to cities, reflecting a growing rural economic and social disadvantage linked to poorer education and incomes, a scarcer availability and higher prices of healthy foods and reduced access and use of public transport and walking than in urban settlements.

“This international study highlighted the need for an integrated approach to rural nutrition, enhancing financial and physical access to healthy foods so as to avoid malnourishment caused by the excessive consumption of low-quality nutrients.”

Dr Ala’a Alkerwi

Building on Luxembourgish public health research

The work relied on data obtained from over 2,000 existing population-based studies, including the ORISCAV-LUX study, which had been conducted in 2007-2008 on more than 1,400 Luxembourg residents with the aim of assessing cardiovascular health and risk factors in Luxembourg.

“We are proud that our data have been used to contribute to such a prestigious international study”, says Dr Alkerwi. “Being underweight or overweight can have detrimental effects on health outcomes and obtaining reliable information on how BMI in rural and urban populations is changing is crucial in order to plan targeted interventions. This international study highlighted the need for an integrated approach to rural nutrition, enhancing financial and physical access to healthy foods so as to avoid malnourishment caused by the excessive consumption of low-quality nutrients”, she concludes.

The research was published in May 2019 in the prestigious journal Nature, with the full title “Rising rural body-mass index is the main driver of the global obesity epidemic in adults”. It was funded by the Wellcome Trust, the Medical Research Council, the Royal Society and the Academy of Medical Sciences. The ORISCAV-LUX study at LIH was jointly supported by the Ministry of Health and the Ministry of Higher Education and Research.
Dr Gloria Aguayo from the LIH Department of Population Health, in collaboration with international academic partners, led a new public health study exploring the association between diabetes and frailty in the elderly. The research has shown that people with diabetes over the age of 60 are more vulnerable than people without the disease, possibly implying that patients suffering from diabetes age more quickly. The study was published in October 2019 in Diabetes Care, a renowned scientific journal in the field of diabetes research.

Diabetes is a public health issue...

The life expectancy of the world population continues to rise. According to statistics of the World Health Organisation (WHO), about one third of the European population will be aged over 60 by 2050. As diabetes is mainly observed in the elderly, the prevalence of this disease and the associated complications are also predicted to increase.
According to the European Health Examination Survey (EHES), conducted in Luxembourg between 2013 and 2015 among over 1,500 residents, approximately 5% of the population suffers from diabetes, with up to a quarter showing signs of prediabetes. Among the 55-64 year olds, up to 18.5% have diabetes, with men reportedly being more affected by glucose metabolism disorders than women.

...and makes us frail

LIH recently evaluated the data of a large English cohort with the aim of better understanding the consequences of chronic disease on ageing. The results clearly show that diabetes and frailty are associated: at a same age, people with diabetes are generally frailer than people without diabetes. Frailty is an essentially age-related condition of vulnerability. Among other things, it affects the posture and sense of balance of elderly people and increases the risk of falling and ensuing fractures, hospitalisation and death.

At the start of the study, 12% of the participants had diabetes and 35% were considered frail. Participants were subsequently monitored over a period of 10 years. The researchers found that frailty increased more rapidly in people with diabetes than in people without diabetes, regardless of the degree of frailty at the beginning of the study. A 60-year-old man with diabetes therefore displays the same frailty index as a 72-year-old man without diabetes.

"In simple terms, diabetes makes us age by 12 years, increasing the risk of rapid health decline. We become frail earlier, meaning that we have a higher risk of falls leading to injuries or fractures, we lose our independence earlier and may need healthcare in hospitals", explains Dr Gloria Aguayo, leader of the study.

Prediabetes is also a concern

Remarkably, the study also indicated a link between prediabetes and frailty. Prediabetes can be detected by measuring glycated haemoglobin HbA1c in blood samples. HbA1c is a marker that is used to assess blood glucose levels over several months. The results show that people with slightly elevated levels of HbA1c at the beginning of the study progressed more rapidly towards frailty than people with a normal level. This result is highly relevant, underlining the importance of addressing elevated blood glucose levels as early as possible.

Causality needs to be determined

The observations of the study may indicate that the complications resulting from diabetes play a role in frailty development. Another possibility could be that common earlier determinants contribute to the development of diabetes and the risk of frailty later in life. Future research should therefore investigate the causes and mechanisms of the relationship between diabetes (or prediabetes) and frailty. At present, the possibility of the reverse phenomenon - that frailty could be a factor contributing to the development of diabetes - cannot be ruled out.

Slowing the progression of frailty

The results of the study underline the relevance of early diagnosis of diabetes to prevent accelerated progression of frailty in the elderly. “Our research suggests that diabetes and the signs of prediabetes affect the frailty of people over 60”, adds Dr Aguayo. “In an ageing population, it is particularly important that metabolic disorders be diagnosed as early as possible to prevent complications. In addition, the population could be made more aware of better lifestyles with a healthier diet and more exercise through increased preventive measures, thus improving their chances of healthy ageing”, she concludes.

The study was conducted with data from around 5,400 individuals aged 60 or more from the English Longitudinal Study of Ageing (ELSA). Participants were asked to complete a 36-point questionnaire every two years between 2004 and 2015 on the condition of their frailty, and this over a period of 10 years. In addition, they underwent a medical check-up every four years including physical ability tests and blood sampling. From all the collected information, a frailty index between 0 and 1 was determined for each person. An index of 0.2 was considered as threshold for frailty.

The research, first-authored by Dr Aguayo, was published in Diabetes Care with the title “Prospective Association Among Diabetes Diagnosis, HbA1c, Glycemia, and Frailty Trajectories in an Elderly Population”. It is a collaboration with researchers from the Universities of Aarhus (Denmark), Liège (Belgium), Western Ontario (Canada) and INSERM in Paris (France).
How do gliomas evolve?

Contribution to a Nature publication

Department of Oncology

Prof Simone P. Niclou, Director of the LIH Department of Oncology, is a member of the Glioma Longitudinal AnalySiS (GLASS) Consortium, an international scientific community aiming to advance the understanding of glioma brain tumours. The GLASS Consortium recently described diffuse glioma cells both before and after being subjected to therapy, so as to characterise how they change and why this form of malignant brain cancer is so difficult to treat. In November 2019, these findings were published in the prestigious journal “Nature”, providing a foundation for further research and the opportunity for the clinical community to predict the effectiveness of newly developed treatments.

Treatment limitations

Until relatively recently, cancer was viewed as a single disease with different “sub-types”, based on where in the body it arose. The advent of detailed molecular analysis has shown that the situation is far more complex and that there can be many diverse cell populations even within a single tumour. Therein lies a significant problem for effective therapy: eradicating one type of cancer cell may leave another unaffected, and it may actually confer a competitive advantage to it.
The most common malignant brain tumour in adults, glioblastoma, is also one of the most difficult cancers to treat. It invariably relapses despite surgical, radiotherapeutic and chemotherapeutic interventions. While the initial molecular characteristics have been well described in gliomas, their subsequent evolution as a result of treatment stress remains unknown.

**A highly variable tumour evolution**

To address the problem, the GLASS Consortium has begun investigating the dynamics of molecular changes in gliomas over time. Their latest findings point towards the fact that the evolution of genomic alterations in gliomas is highly variable and patient-specific. The researchers obtained data for multiple time points from 285 patients treated at 35 hospitals. In the end, they selected high quality tumour samples representing the three major subtypes of diffuse glioma from 222 patients at two time points each, which they labelled “initial” and “recurrence”. The analyses demonstrated the highly variable nature of gliomas, but provide a framework for effective study of glioma evolution and treatment response.

Interestingly, the study showed that when glioma cells are challenged by anti-cancer treatments such as radiation and chemotherapy, they do not evolve in a consistent manner. There are some common features between patient glioma cell samples in response to treatment, including a high rate of mutations in the genome (hypermutation) and the presence of an abnormal number of chromosomes in the cells (aneuploidy), due to dysfunctions in cell division. Yet, following the early events that drive cancer initiation and progression, the evolution of gliomas often appears to be random, as opposed to proceeding down predictable and “streamlined” paths.

**The role of the immune system**

The researchers also assessed how immune activity can shape glioma evolution. Immunotherapy, which relies on the stimulation of the body’s own immune system to target and eliminate cancer cells, is an exciting new field, and understanding immune interactions in the tumor microenvironment and the mechanisms behind glioma immune evasion is crucial for efficient immunotherapy implementation. The research showed that immune activity in the environment surrounding the tumour does not vary over time between initial and recurrent gliomas, although there were patient-to-patient differences. More work is therefore needed to fully fathom this variability and to be able to understand what immunotherapy strategies might be most effective for gliomas.

“Ultimately, we aim to identify novel therapeutic targets and determine the treatment approaches that will result in the most effective destruction of glioma cells, improving outcomes for both patients and their families”, concludes Niclou.

The joint effort of the international GLASS Consortium offers important insight into how to improve the clinical prognosis for glioma patients worldwide and also provides the largest database of sequential glioma tumour profiles to date.

The publication of the GLASS Consortium was edited by senior author Prof Roel Verhaak and first authors Dr Floris Barthel and Dr Kevin Johnson from the The Jackson Laboratory in the US. It includes contributions of 87 researchers and clinicians from the United States, Europe, Asia and Australia. The study was published in November 2019 in the renowned journal Nature, with the full title “Longitudinal molecular trajectories of diffuse glioma in adults”.

The Glioma Longitudinal AnalySiS (GLASS) Consortium is an international community of clinicians and researchers that was inaugurated in 2015 to accelerate efforts to understand glioma tumour evolution and expose therapeutic vulnerabilities. Prof Niclou and Dr Ann-Christin Hau of the LIH Department of Oncology are among its members. GLASS aims to achieve these goals through molecular profiling of tumour specimens obtained at multiple time points along the course of glioma disease.

“Ultimately, we aim to identify novel therapeutic targets and determine the treatment approaches that will result in the most effective destruction of glioma cells, improving outcomes for both patients and their families.”

Prof Simone Niclou
Tumour adaptation and survival: the many “faces” of cancer cells

Publication in Nature Communications

Until now, researchers have assumed that the growth of solid tumours originates from so-called cancer stem cells, characterised by specific surface markers and developing in a fixed, hierarchical order. Accordingly, such cancer stem cells are responsible for tumour progression and produce specific types of more differentiated cancer cells, whose fates are predetermined. A joint interdisciplinary project led by researchers from the NORLUX Neuro-Oncology Laboratory at the LIH Department of Oncology demonstrated that cancer cells of glioblastomas – conspicuously aggressive solid brain tumours – manifest developmental “plasticity” and flexibility, with their observable characteristics being less strictly defined than previously believed. These findings were published in April 2019 in the leading journal Nature Communications.
Glioblastomas are the most common types of malignant brain tumours. Because of their rapid growth, the prognosis for those affected is usually dismal. Many patients hold out hopes for novel therapeutic approaches, which utilise drug-bound antibodies directed against specific markers present on the surface of a subpopulation of immature glioblastoma cells. These antibody-drug compounds bind to the surface, are then internalised and kill the cancer stem cells. However, the findings of the study suggest that this approach may be misdirected. Cancer stem cells, including the cells that derive from them, are able to adapt to environmental conditions and undergo reversible transformations into various cell types, thereby altering their surface structures. These results imply that novel therapeutic approaches targeting the specific surface structures of cancer stem cells could be of limited utility.

**Remarkable cellular adaptations**

In their study, the researchers exposed cancer cells in the laboratory to certain stress factors, such as drugs or oxygen deficiency. This allowed them to observe that glioblastoma cells reacted flexibly to such stressors and simply transformed themselves at any time into cell types with a different set of surface markers. This plasticity confers them the ability to adapt to their microenvironment — the immediate surroundings of the cancer — and develop a favourable environment-specific heterogeneity that enables them to survive, grow and mostly likely also escape therapeutic attacks.

In addition, the team of scientists from Luxembourg, Norway and Germany, led by Prof Simone P. Niclou at LIH, brought forward the possibility that cells of other tumour types may also be less constrained by defined hierarchical principles, and be similarly able to adapt their characteristics to the prevailing environmental conditions.

“The same phenomenon that we described for glioblastomas has also been observed in breast and skin cancer”, explains Dr Anna Golebiewska, Group Leader at the NORLUX Neuro-Oncology Laboratory at LIH’s Department of Oncology and co-first author of the study. “This finding suggests that therapies specifically directed against the membrane markers of cancer stem cells may not be successful. Indeed, our study highlights the importance of considering the dynamic adaptive modifications occurring in cancer cells when designing new drugs”.

The research could in fact help optimise future standard treatments. In a laboratory setting, the researchers were able to show that environmental factors, such as lack of oxygen in combination with specific signals from the tumour microenvironment, can induce modifications in the surface structure of cancer cells. Indeed, the microenvironment comprises cells and molecules that influence the growth of the tumour.

“The once we understand exactly what causes the flexibility of tumor cells, we can devise combinatorial therapies which target the signals underlying this plasticity, thereby improving treatment effectiveness and patient outcomes”, concludes Prof Niclou, Director of the LIH Department of Oncology and leader of the study.

The work is a collaboration between the NORLUX Neuro-Oncology Laboratory and other research units and platforms at LIH. The researchers from LIH also worked in close collaboration with their long-term national partners, specifically the Luxembourg Centre for Systems Biomedicine (LCSB) at the University of Luxembourg and the Department of Neurosurgery of the Centre Hospitalier de Luxembourg. Moreover, the project was carried out with international partners from the Technische Universität Dresden (Germany), the University of Heidelberg (Germany) and the University of Bergen (Norway). This joint undertaking of different research and clinical players gives a truly interdisciplinary and translational dimension to the study.

The publication, first-authored by Dr Anna Golebiewska and Dr Anne Dirkse, was published in April 2019 in Nature Communications, with the full title “Stem cell-associated heterogeneity in Glioblastoma results from intrinsic tumor plasticity shaped by the microenvironment”. The study was supported by an AFR PhD grant from the Luxembourg National Research Fund (FNR) and a training grant from the Fondation du Pélican de Mie et Pierre Hippert-Faber (Fondation de Luxembourg) to Dr Dirkse. Furthermore, the work received funding from LIH, Sächsisches Staatsministerium für Wissenschaft und Kunst (SMWK), Deutsche Krebshilfe and Deutsche Forschungsgemeinschaft (DFG).

“**Our study highlights the importance of considering the dynamic adaptive modifications occurring in cancer cells when designing new drugs.**”

Dr Anna Golebiewska
Der Spiegel, a widely read news magazine generally considered to be one of the most influential of continental Europe, focused one of its June 2019 cover stories on human gut microbiome research. Specifically, the elaborate, seven-page article by the German weekly magazine features the recognised research work of Prof Mahesh Desai, Group Leader of the Eco-Immunology and Microbiome research group at LIH’s Department of Infection and Immunity. Prof Desai and his research team investigate the interplay between the gut microbiome — the population of bacteria and other microorganisms present in the gastrointestinal tract — dietary fibre and the gut mucosal barrier, in the context of various infectious and chronic diseases.
Dietary fibres for a healthy gut

In a study published in the prestigious journal Cell in 2016, Prof Desai and co-workers showed that a human gut microbiome deprived of dietary fibre compensates the lack of nutrients by degrading the mucus barrier that lines the intestinal wall, which acts as a primary defence against pathogens. This creates “holes” that serve as an entry point for pathogenic microbes, resulting in acute and lethal colitis in animal models. The findings therefore propose a mechanism through which diet alters the activity of gut microorganisms and impacts gut health, which could be used to rationally design future dietary interventions and therapeutics. This suggests that an imbalanced gut microbial community and ensuing dysfunctional intestinal barrier could lead to a variety of chronic diseases affecting the gut, such as Inflammatory Bowel Disease (IBD) and colon cancer, but also related to other body parts, such as the central nervous system.

International recognition

Although it is largely centred on political news across the globe, Der Spiegel chose a health-related topic on the human gut microbiome for its June 29th 2019 cover story, which underlines the significance of this field of research for global public health. The magazine’s cover page schematically represented the human intestine using the term “das Superorgan”, with each letter of the word being illustrated with different food sources of fibre, underscoring the importance of this nutrient not just for humans but also for the gut bacteria. Indeed, the title of the issue was “The intestine and the secret of a long life” (Der Darm und das Geheimnis eines langen Lebens), emphasising the role of a healthy gut and of its microbiome in good health outcomes.

The article gave special credit to the seminal research findings of Prof Desai, who was quoted repeatedly throughout and whose photograph was included to illustrate the text. The piece highlighted the impact of his Cell publication and described it as a major breakthrough in the context of numerous diseases. Targeted to a lay audience, the issue reported the numerous benefits of gut microbes for human health. Researchers currently know that there is an evident link between the gut microbiota, human nutrition and the onset and development of disease. Indeed, gut microorganisms fulfil multiple functions that affect the entire body. They process indigestible dietary fibre, keep the gut mucus barrier intact, synthesise vitamin B12, train immune cells to discriminate between harmless and pathogenic bacteria, prevent inflammation, produce serotonin acting on the brain, and generate fatty acids that have a protective effect on the cardiovascular system. The article therefore gave a clear message: feeding gut microbes well through balanced diets contributes to preserving healthy body functions and preventing the onset of certain diseases.

The cover story also described Prof Desai’s ongoing work on the recruitment of patients suffering from inflammatory bowel disease in order to enhance existing treatments by employing dietary therapeutics. Finally, the importance of the generous financial support granted by the Luxembourg National Research Fund (FNR) to fund microbiome research at LIH, and in Luxembourg as a whole, was also highlighted in the issue.

“The publication of our research in such a prominent magazine goes to show the growing interest and appreciation of the importance of this area, not only among the scientific community, but also among the general public.”

Prof Mahesh Desai

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Prof Mahesh Desai

“The publication of our research in such a prominent magazine goes to show the growing interest and appreciation of the importance of this area, not only among the scientific community, but also among the general public”, says Prof Desai.

“Being able to reach out to such a large readership through Der Spiegel has been a wonderful opportunity to boost the visibility of human microbiome research at LIH and in the Grand Duchy in general, and contribute to further affirming our reputation as a leading research institute in this domain”, concludes Prof Markus Ollert, Director of LIH’s Department of Infection and Immunity.
Communicating science
Aside from carrying out cutting-edge research in the labs, the LIH team is also actively involved in a large number of outreach events in Luxembourg. Through such activities, the institute has a threefold goal. First, making its work – and that of the national biomedical research ecosystem in general – known to the general public, thus helping patients understand how the scientific discoveries originating from the lab translate into concrete therapeutic applications that actually improve their health. Second, informing local researchers, clinicians and policy-makers about the high quality research carried out at LIH, therefore contributing to increasing the country’s visibility among the international scientific community as a centre of excellence in translational and personalised medicine. Third, inspiring the next generation of young scientists in Luxembourg.

January – September
//”Max” workshops

March – November
//Lecture series on e-health

March
//Relais pour la Vie 2019
//Chercheurs à l’école

April
//World Parkinson Day

October
//5th Medical Research Day
//FNR Award for Outstanding Promotion of Science
//Lycée M. Rodange visit

November
//Science Festival 2019
//Innovation Camp on e-health
// Successful lecture series on e-health

LIH’s Department of Population Health coordinated a new lecture series called “Improving patient & population health through innovative e-health interventions”, which started in December 2018 and ended in November 2019. The series, initiated under the lead of Prof Laetitia Huiart, Director of the Department of Population Health, featured 12 lectures by distinguished speakers, focusing on digital technologies that support and advance health services, epidemiology and public health research. Some of the specific topics addressed during the lectures included the economic and ethical aspects of e-health, as well as its applications in oncology, mental health and obesity, among others. The conferences took place at the Centre Hospitalier de Luxembourg (CHL) and were followed by more informal “Meet the speaker” sessions at LIH’s premises. The speaker and lectures, were particularly praised by the attendees, according to the dedicated satisfaction survey. The series was supported by the Luxembourg National Research Fund (FNR) through the Support for Research Communication (RESCOM) funding scheme dedicated to seminars and conferences with an international dimension. The programme was set up with the contribution of the University of Luxembourg, the Luxembourg Institute of Socio-Economic Research (LISER), the Centre Hospitalier du Luxembourg (CHL), the Centre Hospitalier Emile Mayrisch (CHEM), the company Information Technology for Translational Medicine (ITTM) and the Luxembourg Institute of Science and Technology (LIST).

// “Max” workshops

The Communication Department organised several workshops across local schools between January and September 2019, including the French Lycée Vauban and a Spillschoul (precoce, 1.1 and 1.2) in Gasperich, in order to promote its children’s book “Max, the tiny microbe who wants to be a superhero”, which depicts LIH’s research on the human gut microbiome in a fun and simplified way. The half-day sessions entailed the reading of the book to the children, as well as a variety of hands-on activities to illustrate the concept of “good” versus “bad” bacteria. Through the use of blue light and a special gel, children also got the chance to visualise the bacteria present on their hands before and after washing them! At the end of the workshops, each child was gifted a copy of the book, which is available in both French and Luxembourgish.

Prof Jan-Eric Litton, from the Department of Medical Epidemiology and Biostatistics at the Karolinska Institute in Stockholm (Sweden), presented “Patients, trust and ethics in information privacy in e-health - from FAIR to FAIR Health” on May 28th, 2019.
// Relais pour la Vie 2019

On March 23rd and 24th, LIH participated in the 2019 edition of the Relais pour la Vie, an annual relay organised by the Fondation Cancer to support cancer patients. The LIH teams included staff from all departments, from Marketing & Communication to the Clinical and Epidemiological Investigation Centre (CIEC). The event attracted a total of 13,783 runners, organised in 375 teams, and raised almost EUR 7,000.

// Chercheurs à l’école

From March 25th until March 29th, the Clinical and Epidemiological Investigation Centre (CIEC) team took part in the 9th edition of Chercheurs à l’école, an initiative organised by the National Research Fund (FNR) to promote constructive interactions between researchers and high-school pupils. The event saw over 100 researchers giving talks to 75 classes in 30 schools across the country.

// World Parkinson Day

LIH, through the Clinical and Epidemiological Investigation Centre (CIEC) and IBBL, participated in several conferences and awareness-raising events organised both in Luxembourg and the Greater Region throughout the month of April, within the framework of the World Parkinson Day.

// 5th Medical Research Day

The 5th edition of the Medical Research Day (Journée de la Recherche Médicale) was held on October 23rd 2019 at the Centre Hospitalier de Luxembourg (CHL). Jointly organised by CHL, LIH – and specifically the Clinical and Epidemiological Investigation Centre (CIEC) – and the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg, the event aims to promote medical research among high school pupils. The 2019 edition, which attracted about 180 high school pupils, combined interactive workshops and mini-conferences that allowed the young participants to better understand the principles of clinical research and meet physicians from CHL, as well as researchers from LIH and LCSB. The students were introduced to ongoing projects in the fields of oncology, allergology, neurological disorders, infectious diseases and many more. The CIEC team also put in place several hands-on games to illustrate how to predict complications after a heart attack through the identification of biomarkers and how to ‘fix’ the heart following valve failure.
// FNR Award for Outstanding Promotion of Science

On Friday, October 25th 2019, the Luxembourg National Research Fund (FNR) held the 11th edition of the FNR Awards Ceremony to celebrate Luxembourg’s best research and science communication efforts. The LIH/IBBL Marketing & Communication Unit was rewarded for its outstanding promotion of science through the Science Quest, an escape room-style game held in February 2018 that aimed to present the institute’s biomedical research activities to high school classes and the general public in an unconventional and entertaining way. The Science Quest consisted in a two-hour challenge, where more than 300 participants playing in teams were put in the shoes of researchers with the task of finding a cure against cancer. The event was organised in partnership with the Ministry of Health and was supported by a “Promoting Science to the Public” (PSP) grant of the FNR. The FNR Award Ceremony gathered around 200 people, including Claude Meisch, Minister for Higher Education & Research.
Lycée M. Rodange visit to IBBL

On October 15th 2019, IBBL welcomed a group of pupils from the ‘biotechnology’ course of the Luxembourgish Lycée M. Rodange for a guided tour of its state-of-the-art facilities in Dudelange. During the visit, the high school students had the opportunity to understand more about IBBL’s operations, from sample collection and storage, to the sample processing and biospecimen research activities that characterise its integrated offer. Specifically, the visit included a general presentation on biobanking, with particular reference to IBBL’s Luxembourg research projects and partners, followed by a tour of the biorepository and biorefinery departments, where biological samples are stored and processed, respectively. In addition, the pupils attended a demonstration of IBBL’s digital pathology service, which allowed them to visualise healthy versus cancer tissues, as well as cell nuclei and cytoplasm directly on a screen.

Innovation Camp on e-health

The 19th edition of the Innovation Camp, an initiative organised by Jonk Entrepreneuren in partnership with LIH, took place on November 12th at the House of BioHealth in Esch-sur-Alzette. The event brought together 55 students from 17 high schools who, for a whole day, were asked to work in groups to come up with innovative solutions to address a concrete “Business Challenge”. This year’s edition tasked them with developing a start-up that leverages on the data associated with people’s voices to assess their health status and establish diagnoses. The pupils were supervised and advised by a team of LIH scientists composed of Dr Guy Fagherazzi, Dr Gloria Aguayo and Michaël Schnell. A guided tour of the LIH laboratories was also organised. At the end of the day, the groups had the chance to present and defend their projects in front of a jury that included Prof Markus Ollert, Dr Frank Glod and Prof Laetitia Huiart, as well as representatives from FNR and Luxinnovation. The first prize was awarded to the ‘Hear Health’ team for their idea of combining a mobile application with a smart bracelet that allows voice recognition and detection of vocal biomarkers to detect a cardiovascular problem in the patient.

Science Festival 2019: follow the samples of the biobank!

LIH was represented through IBBL at the 12th edition of the Science Festival, which took place from November 7th until November 10th at the premises of the National Museum of Natural History and at Neumunster Abbey. IBBL introduced a completely new workshop consisting of six hands-on activities, each of which corresponding to the different steps of the biobanking process. These included a card game that illustrated patient recruitment and the concept of informed consent prior to sample collection, a collection kit assembly task, a sample transport simulation to IBBL through remote-controlled cars, DNA extraction from saliva and urine aliquoting, as well as sample storage in dry ice at -80°C. The Science Festival, organised by the National Museum of Natural History and the National Research Fund, is an outreach event taking place every two years and aiming to promote science and research in Luxembourg among young people and the general public. The 2019 edition attracted an estimated 12,000 visitors!
Highlights
calendar 2019
News, events, awards and nominations
Legs Kanning award for Dr Jérôme Paggetti

Dr Jérôme Paggetti, Principal Investigator at LIH’s Department of Oncology, received the Legs Kanning award from the association Action Lions Vaincre le Cancer during the 14th Legs Kanning conference, which took place on January 10th 2019 at the headquarters of the Banque Internationale à Luxembourg (BIL). The prize rewards researchers for outstanding achievements in cancer research. Dr Paggetti gave a talk on his research topic and presented the objectives and recent achievements of the “Tumour Stroma Interactions” research group (Laboratory of Experimental Cancer Research, Department of Oncology), which investigates the role of the microenvironment in tumour progression and which he jointly leads with Dr Etienne Moussay. Focusing on haematological malignancies such as chronic lymphocytic leukaemia, Dr Paggetti and his group aim to identify new prognostic biomarkers and therapeutic strategies.

Cancer Foundation/FNR funding for Dr Bassam Janji: Reprogramming the tumour immune landscape

On January 16th 2019, LIH researchers Dr Bassam Janji and Dr Guy Berchem received a EUR 213,125 cheque from Lucienne Thommes, Director of the Cancer Foundation, in the presence of Dr Marc Schiltz, Secretary General of the Luxembourg National Research Fund (FNR). The FNR also committed a matching amount to the project. The study “Improving T-cell and macrophage immune checkpoint blockades, combining autophagy inhibitors” (COMBATIC) aims to improve the effectiveness of immune checkpoint inhibitors in melanoma and colon cancer patients who have not previously been eligible for immunotherapy. The project also plans to test the therapeutic benefit of a combination of pharmacological molecules with immune checkpoint inhibitors. The goal is to ultimately provide a therapeutic strategy capable of reprogramming the immune landscape from cold tumours not eligible for immunotherapy to hot tumours pre-infiltrated by immune cells.

Dr Jacques Zimmer appointed full member of the Institut Grand-Ducal

Dr Jacques Zimmer has been appointed full member of the Institut Grand-Ducal – Section des Sciences Naturelles, Physiques et Mathématiques during a plenary meeting held on February 18th 2019. The appointment underscores his important contribution to science in Luxembourg. Holding both a medical degree and a PhD, he is a recognised scientist in inflammation research with a focus on immune mechanisms involving Natural Killer cells. He is part of the Innate Cellular Immunity and Chronic Inflammation research group at LIH’s Department of Infection and Immunity. Through different initiatives such as yearly conference cycles, Luxembourg’s Institut Grand-Ducal aims to promote science, literature and the arts at the national and international levels.
Strasbourg Society of Biology rewards excellent PhD thesis

On March 22nd 2019, Dr Antoun Al Absi was awarded a thesis prize for his outstanding PhD thesis by the “Société de Biologie de Strasbourg” (Strasbourg Society of Biology) in Strasbourg, France, on the occasion of the Doctoral School Days 2019 of the University of Strasbourg. Dr Al Absi carried out his PhD from 2014 to 2018 at the Cytoskeleton and Cancer Progression Research Group in the Laboratory of Experimental Cancer Research at LIH’s Department of Oncology, under the supervision of Dr Clément Thomas and with the support of an AFR PhD grant from the Luxembourg National Research Fund (FNR). The young researcher had been investigating the role of the actin cytoskeleton in breast cancer cell resistance and identified a previously unknown mechanism named the “actin response”, which leaves tumour cells unharmed by Natural Killer cell-mediated cytotoxicity.

Photo: Dr Antoun Al Absi receiving the Thesis Prize from the “Société de Biologie de Strasbourg”.

Leukaemia research supported by Plooschter Projet donation

The Luxembourgish non-profit association Plooschter Projet made a EUR 18,000 donation to the Tumour Stroma Interactions Research Group at LIH’s Department of Oncology to support a project that aims to characterise in detail the identity and features of immune cells found in the tumour microenvironment in chronic lymphocytic leukaemia. A better understanding of the T cell subtypes and how their functions are subverted by tumour immune escape mechanisms shall give hints for potential targets for new innovative immunotherapies. The donation will cover the costs associated with the expensive laboratory techniques to be used as part of the study.

Photo: From left to right: Christiane Lieners-Reger (Plooschter Projet asbl), Yannick Lieners (Plooschter Projet asbl) and Dr Etienne Moussay (LIH).

EDEG conference: new perspectives on diabetes prevention and patient care

From May 11th until May 14th, a national conference on diabetes management followed by the annual international meeting of the European Diabetes Epidemiology Group (EDEG) took place in Mondorf-les-Bains, providing a fruitful exchange between scientists and clinicians working on diabetes research and care. The 54th annual EDEG meeting brought together 150 international experts in diabetes epidemiology, who shared their knowledge on the disease, its risk factors and complications. The national conference was organised by LIH in partnership with several national partners, while the international EDEG conference was co-organised by the European Diabetes Epidemiology Group (EDEG) and LIH. The entire event was supported by the Luxembourg National Research Fund (FNR) through a RESCOM grant (12954278) and by the Health Directorate of the Ministry of Health.

Cancer Foundation funding for Dr Clément Thomas: Restoring the anti-tumour immune response

On May 15th 2019, Lucienne Thommes, Director of the Cancer Foundation and Dr Carlo Bock, President of the Cancer Foundation, awarded a EUR 470,177 check to Dr Clément Thomas, Principal Investigator of the Cytoskeleton and Cancer Progression Research Group at LIH’s Department of Oncology. This funding will support the research project “ACTIMMUNE - Overcoming tumour immune evasion by targeting the actin response”. The study aims to validate the role of the actin response in tumour immune evasion and provide a rationale for targeting this process as a therapeutic approach to improve the anti-tumor immune response. Ultimately, the ACTIMMUNE project shall allow the identification of clinically relevant targets to interfere with the actin response and restore an efficient anti-tumour response.

Photo: From left to right: Lucienne Thommes (Director of the Cancer Foundation), Prof Ulf Nehrbass (CEO of LIH), Dr Clément Thomas (LIH) and Dr Carlo Bock (President of the Cancer Foundation).
**Private donation to the Laboratory of Oncolytic Virus Immuno-Therapeutics**

The Laboratory of Oncolytic Virus Immuno-Therapeutics (LOVIT) at LIH’s Department of Oncology received a generous private donation of EUR 10,000 from Mr André Welter, retired engineer and Luxembourg national. The donation supported the research group in the acquisition of new equipment essential for daily laboratory work. These include two incubators and a laminar flow hood for cell culture, as well as an instrument to monitor cell growth to test the effect of treatment on cell proliferation in real time. LOVIT, headed by Dr Antonio Marchini, was founded in 2017 as a joint undertaking between LIH and the German Cancer Research Centre (DKFZ) in Heidelberg, Germany. It develops new innovative strategies to fight cancer in the recently emerged field of oncolytic virotherapy, an approach that uses a specific type of viruses to destroy cancer cells.

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**Cancer Foundation funding for Prof Simone Niclou: a novel therapeutic protein for Glioblastoma**

On June 12th 2019, Dr Carlo Bock and Lucienne Thommes of the Cancer Foundation, granted Prof Simone Niclou, Director of the Department of Oncology and Head of the NorLux Neuro-Oncology Laboratory, and Dr Virginie Neirinckx, postdoctoral researcher, a check of EUR 138,000. This funding supports the project “Soluble LRIG1 for pan-Receptor Tyrosine Kinase targeting in Glioblastoma”, carried out by Dr Neirinckx. The study aims to further explore the properties and mechanism of action of LRIG1 (Leucine-rich repeats and immunoglobulin-like domains 1), a protein that the NorLux Neuro-Oncology Laboratory had previously shown to reduce the growth and proliferation of glioblastoma cancer cells by inhibiting receptor tyrosine kinases (RTKs). Ultimately, these findings team aim to pave the way for the development of a therapeutic molecule that can be tested in clinical trials.

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**Visit of RIKEN delegation**

Representatives of the Japanese RIKEN Institute, the University of Luxembourg and LIH signed a Memorandum of Understanding on July 9th 2019, in which the three institutions declare their intention to further strengthen future scientific cooperation. The fundamental element of this agreement are the so-called joint RIKEN Outpost Labs in Luxembourg, where senior scientists from the RIKEN Institute will undertake research on the “gut-brain axis” to elucidate the role of an altered gut microbiome and immune system in the onset of neurodegenerative diseases.
Dr Anna Golebiewska awarded for best preclinical oral presentation at EANO meeting

The NorLux Neuro-Oncology Laboratory from LIH’s Department of Oncology was represented at the 14th annual meeting of the European Association of Neuro-Oncology (EANO) in Lyon, France, from September 19th to 22nd 2019. Dr Anna Golebiewska, co-group leader of NorLux, was selected to give a presentation on recent findings about the plasticity of brain cancer stem cells and was subsequently rewarded for the best abstract in preclinical sciences during a plenary session on hot topics and late breaking abstracts. Dr Golebiewska presented her findings to the audience through her presentation “Intrinsic tumour plasticity in Glioblastoma allows for recreation of stem like-states and efficient tumour cell adaptation to new microenvironments”.

Life Sciences and Euron PhD Days

The 2019 edition of the PhD Days, a yearly scientific event for doctoral candidates in Luxembourg, was held from September 23rd to 25th on the Belval Campus in Esch-sur-Alzette. The scientific meeting combined a traditional Life Sciences PhD Day with the Euron conference, jointly organised by the Doctoral School in Science and Engineering of the University of Luxembourg and the European Graduate School of Neuroscience (Euron). Yue Zhang, PhD candidate at LIH’s Quantitative Biology Unit was part of the organising committee. Moreover, Catherine Delbrout, PhD candidate in the Cancer Metabolism Group at LIH’s Department of Oncology, received the first prize for her poster presentation on “metabolism mediated control of cancer cell invasion”, while Yolanda Pires Afonso, PhD candidate in the Neuro-Immunology Group at LIH’s Department of Oncology was awarded the second prize for her oral presentation on “tumour-associated microglia/macrophages heterogeneity in Glioblastoma”.

NK 2019 Meeting

From September 30th to October 3rd 2019, close to 500 scientists from all over the world gathered at the 18th edition of the Congress of the Society for Natural Immunity NK 2019, organised in Luxembourg for the first time. It was an occasion to discuss the latest discoveries in immunology and new strategies for fighting diseases such as cancer and viral infections. The scientific discussions focused on Natural Killer (NK) cells, specialised immune cells that are able to attack and destroy abnormal or infected cells of the body. The event was supported by FNR’s funding instrument “RESCOM - Scientific events”. It was organised in partnership with the Society for Natural Immunity by a local organising committee composed of LIH staff Dr Tatiana Michel, Dr Jacques Zimmer, Dr Aurélie Poli, Prof Markus Ollert, Juliette Pertuy, Dr Bassam Janji and Prof Nathalie Jacobs (GIGA Institute, Liège, Belgium).

Accreditation of WHO European Regional Reference Laboratory for Measles and Rubella at LIH

LIH has been hosting the Luxembourg National Reference Laboratory for Measles and Rubella, as well as a European Regional Reference Laboratory for Measles and Rubella (RRL-Lux), located at LIH’s Department of Infection and Immunity and led by Dr Judith Hübchen. The laboratory assists the WHO in supervising national laboratories by providing external quality assurance, expertise and training on diagnosis and disease monitoring to strengthen overall laboratory capacity. RRL-Lux was successfully reaccredited in October 2019 until January 2022, following a thorough onsite quality assessment by WHO representatives that took place in March 2019.
National PhD Welcome Day 2019

On 21st November 2019, the fourth edition of the National PhD Welcome Day was held at the Halle des Poches à Fonte on the Belval Campus, gathering doctoral candidates from all disciplines who recently started their PhD in Luxembourg. The event provided the opportunity for PhD candidates to get useful information and advice regarding their PhD, network with stakeholders in doctoral training and socialise with their peers. The National PhD Welcome Day 2019 was organised under the lead of LIH, in partnership with the University of Luxembourg (UL), the Luxembourg Institute of Socio-Economic Research (LISER), the Luxembourg Institute of Science and Technology (LIST), the Max Planck Institute Luxembourg for International, European and Regulatory Procedural Law (MPI), the Luxembourg National Research Fund (FNR), EURAXESS Luxembourg and LuxDoc asbl.

Photo: Organising committee

Young Investigator Award - annual meeting of the Society for Neuro-Oncology

From November 20th to 24th 2019, the 24th Annual Meeting of the Society for Neuro-Oncology (SNO) was held in Phoenix, Arizona, United States. At this important international meeting, Dr Ann-Christin Hau, postdoctoral researcher at the NORLUX Neuro-Oncology Laboratory at LIH’s Department of Oncology, received the Young Investigator Award in recognition of her research work. Following the award ceremony, she presented her noteworthy findings and introduced solutions towards personalised treatment for recurrent high-grade glioma.

Photo: Dr Ann-Christin Hau receiving the Young Investigator Award at the 24th Annual Meeting of the SNO

Pelican grant awarded to Yahaya Abubakar Yabo for glioblastoma research project

Yahaya Abubakar Yabo, PhD candidate in the NorLux Neuro-Oncology Laboratory at LIH’s Department of Oncology, is one of the winners of the 2019 Pelican Grant, awarded by the Fondation du Pélican de Mie et Pierre Hippert-Faber to PhD candidates affiliated with the Doctoral Programme in Systems and Molecular Biomedicine of the Doctoral School in Science and Engineering (DSSE) at the University of Luxembourg. Yahaya Abubakar Yabo was granted EUR 7,000 from the foundation in support of his PhD project on the characterisation of the factors underpinning glioblastoma cell adaptation to treatment. The grant will allow Yahaya to acquire invaluable skills in the context of his project, by financing his attendance and participation in a series of training courses and meetings both in Europe and in the US.
Institutional organisation and figures
The **Board of Directors** is nominated by the Government and is composed of nine external members of different professional backgrounds. Its mission is to oversee the activities at LIH. It is responsible for the general organisation, for defining internal rules, for budget control, for framework contracts with partner organisations and for approving new strategies.

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

The **Coordinating Council** is a consultative body composed of internal representatives of the researchers, the personal delegation and the research and innovation support personnel. It issues advisory opinions to the Board of Directors regarding research policy, development and innovation 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.
258 Agreements Signed
401 Employees
5 PhD Defences
326 Ongoing Projects
250 Publications
41 New Partnerships with a Private Partner
15.1 Mio Third-Party Income
TOTAL SAMPLES COLLECTED AND ALIQUOTS CREATED

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<td>Others 0.5%, Cerebrospinal fluid 0.3%, Saliva derivatives 0.3%, Stool derivatives 0.3%, Pleural effusion 0.0%</td>
<td>42,771</td>
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</table>

SAMPLES BY PROGRAMME

<table>
<thead>
<tr>
<th>Programme</th>
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<tbody>
<tr>
<td>Service contracts</td>
<td>1,157,095</td>
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<tr>
<td>Neurodegenerative diseases</td>
<td>202,141</td>
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<td>Population studies</td>
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</tr>
</tbody>
</table>
HUMAN RESOURCES
(31st December 2019)

**Staff by Function**

- **Researchers**: 55% (218)
- **Technicians**: 24% (96)
- **Support Staff**: 21% (83)

**Staff Per Department**

- **Administration**: 10% (39)
- **Integrated Biobank of Luxembourg**: 14% (54)
- **Transversal Activities**: 10% (41)
- **Department of Infection and Immunity**: 22% (89)
- **Department of Oncology**: 17% (67)
- **Department of Population Health**: 21% (84)
- **General Management**: 14% (54)
- **Integrated Biobank of Luxembourg**: 14% (54)
- **Institutional Activities**: 6% (23)
**STAFF BY NATIONALITY**

- **French**: 33% (131)
- **Belgian**: 16% (62)
- **Luxembourgish**: 14% (55)
- **German**: 13% (51)
- **Other European nationalities**: 16% (63)
- **Non-European nationalities**: 10% (39)

**STAFF BY GENDER**

- **Male**: 253
- **Female**: 148

**STAFF BY WORK CONTRACT TYPES**

- **Permanent**: 61% (244)
- **Fixed-term**: 39% (153)
- **External**: 1% (4)
**FINANCES**

**STATUTORY EXPENSES**

**LIH**

- **% SOURCES OF FUNDING**
  - 68.6% Ministry of Higher Education and Research
  - 13.8% Collaborative Funding
  - 13.9% Competitive Funding National
  - 2.2% Competitive Funding International
  - 0.2% H2020
  - 1.2% Others

- **% COST CATEGORIES**
  - 7.93% Raw Materials and Consumables
  - 22.28% Other Operating Costs
  - 63.56% Staff Costs
  - 6.22% Depreciations
  - 0.01% Interests and Other Financial Charges

**IBBL**

- **% SOURCES OF FUNDING**
  - 70% Ministry of Higher Education and Research
  - 6% Competitive Funding National & International
  - 20% Collaborative Funding
  - 4% H2020

- **% COST CATEGORIES**
  - 15% Raw Materials and Consumables
  - 32% Other Operating Costs
  - 47% Staff Costs
  - 6% Depreciations
## PROFIT AND LOSS ACCOUNT (EUR)

### A. CHARGES

1. Use of merchandise, raw materials and consumable materials | 4,662,365 | 4,107,959  
2. Other expenses | 12,075,743 | 11,670,625  
3. Staff costs | 30,457,858 | 29,006,624  
4. Value adjustment on intangible and tangible fixed assets | 3,123,539 | 3,554,671  
5. Interests and other financial charges | 3,522 | 3,592  
6. Profit for the financial year | 0 | 0  
**TOTAL CHARGES** | **50,323,027** | **48,343,471**

### B. INCOME

1. Net turnover | 2,961,987 | 1,724,477  
2. Subsidies | 46,577,022 | 45,529,604  
3. Other income | 272,050 | 1,011,436  
4. Interests and other financial income | 22,392 | 25,710  
5. Loss for the financial year | 489,576 | 52,244  
**TOTAL INCOME** | **50,323,027** | **48,343,471**

## FINANCES

PROFIT AND LOSS ACCOUNT

(31st December 2019)
## Finances

### Balance Sheet

**(31st December 2019)**

<table>
<thead>
<tr>
<th></th>
<th>2019</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASSETS (EUR)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>01.01 - 31.12.19</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FIXED ASSETS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible fixed assets</td>
<td>637,950</td>
<td>739,359</td>
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<tr>
<td>Tangible fixed assets</td>
<td>6,647,540</td>
<td>8,012,126</td>
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<tr>
<td>Financial fixed assets</td>
<td>1,380</td>
<td>4,849</td>
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<tr>
<td><strong>TOTAL FIXED ASSETS</strong></td>
<td>7,286,870</td>
<td>8,756,334</td>
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<tr>
<td><strong>CURRENT ASSETS</strong></td>
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</tr>
<tr>
<td>Debtors</td>
<td></td>
<td></td>
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<tr>
<td>1. <strong>Trade debtors</strong></td>
<td>1,631,081</td>
<td>1,294,302</td>
</tr>
<tr>
<td>a. Becoming due and payable within one year</td>
<td>1,629,964</td>
<td>1,275,758</td>
</tr>
<tr>
<td>b. Becoming due and payable after more than one year</td>
<td>1,117</td>
<td>18,544</td>
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<tr>
<td>2. <strong>Other debtors</strong></td>
<td>2,765,657</td>
<td>2,767,222</td>
</tr>
<tr>
<td>a. Becoming due and payable within one year</td>
<td>2,765,657</td>
<td>2,767,222</td>
</tr>
<tr>
<td>Cash at bank and in hand</td>
<td>29,559,929</td>
<td>27,688,452</td>
</tr>
<tr>
<td><strong>TOTAL CURRENT ASSETS</strong></td>
<td>33,956,667</td>
<td>31,749,976</td>
</tr>
<tr>
<td>Prepayments</td>
<td>926,180</td>
<td>791,273</td>
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<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td>42,169,717</td>
<td>41,297,583</td>
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</tbody>
</table>
### Liabilities (EUR)

#### Capital and Reserves

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<thead>
<tr>
<th>Description</th>
<th>2019 01.01 - 31.12.19</th>
<th>2018 01.01 - 31.12.18</th>
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<tbody>
<tr>
<td>Financial wealth</td>
<td>4,099,157</td>
<td>4,099,157</td>
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<tr>
<td>Reserves</td>
<td>1,486,881</td>
<td>1,486,881</td>
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<tr>
<td>Profit or loss brought forward</td>
<td>7,999,544</td>
<td>8,051,788</td>
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<tr>
<td>Profit or loss for the financial year</td>
<td>-489,576</td>
<td>-52,244</td>
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<tr>
<td>Capital investment subsidies</td>
<td>7,601,529</td>
<td>9,632,094</td>
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<tr>
<td><strong>Total Capital and Reserves</strong></td>
<td><strong>20,697,535</strong></td>
<td><strong>23,217,676</strong></td>
</tr>
</tbody>
</table>

#### Available Reserve for Projects

- **2019**: 16,105,399
- **2018**: 12,713,774

#### Provisions

- **2019**: 942,624
- **2018**: 1,271,426

#### Non-Subordinated Debts

1. **Trade creditors**
   - Becoming due and payable within one year: 3,358,475
   - Becoming due and payable after more than one year: 2,915
2. **Tax and social security debts**
   - Tax debts: 9,720
   - Social security debts: 968,002
3. **Other creditors**
   - Becoming due and payable within one year: 77,788

#### Total Available Reserve for Projects, Provisions and Creditors

- **2019**: 21,464,923
- **2018**: 18,079,518

#### Deferred Income

- **2019**: 7,259
- **2018**: 389

#### Total Capital, Reserves and Liabilities

- **2019**: 42,169,717
- **2018**: 41,297,583
Publications
related to a defect in CCR5 addressing at the cell surface. The deletion in African individuals resistant to HIV infection might be


unified phylogenetic classification system and revised nomenclature


unified phylogenetic classification system and revised nomenclature


77


Low serum B12 concentrations are associated with low B12
Allen LH. (2018). QSOX1 and PLBD1 are new independent predictors of left ventricular
Peripheral blood RNA levels of
Moreau Y, Bartunek J, Van De Werf F, Devaux Y, Janssens S, Sinnaeve
Vanhaverbeke M, Vausort M, Veltman D, Zhang L, Wu M, Laenen G, Gillijns
women followed for 20 years: the mediating role of BMI.
Journal of Clinical Oncology and Therapeutics. 2019; 1(1).
IF: NA (2018)


TRANSVERSAL ACTIVITIES


83
Advantages, disadvantages and the role of biospecimen science.


Connecting cheminformatics and high resolution mass spectrometry: potential environmental exposure and neurodegeneration using single-cell analysis.


We would like to thank everyone involved in the development of this Annual Report