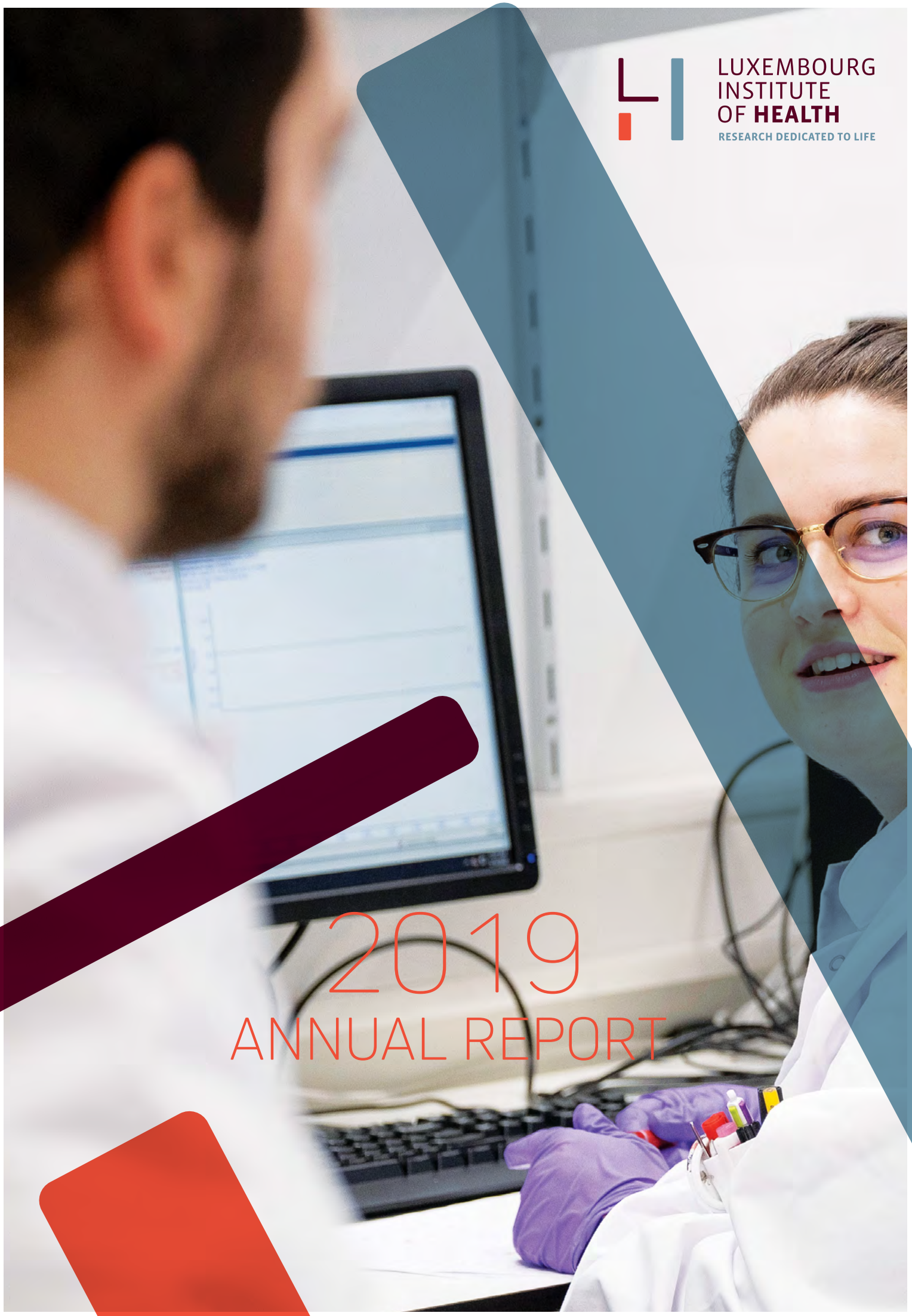


LUXEMBOURG INSTITUTE OF HEALTH

RESEARCH DEDICATED TO LIFE

2019 ANNUAL REPORT

View our corporate video

Prof Dr Ulf Nehrbass, Chief Executive Officer

FOREWORD
MESSAGE FROM THE CEO

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.

Prof Dr Ulf Nehrbass
CEO

CONTENT

MISSION & VISION

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

07

The new Transversal Translational Medicine Initiative

Taking LIH research from the bed to the bench to the bed

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.

Prof Rejko Krüger

> “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*

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.

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

Transversal activities › Transversal Translational Medicine

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*

be key in this recruitment effort. Indeed, communication campaigns and close collaboration with patient associations were instrumental in informing both patients and the general public about the research programme, its aims and benefits, and therefore helped us reach the target", explains Prof Rejko Krüger, Director of Transversal Translational Medicine at LIH and coordinator of NCER-PD. *"The participation of volunteers in the study was also greatly facilitated by a dedicated 'Flying Team' — consisting of a neurologist, a neuropsychologist and a study nurse — which travels directly to patients' residences and recruitment centres to carry out examinations. This is a considerable advantage, especially for participants with reduced mobility",* adds Dr Manon Gantenbein, Head of CIEC.

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

INTEGRATED PATIENT CARE: PARKINSONNET LUXEMBOURG

The close collaboration between Parkinson's patients, researchers, clinicians and health professionals fostered by NCER-PD brought forward the specific need for a novel nation-wide and patient-centred integrated care network to improve the quality of life of people suffering from the disease. Therefore, as a direct consequence of NCER-PD, ParkinsonNet Luxembourg was launched in 2018 with this aim in mind. The network continuously improves patient empowerment and raises awareness on PD by offering reliable and valuable information via its support materials and events. It also allows PD patients to find accredited specialists and define with them their treatment goals.

In 2019, the initiative counted 60 active members, including physiotherapists, occupational therapists, speech and language therapists, nurses and neurologists. Moreover, four ParkinsonNet Luxembourg members became qualified trainers in 2019, which will allow the organisation to qualify new therapists itself to take care of PD patients according to best practices. A total of 13 continuing education events for therapists, neurologists and patients were also organised in 2019. This led to an improved work satisfaction for therapists and to an increase in the number of PD patients treated. Indeed, the number of patients seen by therapists before becoming members of ParkinsonNet was 40 for occupational therapists, 80 for physiotherapists and 35 for speech and language therapists. One year after being members, these numbers rose to 90 for occupational therapists, 140 for physiotherapists and 70 for speech and language therapists.

Together with NCER-PD, ParkinsonNet Luxembourg is a true translational programme, leveraging on fundamental research to tangibly improve patient care.

Prof Simone Niclou

Translational oncology at LIH: the PFP project

Interview with Prof Simone Niclou

Cancer research at LIH is becoming increasingly patient-centric, acting as a bridge between fundamental research and clinical practice. This translational oncology vision was reinforced by the appointment of Prof Simone Niclou as Director of the Department of Oncology (DONC) in May 2019, and by the subsequent launch of Personalised Functional Profiling (PFP), a clinical feasibility study aiming to tailor cancer treatments to the individual characteristics of a patient's cancer. Prof Simone Niclou explains the translational and transversal dimension of the Department's research activities.

Prof 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, allows 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, aunched 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.

Dr Guy Berchem

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.

> “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.”
>
> *Prof Laetitia Huiart*

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 Interventional 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.

The SPRING clinical trial is conducted as part of the WIN (Worldwide Innovative Network in Cancer Personalised Medicine) international consortium, which brings together 37 organisations in 21 countries to accelerate translational and clinical research in the field of personalised medicine for the benefit of patients. The trial is financially supported by the ARC Foundation, with CHL and LIH contributing to the funding of the study in Luxembourg.

Connecting research with clinical practice

Luxembourg's participation in the SPRING clinical trial is coordinated by Dr Guy Berchem, Principal Investigator and oncologist at the CHL. Dr Berchem plays a pivotal role in this respect, acting as a bridge between clinical practice on the one hand, and translational research on the other, and further strengthening the ties between CHL and LIH. Indeed, aside from his position as oncologist in the Oncology Department at the CHL, he has been Head of the Laboratory of Experimental Cancer Research at LIH's Department of Oncology for over 15 years. In addition, he was appointed Associated Medical Director at LIH in May 2019. This dual expertise in both research and healthcare exemplifies the concept of "clinician scientist", which is one of the key pillars of successful translational and personalised medicine.

"In order to improve existing cancer treatments and propose new ones, there must be a close interaction between biomedical research and the clinical world. My role is to facilitate this interaction and guide LIH researchers in ensuring that their research projects address patient needs and clinically relevant issues", states Dr Berchem.

"The SPRING study perfectly illustrates this translational vision, since it leverages on the invaluable clinical research expertise of LIH to tackle the problem of treatment resistance and contribute to the addition of a powerful triple therapy to the existing anti-cancer therapeutic arsenal" he concludes.

> "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*

Prof Laetitia Huiart

Dr Guy Fagherazzi

Leveraging on digital technologies to improve patient health – the CoLive Diabetes study

Interview with Prof Laetitia Huiart and Dr Guy Fagherazzi

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). JITAI 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.

coLive DIABETES
Because your experience matters

Dr Antonio Cosma

Prof Gunnar Dittmar

Shared platforms and services: the pillars of the translational vision

Transversal activities › Quantitative Biology Unit

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.

> "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*

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.

"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 PEVO[SQ] 'basket trial'[1] 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.

The integration of biological and clinical data will allow the development of algorithms that help physicians decide whether a patient is eligible for inclusion in one or more clinical trials, thus optimising patient outcomes. The LIH-IBBL team is in charge of all aspects related to sample logistics, storage and redistribution, as well as sample processing — from DNA and RNA extraction, to the preparation and analysis of patient-derived tissues. Ultimately, the tissue and blood samples collected during the study will be used to identify biomarkers that may predict a patient's response to treatment and the progression of his disease. The project's multidisciplinary consortium is led by the Institut Curie (France) and includes several partners from academia and industry from Luxembourg, Germany, Italy and Hungary.

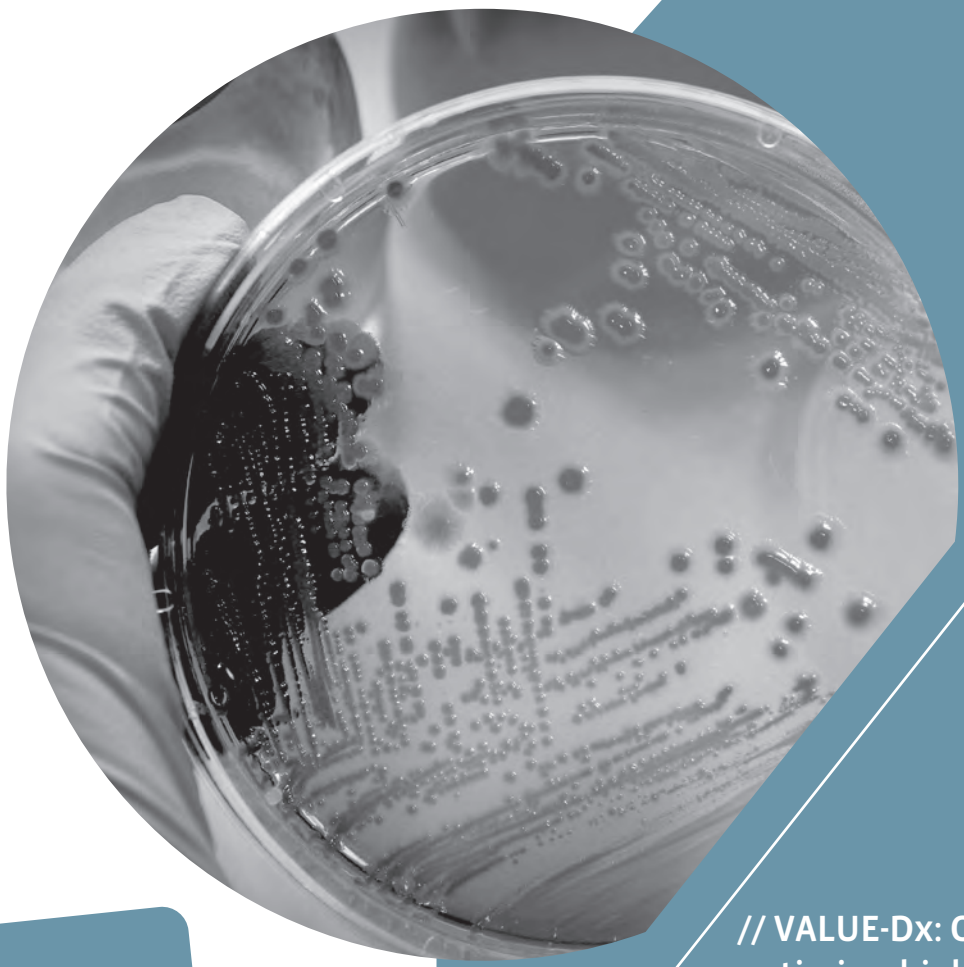
[1] A new type of clinical trial aiming to test a drug on patients presenting the same specific genomic alteration.

// IMMUcan: unraveling immune system-tumour interactions

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.

IMMUCAN

IMMUcan kick-off meeting (EORTC, Brussels, March 2019)



// VALUE-Dx: Combating antimicrobial resistance

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, blood stream 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.

VALUE-Dx

// 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.

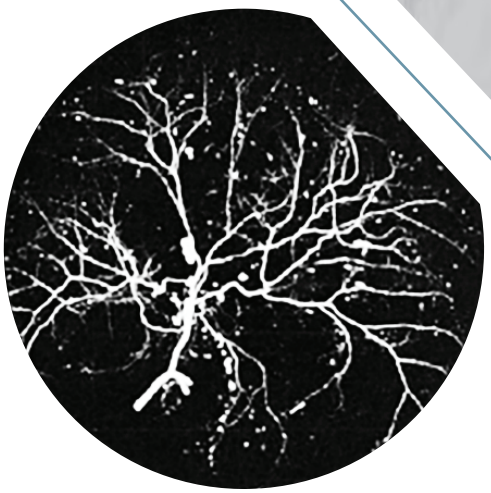
CARDIATEAM Kick-off Meeting (March 2019)

// 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.

Research progress

Prof Dirk Brenner



Micro-Computed Tomography imaging of mice liver arterial vasculature

Controlling antiviral immune responses with acetylcholine

Contribution to a Science publication

Department of Infection and Immunity › Experimental & Molecular Immunology

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.

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.

"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

Global Burden Study: obesity rising faster in rural areas than in cities

Contribution to a Nature publication

Department of Population Health › Epidemiology and Public Health Research Unit

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

Discovery of a link between diabetes and frailty in elderly people

New study results

Department of Population Health › Public Health 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.

> “In simple terms, diabetes makes us age by 12 years, increasing the risk of rapid health decline.”
>
> *Dr Gloria Aguayo*

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.

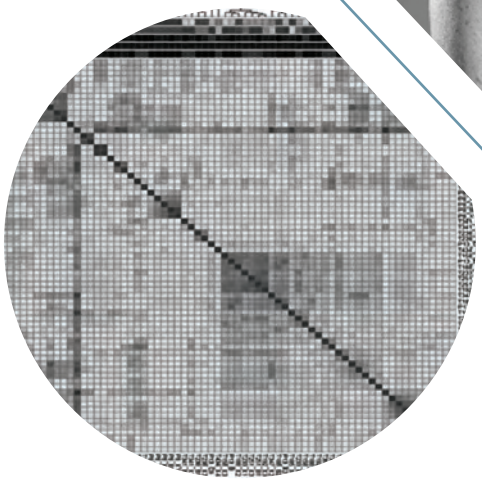
Slowing the progression of frailty

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).

Prof Simone Niclou



Analysis of copy number variations in primary and recurrent gliomas

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.

"More data are needed to fully understand glioma evolution, but our study sets an excellent foundation to more effectively study both evolution and treatment response", says Prof Roel Verhaak from The Jackson Laboratory who led the study.

"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 Prof Niclou.

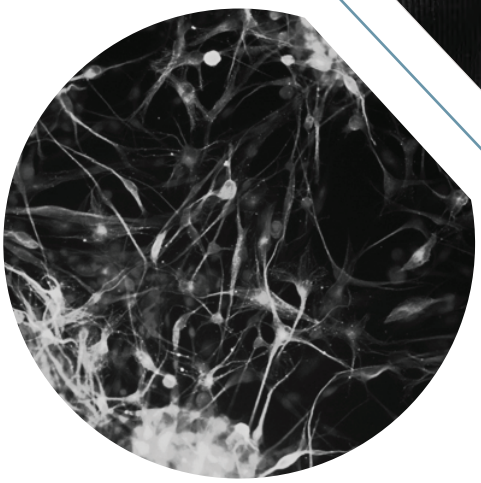
The joint effort of the international GLASS Consortium offers important insight into how to improve the clinical prognosis for glioma patients worldwide and also provides the largest database of sequential glioma tumour profiles to date.

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*

Dr Anna Golebiewska



Plastic glioblastoma cells acquiring transient neuron-like morphology under differentiation conditions

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

Publication in Nature Communications

Department of Oncology › NORLUX Neuro-Oncology Laboratory

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.

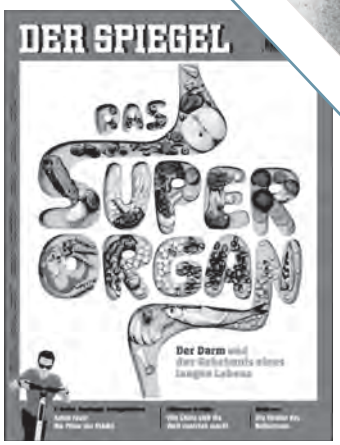
"Once we understand exactly what causes the flexibility of tumor cells, we can devise combinatorial therapies which target the signals underlying this plasticity, thereby improving treatment effectiveness and patient outcomes", concludes Prof Niclou, Director of the LIH Department of Oncology and leader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

Prof Mahesh Desai



"Der Spiegel" cover, June 29th 2019

International press coverage for LIH gut microbiome research

LIH publication as "Der Spiegel" cover story

Department of Infection and Immunity › Allergology, Immunology and Inflammation Research Unit › Eco-Immunology and Microbiome

Der Spiegel, a widely read news magazine generally considered to be one 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 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*

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.

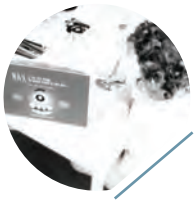
"The publication of our research in such a prominent magazine goes to show the growing interest and appreciation of the importance of this area, not only among the scientific community, but also among the general public", says Prof Desai.

"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

Workshop in Gasperich

// "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.

// 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).

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.

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// Chercheurs à l'école

From March 25th until March 29th, the Clinical and Epidemiological Investigation Centre (CIEC) team took part in the 9th editon 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

// 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.

The LIH/IBBL Marketing & Communication team (from left to right: Juliette Pertuy, Joanna Muz, Arnaud D'Agostini, Laura Star, Federica Amato and Malou Fraiture. Missing: Noémie Guerisse)

// 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.

// 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 Neumünster 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!

// 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.

Highlights calendar 2019

News, events, awards and nominations

1

Legs Kanning award for Dr Jérôme Paggetti

Dr Jérome 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.

Photo: From left to right: Mr Hugues Delcourt (CEO of BIL), Dr Jérôme Paggetti (LIH) and Prof Marc Diederich (president of Action Lions Vaincre le Cancer).

2

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.

Photo: From left to right: Maiti Lommel (Public Health Professional, Cancer Foundation), Dr Guy Berchem (Head of Unit, LIH/CHL), Lucienne Thommes (Director, Cancer Foundation), Dr Bassam Janji (Deputy Head of Unit, LIH), Dr Sean Sapcariu (Programme Manager, FNR) and Dr Marc Schiltz (Secretary General, FNR).

3

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.


4


LUXEMBOURG
INSTITUTE
OF HEALTH
RESEARCH DEDICATED TO LIFE
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6


Fondation
Cancer
470 177 €
De Fondation Cancer
Dr Clément Thomas
Institute of Luxembourg Health
7

MARCH

4

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".

MAY

5

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).

6

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.

7

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)

9

10

8

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.

9

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.

Photo: From left to right: Lucienne Thommes (Director, Cancer Foundation), Dr Virginie Neirinckx, (postdoctoral researcher, LIH), Prof Ulf Nehrbass (CEO, LIH), Prof Simone Niclou (Director of the Department of Oncology, LIH) and Dr Carlo Bock (President, Cancer Foundation).

10

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.


FNR.lu
18th meeting of the Society for Natural Immunity
LUXEMBOURG INSTITUTE OF HEALTH


18th meeting of the Society for Natural Immunity (NK2019)
30th Sept. to 03rd Oct.
2019 Luxembourg
ALVISSE
PARC


FNR.lu
PARC HOTEL

11

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".

12

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 Delbrouck, 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".

13

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).

Photos: NK 2019 meeting

14

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 Hübschen. 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.


LUXEMBOURG
INSTITUTE
OF HEALTH
LISER
uni.lu
LIST
FNR.lu
15


16

15

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

16

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

17

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

Board of Directors (from left to right): Josiane Entringer, Alain Kohl, Viviane Bremer, Robert Müller, Francoise Berthet, Gregor Baertz (president), Xavier Poos, Pierrot Schiltz, Carole Brueckler. Absent: Lysiane Back

BOARDS

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

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

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

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


DEPARTMENT OF ONCOLOGY
DEPARTMENT OF INFECTION & IMMUNITY
TRANSVERSAL ACTIVITIES & PLATFORMS
DEPARTMENT OF POPULATION HEALTH
RESEARCH DEPARTMENTS
RESEARCH SUPPORT SERVICES
CEO LIH
BOARD OF DIRECTORS
CFAO
ADMINISTRATIVE DEPARTMENT & CORE SERVICES
CEO IBBL
INSTITUTE IBBL

KEY FACTS*

2019

1
BIOBANK

40
NATIONALITIES

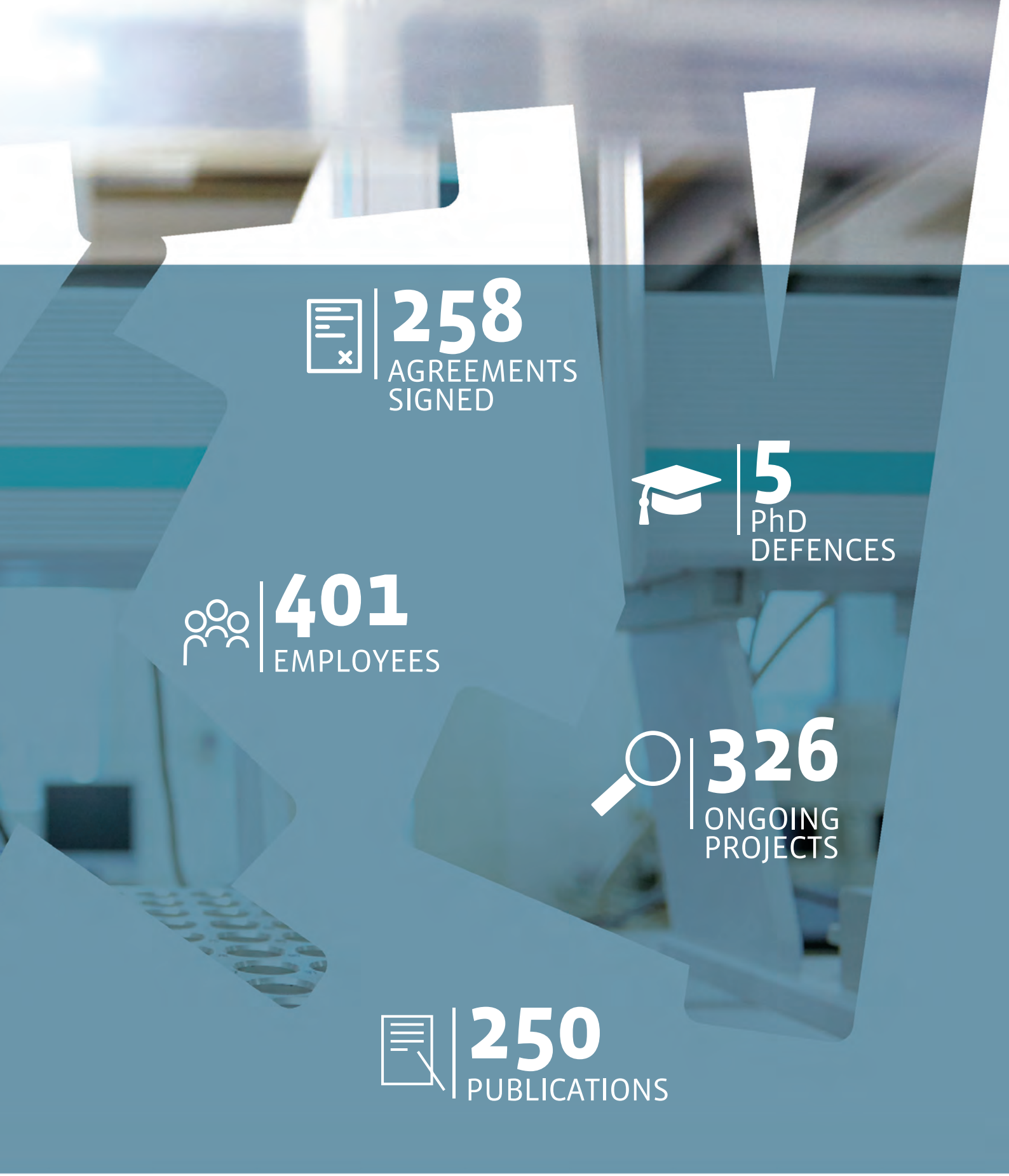
88,417
TOTAL SAMPLES DISTRIBUTED (IBBL)

218
SCIENTISTS

3
PATENT APPLICATIONS

1.6Mill.
TOTAL SAMPLES COLLECTED AND ALIQUOTS CREATED (IBBL)

*figures as of 31st December 2019



258
AGREEMENTS SIGNED

5
PhD DEFENCES

401
EMPLOYEES

326
ONGOING PROJECTS

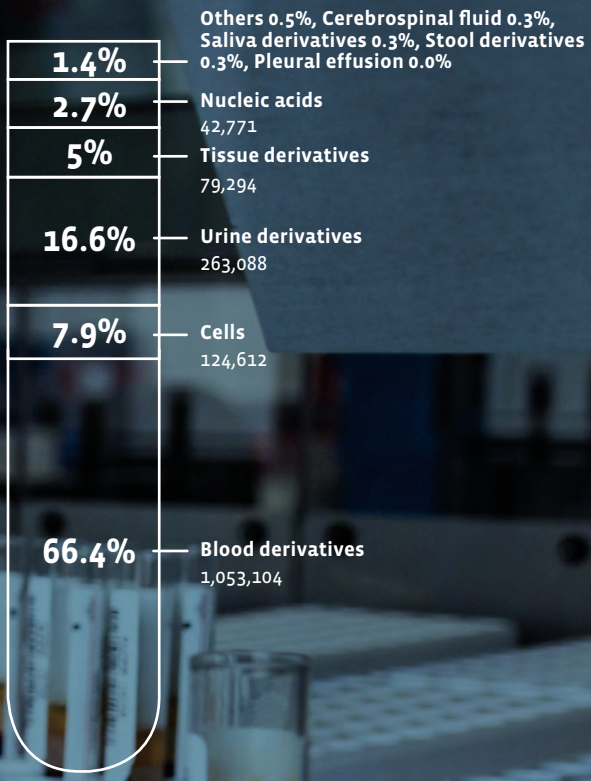
250
PUBLICATIONS

41
NEW PARTNERSHIPS WITH A PRIVATE PARTNER

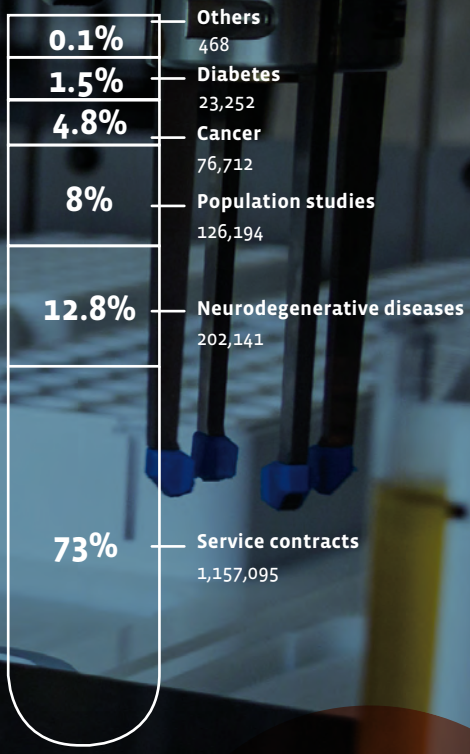
15.1 € MIO
THIRD-PARTY INCOME

COLLECTION STATISTICS

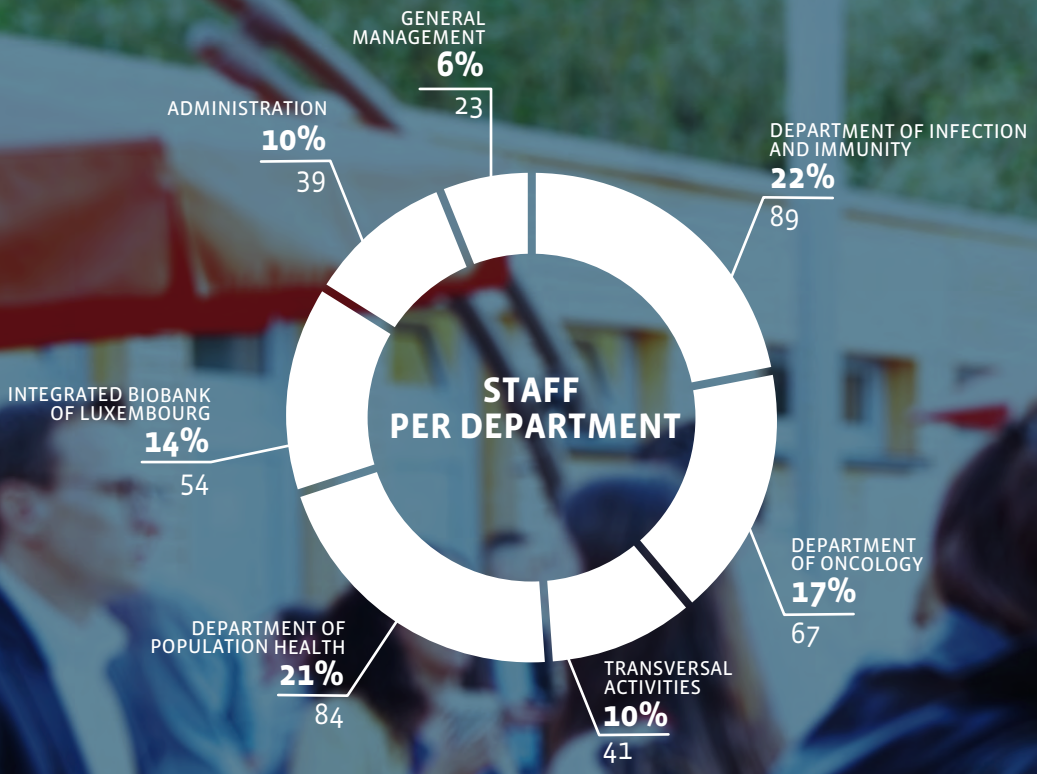
SAMPLES BY TYPE



SAMPLES BY PROGRAMME



IBBL
INTEGRATED BIOBANK OF LUXEMBOURG
FOR NEXT GENERATION HEALTHCARE



STAFF BY FUNCTION

RESEARCHERS
55%
218

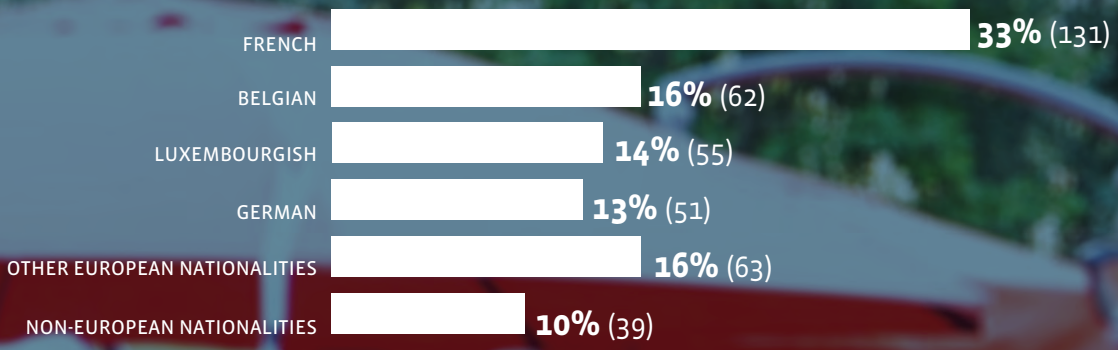
TECHNICIANS
24%
96

SUPPORT STAFF
21%
83

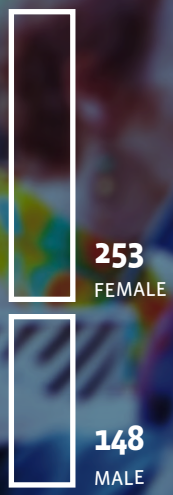
HUMAN RESOURCES

(31st December 2019)

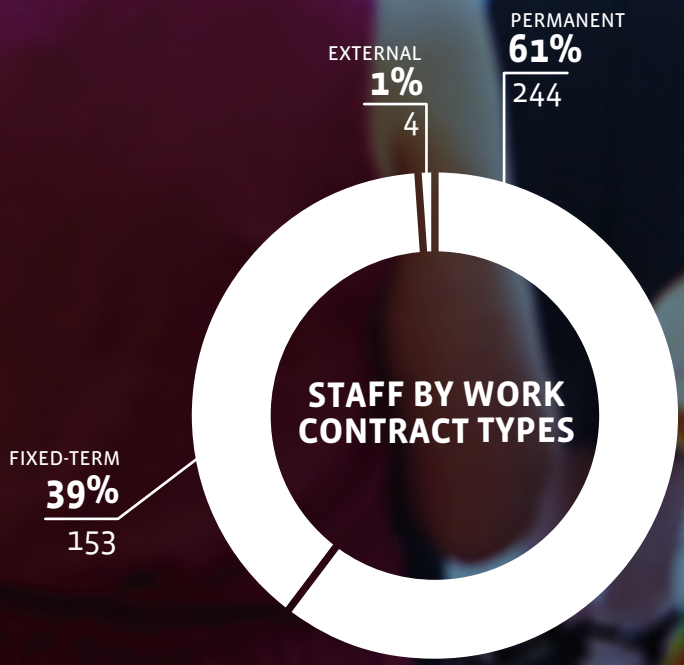
STAFF BY NATIONALITY



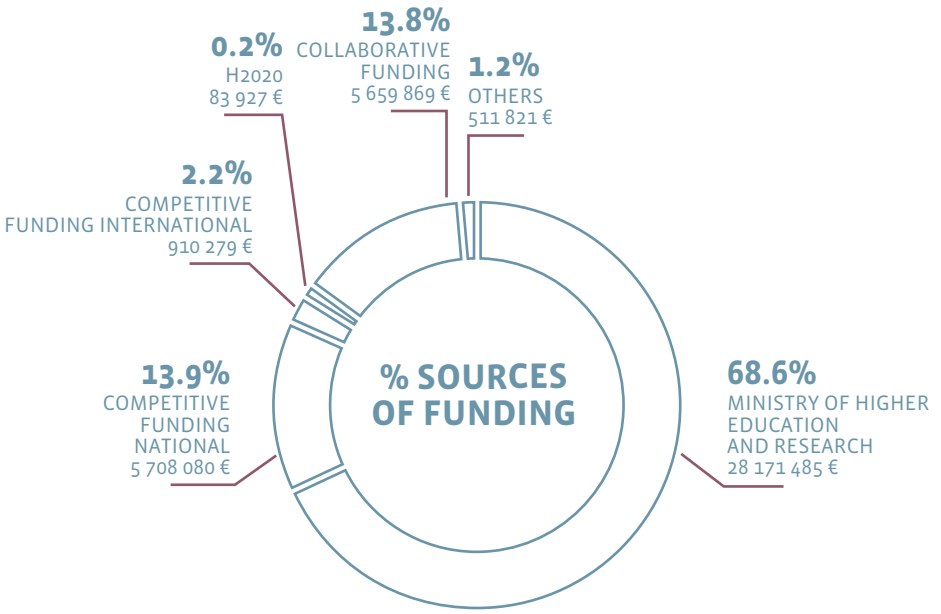
STAFF BY GENDER



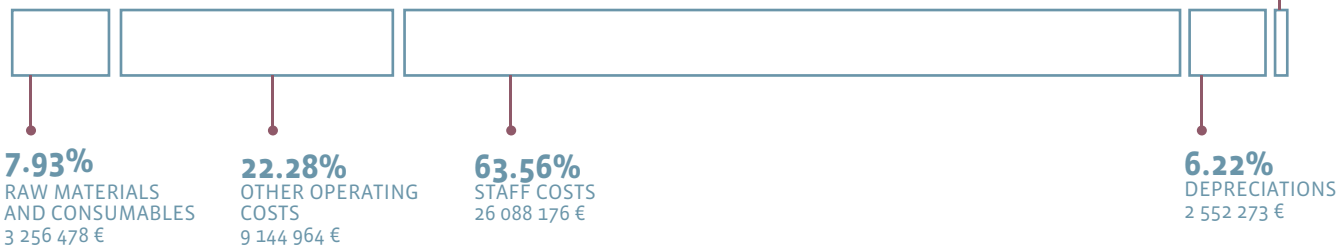
STAFF BY WORK CONTRACT TYPES



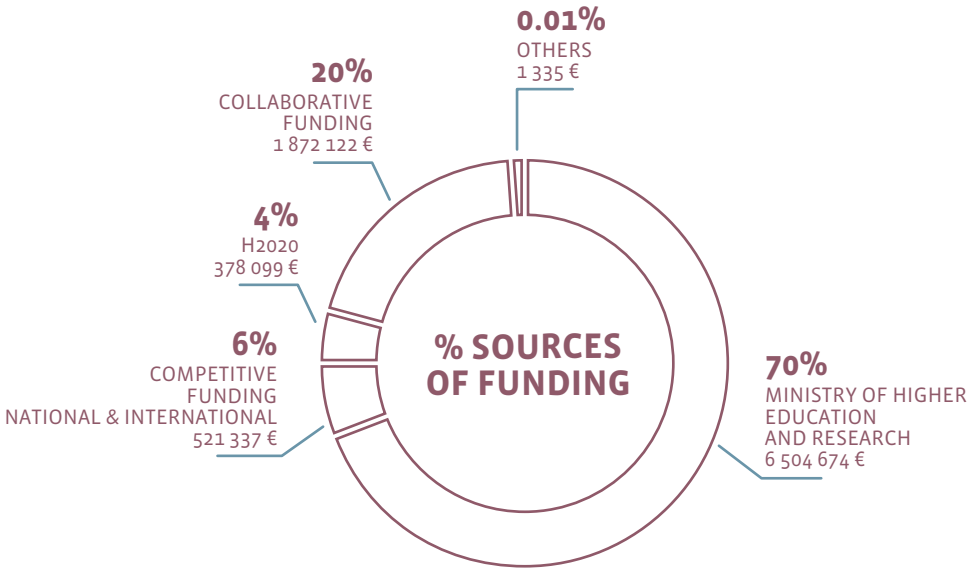
LIH



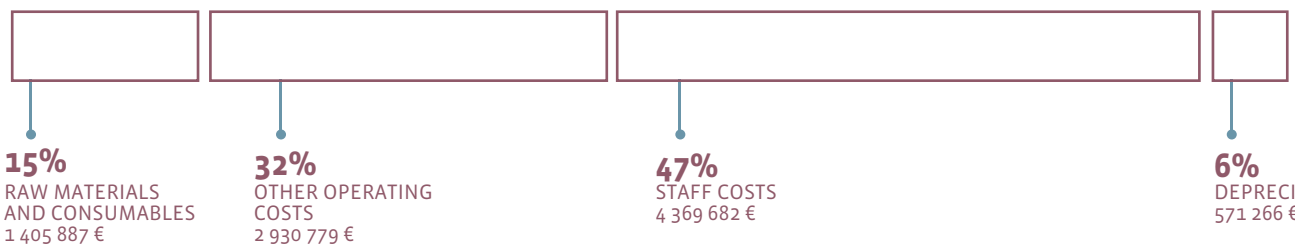
% COST CATEGORIES



IBBL



% COST CATEGORIES



FINANCES

STATUTORY EXPENSES

PROFIT AND LOSS ACCOUNT (EUR)	2019 01.01 - 31.12.19	2018 01.01 - 31.12.18
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)

ASSETS (EUR)	2019 01.01 - 31.12.19	2018 01.01 - 31.12.18
FIXED ASSETS		
Intangible fixed assets	637.950	739.359
Tangible fixed assets	6.647.540	8.012.126
Financial fixed assets	1.380	4.849
TOTAL FIXED ASSETS	**7.286.870**	**8.756.334**
CURRENT ASSETS		
Debtors		
1. Trade debtors	**1.631.081**	**1.294.302**
a. Becoming due and payable within one year	1.629.964	1.275.758
b. Becoming due and payable after more than one year	1.117	18.544
2. Other debtors	**2.765.657**	**2.767.222**
a. Becoming due and payable within one year	2.765.657	2.767.222
Cash at bank and in hand	**29.559.929**	**27.688.452**
TOTAL CURRENT ASSETS	**33.956.667**	**31.749.976**
Prepayments	**926.180**	**791.273**
TOTAL ASSETS	**42.169.717**	**41.297.583**

FINANCES
BALANCE SHEET
(31st December 2019)

LIABILITIES (EUR)	**2019** 01.01 - 31.12.19	**2018** 01.01 - 31.12.18
CAPITAL AND RESERVES		
Financial wealth	4.099.157	4.099.157
Reserves	1.486.881	1.486.881
Profit or loss brought forward	7.999.544	8.051.788
Profit or loss for the financial year	-489.576	-52.244
Capital investment subsidies	7.601.529	9.632.094
TOTAL CAPITAL AND RESERVES	**20.697.535**	**23.217.676**
Available reserve for projects	**16.105.399**	**12.713.774**
Provisions	**942.624**	**1.271.426**
NON-SUBORDINATED DEBTS		
1. Trade creditors	**3.361.390**	**3.073.941**
a. Becoming due and payable within one year	3.358.475	3.052.980
b. Becoming due and payable after more than one year	2.915	20.961
2. Tax and social security debts	**977.722**	**960.976**
a. Tax debts	9.720	5.040
b. Social security debts	968.002	955.936
3. Other creditors	**77.788**	**59.401**
a. Becoming due and payable within one year	77.788	59.401
TOTAL AVAILABLE RESERVE FOR PROJECTS, PROVISIONS AND CREDITORS	**21.464.923**	**18.079.518**
Deferred income	**7.259**	**389**
TOTAL CAPITAL, RESERVES AND LIABILITIES	**42.169.717**	**41.297.583**

Publications

DEPARTMENT OF INFECTION AND IMMUNITY

Dostert C, Grusdat M, Letellier E, Brenner D. **The TNF Family of Ligands and Receptors: Communication Modules in the Immune System and Beyond.** Physiological Reviews. 2019; 99(1): 115-160. *IF: 24.250 (2018) - Prepublished 2018*

Blank S, Haemmerle S, Jaeger T, Russkamp D, Ring J, Schmidt-Weber CB, Ollert M. **Prevalence of Hymenoptera venom allergy and sensitization in the population-representative German KORA cohort.** Allergo Journal International. 2019; 28(6): 183-191. *IF: NA (2018)*

Grova N, Schroeder H, Olivier JL, Turner JD. **Epigenetic and neurological impairments associated with early life exposure to persistent organic pollutants.** International Journal of Genomics. 2019; 2019: 2085496. *IF: 2.303 (2018)*

Hilger C, Fischer J, Wolbing F, Biedermann T. **Role and mechanism of Galactose-Alpha-1,3-Galactose in the elicitation of delayed anaphylactic reactions to red Meat.** Current Allergy and Asthma Reports. 2019; 19(1): 3. *IF: 3.982 (2018)*

Kirpach J. **[Investigation of the possible use of B cells for the diagnosis of acute Lyme disease] (Doctoral thesis)**. Homburg: Saarland University, 2019. 216 p.

Mizera A, Pang J, Yuan Q. **GPU-accelerated steady-state computation of large probabilistic Boolean networks.** Formal Aspects of Computing. 2019; 31(1): 27-46. *IF: 0.784 (2018)*

Cox MA, Duncan GS, Lin GHY, Steinberg BE, Yu LX, Brenner D, Buckler LN, Elia AJ, Wakeham AC, Nieman B, Dominguez-Brauer C, Elford AR, Gill KT, Kubli SP, Haight J, Berger T, Ohashi PS, Tracey KJ, Olofsson PS, Mak TW. **Choline acetyltransferase-expressing T cells are required to control chronic viral infection.** Science. 2019; 363(6427): 639-644. *IF: 41.037 (2018)*

Hofstra LM. **HIV drug resistance. Clinical and public health implications (Doctoral thesis)**. Utrechtht: University of Utrecht, 2019.

Pannus P, Adams P, Willems E, Heyndrickx L, Florence E, Rutsaert S, De Spiegelaere W, Vandekerckhove L, Seguin-Devaux C, Vanham G. **In-vitro viral suppressive capacity correlates with immune checkpoint marker expression on peripheral CD8+ T cells in treated HIV-positive patients.** AIDS. 2019; 33(3): 387-398. *IF: 4.499 (2018)*

Vinken L, Fransen K, Cuypers L, Alexiev I, Balotta C, Debaisieux L, Seguin-Devaux C, Garcia Ribas S, Gomes P, Incardona F, Kaiser R, Ruelle J, Sayan M, Paraschiv S, Paredes R, Peeters M, Sonnerborg A, Vancutsem E, Vandamme AM, Van den Wijngaert S, Van Ranst M, Verhofstede C, Stadler T, Lemey P, Van Laethem K. **Earlier initiation of antiretroviral treatment coincides with an initial control of the HIV-1 Sub-Subtype F1 outbreak among men-having-sex-with-men in Flanders, Belgium.** Frontiers in Microbiology. 2019; 10: 613. *IF: 4.259 (2018)*

Adams P, Vancutsem E, Nicolaizeau C, Servais JY, Pierard D, Francois JH, Schneider T, Paxinos EE, Marins EG, Canchola JA, Seguin-Devaux C. **Multicenter evaluation of the cobas® HIV-1 quantitative nucleic acid test for use on the cobas® 4800 system for the quantification of HIV-1 plasma viral load.** Journal of Clinical Virology. 2019; 114: 43-49. *IF: 3.020 (2018)*

Wilson AS, Law HD, Knobbe-Thomsen CB, Kearney CJ, Oliaro J, Binsfeld C, Burgio G, Starrs L, Brenner D, Randall KL, Brustle A. **Protection from EAE in DOCK8 mutant mice occurs despite increased Th17 cell frequencies in the periphery.** European Journal of Immunology. 2019; (5): 770-781. Epub 2019 Feb 20. *IF: 4.695 (2018)*

Nouanthong P, Hubschen JM, Billamay S, Mongkhoune S, Vilivong K, Khounvisith V, Sinner R, Grandadam M, Phonekeo D, Black AP, Muller CP. **Varicella zoster and fever rash surveillance in Lao People's Democratic Republic.** BMC Infectious Diseases. 2019; 19(1): 392. *IF: 2.565 (2018)*

Arendt V, Guillorit L, Origer A, Sauvageot N, Vaillant M, Fischer A, Goedertz H, Francois JH, Alexiev I, Staub T, Seguin-Devaux C. **Injection of cocaine is associated with a recent HIV outbreak in people who inject drugs in Luxembourg.** PloS one. 2019; 14(5): e0215570. *IF: 2.776 (2018)*

Kirpach J, Colone A, Burckert JP, Faison WJ, Dubois A, Sinner R, Reye AL, Muller CP. **Detection of a low level and heterogeneous B cell immune response in peripheral blood of acute borreliosis patients with high throughput sequencing.** Frontiers in Immunology. 2019; 10: 1105. *IF: 4.716 (2018)*

Raith M, Zach D, Sonnleitner L, Woroszylo K, Focke-Tejkl M, Wank H, Graf T, Kuehn A, Pascal M, Munoz-Cano RM, Wortmann J, Aschauer P, Keller W, Braeuer S, Goessler W, Swoboda I. **Rational design of a hypoallergenic Phl p 7 variant for immunotherapy of polcalcin-sensitized patients.** Scientific Reports. 2019; 9(1): 7802. *IF: 4.011 (2018)*

EMCDDA expert network (Devaux C. as collaborator for DRID network). **Drug-related infectious diseases: Update from the EMCDDA expert network.** Luxembourg: Publications Office of the European Union, 2019. 20 p.

Untersmayr E, Bax HJ, Bergmann C, Bianchini R, Cozen W, Gould HJ, Hartmann K, Josephs DH, Levi-Schaffer F, Penichet ML, O'Mahony L, Poli A, Redegeld FA, Roth-Walter F, Turner MC, Vangelista L, Karagiannis SN, Jensen-Jarolim E. **AllergoOncology: Microbiota in allergy and cancer-A European Academy for Allergy and Clinical Immunology position paper.** Allergy. 2019; 74(6): 1037-1051. Epub 2019 Mar 6. *IF: 6.771 (2018)*

Sjoberg E, Meyrath M, Milde L, Herrera M, Lovrot J, Hagerstrand D, Frings O, Bartish M, Rolny C, Sonnhammer E, Chevigne A, Augsten M, Ostman A. **A novel ACKR2-dependent role of fibroblast-derived CXCL14 in epithelial-to-mesenchymal transition and metastasis of breast cancer.** Clinical Cancer Research. 2019; 25(12): 3702-3717. Epub 2019 Mar 8. *IF: 8.911 (2018)*

Reynders N, Abboud D, Baragli A, Noman MZ, Rogister B, Niclou SP, Heveker N, Janji B, Hanson J, Szpakowska M, Chevigne A. **The distinct roles of CXCR3 variants and their ligands in the tumor microenvironment.** Cells. 2019; 8(6). *IF: 5.656 (2018)*

Maria Matricardi P, Dramburg S, Alvarez-Perea A, Antolin-Amerigo D, Apfelbacher C, Atanaskovic-Markovic M, Berger U, Blaiss MS, Blank S, Boni E, Bonini M, Bousquet J, Brockow K, Buters J, Cardona V, Caubet JC, Cavkaytar O, Elliott T, Esteban-Gorgojo I, Fonseca JA, Gardner J, Gevaert P, Ghiordanescu I, Hellings P, Hoffmann-Sommergruber K, Fusun Kalpaklioglu A, Marmouz F, Meijide Calderon A, Mosges R, Nakonechna A, Ollert M, Oteros J, Pajno G, Panaitescu C, Perez-Formigo D, Pfaar O, Pitsios C, Rudenko M, Ryan D, Sanchez-Garcia S, Shih J, Tripodi S, Van der Poel LA, van Os-Medendorp H, Varricchi G, Wittmann J, Worm M, Agache I. **The role of mobile health technologies in allergy care: An EAACI position paper.** Allergy. 2019. [Epub ahead of print]. *IF: 6.771 (2018)*

Kolie D, Camara BS, Kourouma K, Grovogui FM, Delamou A, Beavogui AH, Hermans V, Muller CP, Edwards JK, Van Griensven J, Zachariah R. **Effects of the 2014/2015 Ebola outbreak on malaria management in pregnant women: A comparative study of an Ebola affected and unaffected rural district of Guinea.** Central African Journal of Public Health. 2019; 5(4): 149-155. *IF: NA (2018)*

Devaux C, Arendt V. **EMCDDA Case study 5 — Expanding HCV screening and hepatitis treatment and care for PWID to harm reduction centres.** In *Hepatitis C: new models of care for drugs services*. EMCDDA, 2019. p.43-49.

Ribas MLA, Tejero Y, Cordero Y, Perez D, Sausy A, Muller CP, Hubschen JM. **Identification of human parvovirus B19 among measles and rubella suspected patients from Cuba.** Journal of Medical Virology. 2019; 91(7): 1351-1354. Epub 2019 Mar 14. *IF: 2.049 (2018)*

Seguin-Devaux C, Plesseria JM, Verschueren C, Masquelier C, Iserentant G, Fullana M, Jozsi M, Cohen JHM, Dervillez X. **FHR4-based immunoconjugates direct complement-dependent cytotoxicity and phagocytosis towards HER2-positive cancer cells.** Molecular Oncology. 2019; 13(12): 2531-2553. Epub 2019 Sep 30. *IF: 5.962 (2018)*

van Meteren N, Lagadic-Gossmann D, Chevanne M, Gallais I, Gobart D, Burel A, Bucher S, Grova N, Fromenty B, Appenzeller BMR, Chevance S, Gauffre F, Le Ferrec E, Sergent O. **Polycyclic aromatic hydrocarbons can trigger hepatocyte release of extracellular vesicles by various mechanisms of action depending on their affinity for the aryl hydrocarbon receptor.** Toxicological Sciences. 2019. [Epub ahead of print]. *IF: 3.564 (2018)*

Dina J, Omnes J, Vauloup-Fellous C, Collet L, Hamel J, Antona D, Hubschen JM, Ben Mamou M, Vabret A. **True measles cases undetected by Reverse Transcription-PCR (RT-PCR): Effect of genetic variability on assay sensitivity needs to be regularly surveyed.** Journal of Clinical Microbiology. 2019; 57(8). Print 2019 Aug. *IF: 4.959 (2018)*

Russkamp D, Aguilar-Pimentel A, Alessandrini F, Gailus-Durner V, Fuchs H, Ohnmacht C, Chaker A, de Angelis MH, Ollert M, Schmidt-Weber CB, Blank S. **IL-4 receptor alpha blockade prevents sensitization and alters acute and long-lasting effects of allergen-specific immunotherapy of murine allergic asthma.** Allergy. 2019; 74(8): 1549-1560. Epub 2019 Apr 11. *IF: 6.771 (2018)*

Elwenspoek MMC, Hengesch X, Leenen FAD, Sias K, Fernandes SB, Schaan VK, Meriaux SB, Schmitz S, Bonnemberger F, Schachinger H, Vogele C, Muller CP, Turner JD. **Glucocorticoid receptor signaling in leukocytes after early life adversity.** Development and Psychopathology. 2019: 1-11. [Epub ahead of print]. *IF: 3.593 (2018)*

Ogundipe OF, Van den Bergh R, Thierry B, Takarinda KC, Muller CP, Timire C, Caluwaerts S, Chaillet P, Zuniga I. **Better care for babies: the added value of a modified reverse syphilis testing algorithm for the treatment of congenital syphilis in a maternity Hospital in Central African Republic.** BMC Pediatrics. 2019; 19(1): 284. *IF: 1.983 (2018)*

Arendt V, Amand M, Iserentant G, Lemaire M, Masquelier C, Ndayisaba GF, Verhofstede C, Karita E, Allen S, Chevigne A, Schmit JC, Bercoff DP, Seguin-Devaux C. **Predominance of the heterozygous CCR5 delta-24 deletion in African individuals resistant to HIV infection might be related to a defect in CCR5 addressing at the cell surface.** Journal of the International AIDS Society. 2019; 22(9): e25384. *IF: 5.192 (2018)*

Zeng N. **Investigation of the immune functions of DJ-1 (Doctoral thesis)**. Université de Luxembourg, 2019.

Cossarizza A, Chang HD, Radbruch A, Acs A, Adam D, Adam-Klages S, Agace WW, Aghaeepour N, Akdis M, Allez M, Almeida LN, Alvisi G, Anderson G, Andra I, Annunziato F, Anselmo A, Bacher P, Baldari CT, Bari S, Barnaba V, Barros-Martins J, Battistini L, Bauer W, Baumgart S, Baumgarth N, Baumjohann D, Baying B, Bebawy M, Becher B, Beisker W, Benes V, Beyaert R, Blanco A, Boardman DA, Bogdan C, Borger JG, Borsellino G, Boulais PE, Bradford JA, Brenner D, Brinkman RR, Brooks AES, Busch DH, Buscher M, Bushnell TP, Calzetti F, Cameron G, Cammarata I, Cao X, Cardell SL, Casola S, Cassatella MA, Cavani A, Celada A, Chatenoud L, Chattopadhyay PK, Chow S, Christakou E, Cicin-Sain L, Clerici M, Colombo FS, Cook L, Cooke A, Cooper AM, Corbett AJ, Cosma A, Cosmi L, Coulie PG, Cumano A, Cvetkovic L, Dang VD, Dang-Heine C, Davey MS, Davies D, De Biasi S, Del Zotto G, Dela Cruz GV, Delacher M, Della Bella S, Dellabona P, Deniz G, Dessing M, Di Santo JP, Diefenbach A, Dieli F, Dolf A, Dorner T, Dress RJ, Dudziak D, Dustin M, Dutertre CA, Ebner F, Eckle SBG, Edinger M, Eede P, Ehrhardt GRA, Eich M, Engel P, Engelhardt B, Erdei A, Esser C, Everts B, Evrard M, Falk CS, Fehniger TA, Felipo-Benavent M, Ferry H, Feuerer M, Filby A, Filkor K, Fillatreau S, Follo M, Forster I, Foster J, Foulds GA, Frehse B, Frenette PS, Frischbutter S, Fritzsche W, Galbraith DW, Gangaev A, Garbi N, Gaudilliere B, Gazzinelli RT, Geginat J, Gerner W, Gherardin NA, Ghoreschi K, Gibellini L, Ginhoux F, Goda K, Godfrey DI, Goettlinger C, Gonzalez-Navajas JM, Goodyear CS, Gori A, Grogan JL, Grummitt D, Grutzkau A, Haftmann C, Hahn J, Hammad H, Hammerling G, Hansmann L, Hansson G, Harpur CM, Hartmann S, Hauser A, Hauser AE, Haviland DL, Hedley D, Hernandez DC, Herrera G, Herrmann M, Hess C, Hofer T, Hoffmann P, Hogquist K, Holland T, Hollt T, Holmdahl R, Hombrink P, Houston JP, Hoyer BF, Huang B, Huang FP, Huber JE, Huehn J, Hundemer M, Hunter CA, Hwang WYK, Iannone A, Ingelfinger F, Ivison SM, Jack HM, Jani PK, Javega B, Jonjic S, Kaiser T, Kalina T, Kamradt T, Kaufmann SHE, Keller B, Ketelaars SLC, Khalilnezhad A, Khan S, Kisielow J, Klenerman P, Knopf J, Koay HF, Kobow K, Kolls JK, Kong WT, Kopf M, Korn T, Kriegsmann K, Kristyanto H, Kroneis T, Krueger A, Kuhne J, Kukat C, Kunkel D, Kunze-Schumacher H, Kurosaki T, Kurts C, Kvistborg P, Kwok I, Landry J, Lantz O, Lanuti P, LaRosa F, Lehuen A, LeibundGut-Landmann S, Leipold MD, Leung LYT, Levings MK, Lino AC, Liotta F, Litwin V, Liu Y, Ljunggren HG, Lohoff M, Lombardi G, Lopez L, Lopez-Botet M, Lovett-Racke AE, Lubberts E, Luche H, Ludewig B, Lugli E, Lunemann S, Maecker HT, Maggi L, Maguire O, Mair F, Mair KH, Mantovani A, Manz RA, Marshall AJ, Martinez-Romero A, Martrus G, Marventano I, Maslinski W, Matarese G, Mattioli AV, Maueroder C, Mazzoni A, McCluskey J, McGrath M, McGuire HM, McInnes IB, Mei HE, Melchers F, Melzer S, Mielenz D, Miller SD, Mills KHG, Minderman H, Mjosberg J, Moore J, Moran B, Moretta L, Mosmann TR, Muller S, Multhoff G, Munoz LE, Munz C, Nakayama T, Nasi M, Neumann K, Ng LG, Niedobitek A, Nourshargh S, Nunez G, O'Connor JE, Ochel A, Oja A, Ordonez D, Orfao A, Orlowski-Oliver E, Ouyang W, Oxenius A, Palankar R, Panse I, Pattanapanyasat K, Paulsen M, Pavlinic D, Penter L, Peterson P, Peth C, Petriz J, Piancone F, Pickl WF, Piconese S, Pinti M, Pockley AG, Podolska MJ, Poon Z, Pracht K, Prinz I, Pucillo CEM, Quataert SA, Quatrini L, Quinn KM, Radbruch H, Radstake T, Rahmig S, Rahn HP, Rajwa B, Ravichandran G, Raz Y, Rebhahn JA, Recktenwald D, Reimer D, Reis ESC, Remmerswaal EBM, Richter L, Rico LG, Riddell A, Rieger AM, Robinson JP, Romagnani C, Rubartelli A, Ruland J, Saalmuller A, Saeys Y, Saito T, Sakaguchi S, Sala-de-Oyanguren F, Samstag Y, Sanderson S, Sandrock I, Santoni A, Sanz RB, Saresella M, Sautes-Fridman C, Sawitzki B, Schadt L, Scheffold A, Scherer HU, Schiemann M, Schildberg FA, Schimisky E, Schlitzer A, Schlosser J, Schmid S, Schmitt S, Schober K, Schraivogel D, Schuh W, Schuler T, Schulte R, Schulz AR, Schulz SR, Scotta C, Scott-Algara D, Sester DP, Shankey TV, Silva-Santos B, Simon AK, Sitnik KM, Sozzani S, Speiser DE, Spidlen J, Stahlberg A, Stall AM, Stanley N, Stark R, Stehle C, Steinmetz T, Stockinger H, Takahama Y, Takeda K, Tan L, Tarnok A, Tiegs G, Toldi G, Tornack J, Traggiai E, Trebak M, Tree TIM, Trotter J, Trowsdale J, Tsoumakidou M, Ulrich H, Urbanczyk S, van de Veen W, van den Broek M, van der Pol E, Van Gassen S, Van Isterdael G, van Lier RAW, Veldhoen M, Vento-Asturias S, Vieira P, Voehringer D, Volk HD, von Borstel A, von Volkmann K, Waisman A, Walker RV, Wallace PK, Wang SA, Wang XM, Ward MD, Ward-Hartstonge KA, Warnatz K, Warnes G, Warth S, Waskow C, Watson JV, Watzl C, Wegener L, Weisenburger T, Wiedemann A, Wienands J, Wilharm A, Wilkinson RJ, Willimsky G, Wing JB, Winkelmann R, Winkler TH, Wirz OF, Wong A, Wurst P, Yang JHM, Yang J, Yazdanbakhsh M, Yu L, Yue A, Zhang H, Zhao Y, Ziegler SM, Zielinski C, Zimmermann J, Zychlinsky A. **Guidelines for the use of flow cytometry and cell sorting in immunological studies (second edition).** European Journal of Immunology. 2019; 49(10): 1457-1973. *IF: 4.695 (2018)*

Dimitrov KM, Abolnik C, Afonso CL, Albina E, Bahl J, Berg M, Briand FX, Brown IH, Choi KS, Chvala I, Diel DG, Durr PA, Ferreira HL, Fusaro A, Gil P, Goujgoulova GV, Grund C, Hicks JT, Joannis TM, Torchetti MK, Kolosov S, Lambrecht B, Lewis NS, Liu H, Liu H, McCullough S, Miller PJ, Monne I, Muller CP, Munir M, Reischak D, Sabra M, Samal SK, Servan de Almeida R, Shittu I, Snoeck CJ, Suarez DL, Van Borm S, Wang Z, Wong FYK. **Updated unified phylogenetic classification system and revised nomenclature for Newcastle disease virus.** Infection, Genetics and Evolution. 2019; 74: 103917. Epub 2019 Jun 11. *IF: 2.611 (2018)*

Zimmer J. **Alessandro Moretta and Transporter associated with Antigen Processing (TAP) deficiency: on Giant's shoulders.** Frontiers in Immunology. 2019; 10: 2404. *IF: 4.716 (2018)*

Medic S, Petrovic V, Loncarevic G, Kanazir M, Begovic Lazarevic I, Rakic Adrovic S, Bancevic M, Muller CP, Hubschen JM. **Epidemiological, clinical and laboratory characteristics of the measles resurgence in the Republic of Serbia in 2014-2015.** PLoS One. 2019; 14(10): e0224009. *IF: 2.776 (2018)*

Kirschner S. **Epigenetic consequences of early-life infection in a mouse model (Doctoral thesis)**. Trier: University of Trier, 2019. 195 p.

Klueber J, Schrama D, Rodrigues P, Dickel H, Kuehn A. **Fish allergy management: from component-resolved diagnosis to unmet diagnostic needs.** Current Treatment Options in Allergy. 2019; 6(4): 322-337. *IF: NA (2018)*

Bachmann P, Finke JB, Rebeck D, Zhang X, Larra MF, Koch KP, Turner JD, Schachinger H. **Test-retest reproducibility of a combined physical and cognitive stressor.** Biological Psychology. 2019; 148: 107729. Epub 2019 Jul 29. *IF: 2.627 (2018)*

Pauly M, Sayasinh K, Muller CP, Sayasone S, Black AP. **High prevalence of helminth infections in mother-child pairs from three central provinces of Lao People's Democratic Republic.** Parasite Epidemiology and Control. 2019; 7: e00122. *IF: NA (2018)*

Wouters E, Walraed J, Robertson MJ, Meyrath M, Szpakowska M, Chevigné A, Skiniotis G, Stove C. **Assessment of biased agonism among distinct synthetic cannabinoid receptor agonist scaffolds.** ACS Pharmacology & Translational Science. 2019. In Press. *IF: NA (2018)*

Chan SK, Pomes A, Hilger C, Davies JM, Mueller G, Kuehn A, Lopata AL, Gadermaier G, van Hage M, Raulf M, Goodman RE. **Keeping allergen names clear and defined.** Frontiers in Immunology. 2019; 10: 2600. *IF: 4.716 (2018)*

Hefele L, Syphan S, Xayavong D, Homsana A, Kleine D, Chanthavilay P, Nouanthong P, Xaydalasouk K, Phathammavong O, Billamay S, Xeuatvongsa A, Reinharz D, Muller CP, Black AP. **Seroprotection at different levels of the health care system after routine vaccination with Diphtheria-Tetanus-Pertussis whole cell-Hepatitis B-Haemophilus influenzae Type B in Lao People's Democratic Republic.** Clinical Infectious Diseases. 2019; 69(12): 2136-2144. *IF: 9.055 (2018)*

Berndt N, Devaux C, Seixas R. **Combattre l'hépatite C chez les usagers de drogues injectables au Luxembourg : illustration d'une approche intersectorielle.** Addiction(s) : recherches et pratiques. 2019; (4): 22-25. *IF: NA (2018)*

Bilo MB, Ollert M, Blank S. **The role of component-resolved diagnosis in Hymenoptera venom allergy.** Current Opinion in Allergy and Clinical Immunology. 2019; 19(6): 614-622. *IF: 3.014 (2018)*

Le Goff M, Lagadic-Gossmann D, Latour R, Podechard N, Grova N, Gauffre F, Chevance S, Burel A, Appenzeller BMR, Ulmann L, Sergent O, Le Ferrec E. **PAHs increase the production of extracellular vesicles both in vitro in endothelial cells and in vivo in urines from rats.** Environmental pollution. 2019; 255(Pt 1): 113171. Epub 2019 Sep 10. *IF: 5.714 (2018)*

Pauly M, Snoeck CJ, Phoutana V, Keosengthong A, Sausy A, Khenkha L, Nouanthong P, Samountry B, Jutavijittum P, Vilivong K, Hubschen JM, Black AP, Pommasichan S, Muller CP. **Cross-species transmission of poultry pathogens in backyard farms: ducks as carriers of chicken viruses.** Avian Pathology. 2019; 48(6): 503-511. Epub 2019 Jul 24. *IF: 1.961 (2018)*

Williams A, Amand M, Van den Bergh R, De Clerck H, Antierens A, Chaillet P. **Ensuring on-site Ebola patient monitoring and follow-up: Development of a laboratory structure embedded in an Ebola treatment center.** Disaster Medicine & Public Health Preparedness. 2019; 13(5-6): 1028-1034. *IF: 1.031 (2018)*

Vagvolgyi M, Girst G, Kusz N, Otvos SB, Fulop F, Hohmann J, Servais JY, Seguin-Devaux C, Chang FR, Chen MS, Chang LK, Hunyadi A. **Less cytotoxic protoflavones as antiviral agents: Protoapigenone 1'-O-isopropyl Ether shows improved selectivity against the Epstein-Barr Virus lytic cycle.** International Journal of Molecular Sciences. 2019; 20(24): 6269. *IF: 4.183 (2018)*

Maltezou HC, Botelho-Nevers E, Brantsaeter AB, Carlsson RM, Heininger U, Hubschen JM, Josefsdottir KS, Kassianos G, Kyncl J, Ledda C, Medic S, Nitsch-Osuch A, de Lejarazu RO, Theodoridou M, Van Damme P, van Essen GA, Wicker S, Wiedermann U, Poland GA, Vaccination Policies for H.C P in Europe Study Group. **Vaccination of healthcare personnel in Europe: Update to current policies.** Vaccine. 2019; 37(52): 7584. Epub 2019 Oct 14. *IF: 3.269 (2018)*

Redegeld F, Hermann K, Ollert M, Ring J. **Antibody Detection.** In *Nijkamp and Parnham's Principles of Immunopharmacology*. Fourth revised and extended ed. Parnham MJ, Nijkamp FP and Rossi AG, eds. Cham: Springer International Publishing, 2019. p.233-241.

Luckel C, Picard F, Raifer H, Campos Carrascosa L, Guralnik A, Zhang Y, Klein M, Bittner S, Steffen F, Moos S, Marini F, Gloury R, Kurschus FC, Chao YY, Bertrams W, Sexl V, Schmeck B, Bonetti L, Grusdat M, Lohoff M, Zielinski CE, Zipp F, Kallies A, Brenner D, Berger M, Bopp T, Tackenberg B, Huber M. **IL-17(+) CD8(+) T cell suppression by dimethyl fumarate associates with clinical response in multiple sclerosis.** Nat Commun. 2019; 10(1): 5722. *IF: 11.878 (2018)*

Klueber J, Costa J, Randow S, Codreanu-Morel F, Verhoeckx K, Bindslev-Jensen C, Ollert M, Hoffmann-Sommergruber K, Morisset M, Holzhauser T, Kuehn A. **Homologous tropomyosins from vertebrate and invertebrate: Recombinant calibrator proteins in functional biological assays for tropomyosin allergenicity assessment of novel animal foods.** Clinical and Experimental Allergy. 2020; 50(1): 105-106. Epub 2019 Oct 11. *IF: 4.741 (2018)*

Zhuang Y, Xu HC, Shinde PV, Warfsmann J, Vasilevska J, Sundaram B, Behnke K, Huang J, Hoell JI, Borkhardt A, Pfeffer K, Taha MS, Herebian D, Mayatepek E, Brenner D, Ahmadian MR, Keitel V, Wieczorek D, Haussinger D, Pandyra AA, Lang KS, Lang PA. **Fragile X mental retardation protein protects against tumour necrosis factor-mediated cell death and liver injury.** Gut. 2020; 69(1): 133-145. Epub 2019 Aug 13. *IF: 17.943 (2018)*

Adam O, Musa A, Kamer A, Sausy A, Tisserand E, Hubschen JM. **Seroprevalence of measles, mumps, and rubella and genetic characterization of mumps virus in Khartoum, Sudan.** International Journal of Infectious Diseases. 2020; 91: 87-93. Epub 2019 Nov 20. *IF: 3.538 (2018)*

De Magalhaes CR, Schrama D, Fonseca F, Kuehn A, Morisset M, Ferreira SR, Goncalves A, Rodrigues PM. **Effect of EDTA enriched diets on farmed fish allergenicity and muscle quality; a proteomics approach.** Food Chemistry. 2020; 305: 125508. Epub 2019 Sep 11. *IF: 5.399 (2018)*

DEPARTMENT OF ONCOLOGY

Walner H, Bartoš M, Mangová M, Keunen O, Bjerkvig R, Jiřík R, Šorel M. **Iterative methods for fast reconstruction of undersampled dynamic contrast-enhanced MRI data.** In *World Congress on Medical Physics and Biomedical Engineering 2018*. Ibbott GS, Lhotska L, Sukupova L and Lackovic I, eds. Singapore: Springer Verlag, 2019. p.267-271. (IFMBE, Vol. 68, N°1).

Wierz M, Pierson S, Gargiulo E, Guerin C, Moussay E, Paggetti J. **Purification of leukemia-derived exosomes to study microenvironment modulation.** Methods in Molecular Biology. 2019; 1884: 231-245. *IF: NA (2018)*

Kindt N, Descamps G, Lechien JR, Remmelink M, Colet JM, Wattiez R, Berchem G, Journe F, Saussez S. **Involvement of HPV infection in the release of macrophage migration Inhibitory factor in head and neck squamous cell carcinoma.** Journal of Clinical Medicine. 2019; 8(1). *IF: 5.688 (2018)*

Sulheim E, Morch Y, Snipstad S, Borgos SE, Miletic H, Bjerkvig R, Davies CL, Aslund AKO. **Therapeutic effect of cabazitaxel and blood-brain barrier opening in a patient-derived glioblastoma model.** Nanotheranostics. 2019; 3(1): 103-112. *IF: NA (2018)*

Bjerkvig R, Thorsen F. **Glioblastoma: a prognostic value of AMT-PET?** Neuro-Oncology. 2019; 21(2): 146-147. *IF: 10.091(2018)*

Koelsche C, Stichel D, Griewank KG, Schrimpf D, Reuss DE, Bewerunge-Hudler M, Vokuhl C, Dinjens WNM, Petersen I, Mittelbronn M, Cuevas-Bourdier A, Buslei R, Pfister SM, Flucke U, Mechtersheimer G, Mentzel T, von Deimling A. **Genome-wide methylation profiling and copy number analysis in atypical fibroxanthomas and pleomorphic dermal sarcomas indicate a similar molecular phenotype.** Clinical Sarcoma Research. 2019; 9: 2. *IF: NA (2018)*

Buus-Gehrig C, Lehrnbecher T, Porto L, Becker M, Freiman T, Mittelbronn M, Bochennek K. **Pontine tumor in a neonate: case report and analysis of the current literature.** Journal of Neurosurgery. Pediatrics. 2019; 23(5): 606-612. [Epub ahead of print]. *IF: NA (2018)*

Eisemann T, Costa B, Harter PN, Wick W, Mittelbronn M, Angel P, Peterziel H. **Podoplanin expression is a prognostic biomarker but may be dispensable for the malignancy of glioblastoma.** Neuro-Oncology. 2019; 21(3): 326-336. *IF: 10.091(2018)*

Sharma AB, Dimitrov S, Hamiche A, Van Dyck E. **Centromeric and ectopic assembly of CENP-A chromatin in health and cancer: old marks and new tracks.** Nucleic Acids Research. 2019; 47(3): 1051-1069. *IF: 11.147 (2018)*

Foltyn M, Luger AL, Lorenz NI, Sauer B, Mittelbronn M, Harter PN, Steinbach JP, Ronellenfitsch MW. **The physiological mTOR complex 1 inhibitor DDIT4 mediates therapy resistance in glioblastoma.** British Journal of Cancer. 2019; 120(5): 481-487. Epub 2019 Feb 12. *IF: 5.416 (2018)*

Daubon T, Leon C, Clarke K, Andrique L, Salabert L, Darbo E, Pineau R, Guerit S, Maitre M, Dedieu S, Jeanne A, Bailly S, Feige JJ, Miletic H, Rossi M, Bello L, Falciani F, Bjerkvig R, Bikfalvi A. **Deciphering the complex role of thrombospondin-1 in glioblastoma development.** Nature Communications. 2019; 10(1): 1146. *IF: 11.878 (2018)*

Linder B, Weirauch U, Ewe A, Uhmann A, Seifert V, Mittelbronn M, Harter PN, Aigner A, Kogel D. **Therapeutic targeting of Stat3 using lipopolyplex nanoparticle-formulated siRNA in a syngeneic orthotopic mouse glioma model.** Cancers. 2019; 11(3). *IF: 6.162 (2018)*

Gobin M. **Targeted DNA repair gene expression study in glioblastoma patient biopsies: clinical impact and characterisation of the NEIL3 DNA glycosylase, a novel candidate target for therapy (Doctoral thesis)**. Luxembourg: Université de Luxembourg 2019. 156 p.

Gobin M, Nazarov PV, Warta R, Timmer M, Reifenberger G, Felsberg J, Vallar L, Chalmers AJ, Herold-Mende CC, Goldbrunner R, Niclou SP, Van Dyck E. **A DNA repair and cell-cycle gene expression signature in primary and recurrent glioblastoma: prognostic value and clinical implications.** Cancer Research. 2019; 79(6): 1226-1238. Epub 2019 Jan 23. *IF: 8.378 (2018)*

Wurzer H, Al Absi A, Hoffmann C, Thomas C. **Do tumor cells escape from natural killer cell cytotoxicity by mimicking dendritic cells?** Oncotarget. 2019; 10(25): 2419-2420. *IF: 5.168 (2016), IF 2018 not yet available*

Nesseler JP, Schaue D, McBride WH, Lee MH, Kaprealian T, Niclou SP, Nickers P. **Irradiation to improve the response to immunotherapeutic agents in glioblastomas.** Advances in Radiation Oncology. 2019; 4(2): 268-282. *IF: NA (2018)*

Sundstrom T, Prestegarden L, Azuaje F, Aasen SN, Rosland GV, Varughese JK, Bahador M, Bernatz S, Braun Y, Harter PN, Skaftnesmo KO, Ingham ES, Mahakian LM, Tam S, Tepper CG, Petersen K, Ferrara KW, Tronstad KJ, Lund-Johansen M, Beschorner R, Bjerkvig R, Thorsen F. **Inhibition of mitochondrial respiration prevents BRAF-mutant melanoma brain metastasis.** Acta Neuropathologica Communications. 2019; 7(1): 55. *IF: 5.883 (2018)*

Dirkse A, Golebiewska A, Buder T, Nazarov PV, Muller A, Poovathingal S, Brons NHC, Leite S, Sauvageot N, Sarkisjan D, Seyfrid M, Fritah S, Stieber D, Michelucci A, Hertel F, Herold-Mende C, Azuaje F, Skupin A, Bjerkvig R, Deutsch A, Voss-Bohme A, Niclou SP. **Stem cell-associated heterogeneity in Glioblastoma results from intrinsic tumor plasticity shaped by the microenvironment.** Nature Communications. 2019; 10(1): 1787. *IF: 11.878 (2018)*

Mastrella G, Hou M, Li M, Stoecklein VM, Zdouc N, Volmar MNM, Miletic H, Reinhard S, Herold-Mende CC, Kleber S, Eisenhut K, Gargiulo G, Synowitz M, Vescovi AL, Harter PN, Penninger JM, Wagner E, Mittelbronn M, Bjerkvig R, Hambardzumyan D, Schuller U, Tonn JC, Radke J, Glass R, Kalin RE. **Targeting APLN/APLNR improves anti-angiogenic efficiency and blunts pro-invasive side effects of VEGFA/VEGFR2-blockade in glioblastoma.** Cancer Research. 2019; 29(9): 2298-2313. Epub 2019 Feb 4. *IF: 8.378 (2018)*

Largeot A, Pagano G, Gonder S, Moussay E, Paggetti J. **The B-side of Cancer Immunity: The Underrated Tune.** Cells. 2019; 8(5): pii: E449. *IF: 5.656 (2018)*

Wurzer H, Hoffmann C, Al Absi A, Thomas C. **Actin cytoskeleton straddling the immunological synapse between cytotoxic lymphocytes and cancer cells.** Cells. 2019; 8(5). *IF: 5.656 (2018)*

Gargiulo E, Paggetti J, Moussay E. **Hematological malignancy-derived small extracellular vesicles and tumor microenvironment: The art of turning foes into friends.** Cells. 2019; 8(5): pii: E511. *IF: 5.656 (2018)*

Exner ND, Valenzuela JAC, Abou-El-Ardat K, Miletic H, Huszthy PC, Radehaus PM, Schrock E, Bjerkvig R, Kaderali L, Klink B, Nigro JM. **Deep sequencing of a recurrent oligodendroglioma and the derived xenografts reveals new insights into the evolution of human oligodendroglioma and candidate driver genes.** Oncotarget. 2019; 10(38): 3641-3653. *IF: 5.168 (2016) - IF 2018 not yet available*

Bretscher C, Marchini A. **H-1 Parvovirus as a Cancer-Killing Agent: Past, Present, and Future.** Viruses. 2019; 11(6). *IF: 3.811 (2018)*

Zeiner PS, Preusse C, Golebiewska A, Zinke J, Iriondo A, Muller A, Kaoma T, Filipski K, Muller-Eschner M, Bernatz S, Blank AE, Baumgarten P, Ilina E, Grote A, Hansmann ML, Verhoff MA, Franz K, Feuerhake F, Steinbach JP, Wischhusen J, Stenzel W, Niclou SP, Harter PN, Mittelbronn M. **Distribution and prognostic impact of microglia/macrophage subpopulations in gliomas.** Brain Pathology. 2019; 29(4): 513-529. Epub 2019 Jan 15. *IF: 6.155 (2018)*

Schotterl S, Miemietz JT, Ilina EI, Wirsik NM, Ehrlich I, Gall A, Huber SM, Lentzen H, Mittelbronn M, Naumann U. **Mistletoe-based drugs work in synergy with radio-chemotherapy in the treatment of glioma in vitro and in vivo in glioblastoma bearing mice.** Evidence-Based Complementary and Alternative Medicine. 2019; 2019: 2019/07/30. *IF: 1.984 (2018)*

Pietzke M, Meiser J, Vazquez A. **Formate metabolism in health and disease.** Molecular Metabolism. 2019. In Press. *IF: 6.181 (2018)*

Filipski K, Braun Y, Zinke J, Roller B, Baumgarten P, Wagner M, Senft C, Zeiner PS, Ronellenfitsch MW, Steinbach JP, Plate KH, Gasparoni G, Mittelbronn M, Capper D, Harter PN. **Lack of H3K27 trimethylation is associated with 1p/19q codeletion in diffuse gliomas.** Acta Neuropathologica. 2019; 138(2): 331-334. Epub 2019 May 7. *IF: 18.174 (2018)*

Marchini A, Daeffler L, Pozdeev VI, Angelova A, Rommelaere J. **Immune conversion of tumor microenvironment by oncolytic viruses: the protoparvovirus H-1PV case study.** Frontiers in Immunology. 2019; 10: 1848. *IF: 4.716 (2018)*

Lequeux A, Noman MZ, Xiao M, Sauvage D, Van Moer K, Viry E, Bocci I, Hasmim M, Bosseler M, Berchem G, Janji B. **Impact of hypoxic tumor microenvironment and tumor cell plasticity on the expression of immune checkpoints.** Cancer Letters. 2019; 458: 13-20. Epub 2019 May 25. *IF: 6.508 (2018)*

Aasen SN, Parajuli H, Hoang T, Feng Z, Stokke K, Wang J, Roy K, Bjerkvig R, Knappskog S, Thorsen F. **Effective Treatment of Metastatic Melanoma by Combining MAPK and PI3K Signaling Pathway Inhibitors.** International Journal of Molecular Sciences. 2019; 20(17). *IF: 4.183 (2018)*

Neirinckx V, Hau A-C, Schuster A, Fritah S, Tiemann K, Klein E, Nazarov PV, Matagne A, Szpakowska M, Meyrath M, Chevigné A, Schmidt MHH, Niclou SP. **The soluble form of pan-RTK inhibitor and tumor suppressor LRIG1 mediates downregulation of AXL through direct protein-protein interaction in glioblastoma.** Neuro-oncology Advances. 2019; 1(1). Accepted. *IF: NA (2018)*

Noman MZ, Hasmim M, Lequeux A, Xiao M, Duhem C, Chouaib S, Berchem G, Janji B. **Improving cancer immunotherapy by targeting the hypoxic tumor microenvironment: new opportunities and challenges.** Cells. 2019; 8(9). *IF: 5.656 (2018)*

Daubon T, Guyon J, Raymond A-A, Dartigues B, Rudewicz J, Ezzoukhry Z, Dupuy J-W, Herbert JMJ, Saltel F, Bjerkvig R, Nikolski M, Bikfalvi A. **The invasive proteome of glioblastoma revealed by laser-capture microdissection.** Neuro-Oncology Advances. 2019; 1(1). In press. *IF: NA (2018)*

Gulberti S, Mao X, Bui C, Fournel-Gigleux S. **The role of heparan sulfate maturation in cancer: a focus on the 3O-sulfation and the enigmatic 3O-sulfotransferases (HS3STs).** Seminars in Cancer Biology. 2019. In Press. *IF: 9.658 (2018)*

Baumann C, Tichy J, Schaefer JH, Steinbach JP, Mittelbronn M, Wagner M, Foerch C. **Delay in diagnosing patients with right-sided glioblastoma induced by hemispheric-specific clinical presentation.** Journal of Neuro-Oncology. 2019. [Epub ahead of print]. *IF: I3.129 (2018)*

Braczynski AK, Capper D, Jones DTW, Schittenhelm J, Stichel D, von Deimling A, Harter PN, Mittelbronn M. **High density DNA methylation array is a reliable alternative for PCR-based analysis of the MGMT promoter methylation status in glioblastoma.** Pathology, Research and Practice. 2019: 152728. [Online ahead of print]. *IF: 1.794 (2018)*

Ji J, Xu R, Ding K, Bao G, Zhang X, Huang B, Wang X, Martinez A, Wang X, Li G, Miletic H, Thorsen F, Bjerkvig R, Xiang L, Han B, Chen A, Li X, Wang J. **Long Noncoding RNA SChLAP1 forms a Growth-Promoting Complex with HNRNPL in human glioblastoma through stabilization of ACTN4 and activation of NF-κB signaling.** Clinical Cancer Research. 2019; 25(22): 6868-6881. Epub 2019 Sep 6. *IF: 8.911 (2018)*

Barthel FP, Johnson KC, Varn FS, Moskalik AD, Tanner G, Kocakavuk E, Anderson KJ, Abiola O, Aldape K, Alfaro KD, Alpar D, Amin SB, Ashley DM, Bandopadhayay P, Barnholtz-Sloan JS, Beroukhim R, Bock C, Brastianos PK, Brat DJ, Brodbelt AR, Bruns AF, Bulsara KR, Chakrabarty A, Chakravarti A, Chuang JH, Claus EB, Cochran EJ, Connelly J, Costello JF, Finocchiaro G, Fletcher MN, French PJ, Gan HK, Gilbert MR, Gould PV, Grimmer MR, Iavarone A, Ismail A, Jenkinson MD, Khasraw M, Kim H, Kouwenhoven MCM, LaViolette PS, Li M, Lichter P, Ligon KL, Lowman AK, Malta TM, Mazor T, McDonald KL, Molinaro AM, Nam DH, Nayyar N, Ng HK, Ngan CY, Niclou SP, Niers JM, Noushmehr H, Noorbakhsh J, Ormond DR, Park CK, Poisson LM, Rabadan R, Radlwimmer B, Rao G, Reifenberger G, Sa JK, Schuster M, Shaw BL, Short SC, Smitt PAS, Sloan AE, Smits M, Suzuki H, Tabatabai G, Van Meir EG, Watts C, Weller M, Wesseling P, Westerman BA, Widhalm G, Woehrer A, Yung WKA, Zadeh G, Huse JT, De Groot JF, Stead LF, Verhaak RGW, Glass Consortium. **Longitudinal molecular trajectories of diffuse glioma in adults.** Nature. 2019: 10.1038/s41586-019-1775-1. [Online ahead of print]. *IF: 43.070 (2018)*

Qureshi-Baig K, Kuhn D, Viry E, Pozdeev VI, Schmitz M, Rodriguez F, Ullmann P, Koncina E, Nurmik M, Frasquilho S, Nazarov PV, Zuegel N, Boulmont M, Karapetyan Y, Antunes L, Val D, Mittelbronn M, Janji B, Haan S, Letellier E. **Hypoxia-induced autophagy drives colorectal cancer initiation and progression by activating the PRKC/PKC-EZR (ezrin) pathway.** Autophagy. 2019: 1-17. [Online ahead of print]. *IF: 11.059 (2018)*

Feng Z, Zhou W, Wang J, Qi Q, Han M, Kong Y, Hu Y, Zhang Y, Chen A, Huang B, Chen A, Zhang D, Li W, Zhang Q, Bjerkvig R, Wang J, Thorsen F, Li X. **Reduced expression of proteolipid protein 2 increases ER stress-induced apoptosis and autophagy in glioblastoma.** Journal of Cellular and Molecular Medicine. 2019. [Online ahead of print]. *IF: 4.658 (2018)*

Han M, Wang S, Yang N, Wang X, Zhao W, Saed HS, Daubon T, Huang B, Chen A, Li G, Miletic H, Thorsen F, Bjerkvig R, Li X, Wang J. **Therapeutic implications of altered cholesterol homeostasis mediated by loss of CYP46A1 in human glioblastoma.** EMBO Molecular Medicine. 2019: e10924. [Online ahead of print]. *IF: 10.624 (2018)*

Bartos M, Rajmic P, Sorel M, Mangova M, Keunen O, Jirik R. **Spatially regularized estimation of the tissue homogeneity model parameters in DCE-MRI using proximal minimization.** Magnetic Resonance in Medicine. 2019; 82(6): 2257-2272. Epub 2019 Jul 17. *IF: 3.858 (2018)*

Sen NE, Canet-Pons J, Halbach MV, Arsovic A, Pilatus U, Chae WH, Kaya ZE, Seidel K, Rollmann E, Mittelbronn M, Meierhofer D, De Zeeuw CI, Bosman LWJ, Gispert S, Auburger G. **Generation of an Atxn2-CAG100 knock-in mouse reveals N-acetylaspartate production deficit due to early Nat8l dysregulation.** Neurobiology of Disease. 2019; 132: 104559. Epub 2019 Jul 31. *IF: 5.160 (2018)*

Biedermann J, Preussler M, Conde M, Peitzsch M, Richter S, Wiedemuth R, Abou-El-Ardat K, Kruger A, Meinhardt M, Schackert G, Leenders WP, Herold-Mende C, Niclou SP, Bjerkvig R, Eisenhofer G, Temme A, Seifert M, Kunz-Schughart LA, Schrock E, Klink B. **Mutant IDH1 differently affects redox state and metabolism in glial cells of normal and tumor origin.** Cancers. 2019; 11(12): 2028. *IF: 6.182 (2018)*

Johannessen TA, Bjerkvig R. **A new chance for EGFR inhibition in glioblastoma?** Neuro-Oncology. 2019; 21(12): 1487-1488. *IF: 10.091(2018)*

Han M, Wang S, Fritah S, Wang X, Zhou W, Yang N, Ni S, Huang B, Chen A, Li G, Miletic H, Thorsen F, Bjerkvig R, Li X, Wang J. **Interfering with long non-coding RNA MIR22HG processing inhibits glioblastoma progression through suppression of Wnt/β-catenin signalling.** Brain. 2019. [Online ahead of print]. *IF: 11.814 (2018)*

Gratz R, Brumbarova T, Ivanov R, Trofimov K, Tunnermann L, Ochoa-Fernandez R, Blomeier T, Meiser J, Weidtkamp-Peters S, Zurbriggen MD, Bauer P. **Phospho-mutant activity assays provide evidence for alternative phospho-regulation pathways of the transcription factor FER-LIKE IRON DEFICIENCY-INDUCED TRANSCRIPTION FACTOR.** New Phytologist. 2020; 225(1): 250-267. Epub 2019 Oct 13. *IF: 7.299 (2018)*

Ji J, Ding K, Luo T, Xu R, Zhang X, Huang B, Chen A, Zhang D, Miletic H, Bjerkvig R, Thorsen F, Wang J, Li X. **PMEPA1 isoform a drives progression of glioblastoma by promoting protein degradation of the Hippo pathway kinase LATS1.** Oncogene. 2020; 39(5): 1125-1139. Epub 2019 Oct 11. *IF: 6.634 (2018)*

Wefers AK, Stichel D, Schrimpf D, Coras R, Pages M, Tauziede-Espariat A, Varlet P, Schwarz D, Soylemezoglu F, Pohl U, Pimentel J, Meyer J, Hewer E, Japp A, Joshi A, Reuss DE, Reinhardt A, Sievers P, Casalini MB, Ebrahimi A, Huang K, Koelsche C, Low HL, Rebelo O, Mamoto D, Becker AJ, Staszewski O, Mittelbronn M, Hasselblatt M, Schittenhelm J, Cheesman E, de Oliveira RS, Queiroz RGP, Valera ET, Hans VH, Korshunov A, Olar A, Ligon KL, Pfister SM, Jaunmuktane Z, Brandner S, Tatevossian RG, Ellison DW, Jacques TS, Honavar M, Aronica E, Thom M, Sahm F, von Deimling A, Jones DTW, Blumcke I, Capper D. **Isomorphic diffuse glioma is a morphologically and molecularly distinct tumour entity with recurrent gene fusions of MYBL1 or MYB and a benign disease course.** Acta Neuropathologica. 2020; 139(1): 193-209. Epub 2019 Sep 28. *IF: 18.174 (2018)*

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Bohn T, Desmarchelier C, El SN, Keijer J, van Schothorst E, Ruhl R, Borel P. **beta-Carotene in the human body: metabolic bioactivation pathways - from digestion to tissue distribution and excretion.** The Proceedings of the Nutrition Society. 2019; 78(1): 68-87. *IF: 5.017 (2018)*

Bocquet V, Ruiz-Castell M, de Beaufort C, Barre J, de Rekeneire N, Michel G, Donahue RP, Kuemmerle A, Stranges S. **Public health burden of pre-diabetes and diabetes in Luxembourg: finding from the 2013-2015 European Health Examination Survey.** BMJ Open. 2019; 9(1): e022206. *IF: 2.376 (2018)*

Mouton C, De Girolamo L, Theisen D, Seil R. **How to document a clinical study and avoid common mistakes in study conduct?** In *Basic methods handbook for clinical orthopaedic research: A practical guide and case based research approach*. Musahl V, Karlsson J, Hirschmann MT, Ayeni OR, Marx RG, Koh JL and Nakamura N, eds. Berlin, Heidelberg: Springer, 2019. p.121-132.

Theisen D, Moksnes H, Hardy C, Engebretsen L, Seil R. **How to Organise an International Register in Compliance with the European GDPR: Walking in the Footsteps of the PAMI Project (Paediatric ACL Monitoring Initiative).** In *Basic methods handbook for clinical orthopaedic research: A practical guide and case based research approach*. Musahl V, Karlsson J, Hirschmann MT, Ayeni OR, Marx RG, Koh JL and Nakamura N, eds. Berlin, Heidelberg: Springer, 2019. p.427-434.

Kindermann W, Urhausen A, Scharhag J. **Comment on: Athlete's Heart: Is the Morganroth Hypothesis Obsolete?** Heart, Lung & Circulation. 2019; 28(2): e12-e13. *IF: 2.078 (2018)*

Alkerwi A, Pastore J, Sauvageot N, Coroller GL, Bocquet V, d'Incau M, Aguayo G, Appenzeller B, Bejko D, Bohn T, Malisoux L, Couffignal S, Noppe S, Delagardelle C, Beissel J, Chioti A, Stranges S, Schmit JC. **Challenges and benefits of integrating diverse sampling strategies in the observation of cardiovascular risk factors (ORISCAV-LUX 2) study.** BMC Medical Research Methodology. 2019; 19(1): 27. *IF: 2.509 (2018)*

Djimde M, Samouda H, Jacobs J, Niangaly H, Tekete M, Sombie SB, Mgina EJ, Fofana B, Sagara I, Doumbo OK, Vaillant M, Djimde AA. **Relationship between weight status and anti-malarial drug efficacy and safety in children in Mali.** Malaria Journal. 2019; 18(1): 40. *IF: 2.798 (2018)*

Gao L, Madry H, Chugaev DV, Denti M, Frolov A, Burtsev M, Magnitskaya N, Mukhanov V, Neyret P, Solomin LN, Sorokin E, Staubli AE, Stone KR, Vilenskiy V, Zayats V, Pape D, Korolev A. **Advances in modern osteotomies around the knee : Report on the Association of Sports Traumatology, Arthroscopy, Orthopaedic surgery, Rehabilitation (ASTAOR) Moscow International Osteotomy Congress 2017.** Journal of Experimental Orthopaedics. 2019; 6(1): 9. *IF: NA (2018)*

Seil R. **Why ESSKA? On what it takes for orthopaedic surgeons and their scientific societies to adapt to societal changes in 2018.** Knee Surgery, Sports Traumatology, Arthroscopy. 2019; 27(3): 665-672. Epub 2019 Feb 7. *IF: 3.149 (2018)*

Senn S, Schmitz S, Schritz A, Salah S. **Random main effects of treatment: A case study with a network meta-analysis.** Biometrical journal. 2019; 61(2): 379-390. Epub 2019 Jan 9. *IF: 1.255 (2018)*

Verweij J, Hendriks HR, Zwierzina H, on behalf of the Cancer Drug Development Forum (Collignon O as contributor). **Innovation in oncology clinical trial design.** Cancer Treatment Reviews. 2019; 74: 15-20. Epub 2019 Jan 4. *IF: 8.332 (2018)*

Senn SJ, Lewis RJ. **Treatment effects in multicenter randomized clinical trials.** JAMA. 2019; 321(12): 1211-1212. *IF: 51.273 (2018)*

Gomes CPC, Agg B, Andova A, Arslan S, Baker A, Bartekova M, Beis D, Betsou F, Wettinger SB, Bugarski B, Condorelli G, Silva G, Danilin S, de Gonzalo-Calvo D, Buil A, Carmo-Fonseca M, Enguita FJ, Felekkis K, Ferdinandy P, Gyongyosi M, Hackl M, Karaduzovic-Hadziabdic K, Hellemans J, Heymans S, Hlavackova M, Hoydal MA, Jankovic A, Jusic A, Kardassis D, Kerkela R, Kuster GM, Lakkisto P, Leszek P, Lustrek M, Maegdefessel L, Martelli F, Novella S, O'Brien T, Papaneophytou C, Pedrazzini T, Pinet F, Popescu O, Potocnjak I, Robinson E, Sasson S, Scholz M, Simionescu M, Stoll M, Varga ZV, Vinciguerra M, Xuereb A, Yilmaz MB, Emanueli C, Devaux Y, On Behalf Of The Eu-CardioRN A. Cost Action (CA17129). **Catalyzing transcriptomics research in cardiovascular disease: The CardioRNA COST Action CA17129.** Non-coding RNA. 2019; 5(2). *IF: NA (2018)*

Brodkorb A, Egger L, Alminger M, Alvito P, Assuncao R, Ballance S, Bohn T, Bourlieu-Lacanal C, Boutrou R, Carriere F, Clemente A, Corredig M, Dupont D, Dufour C, Edwards C, Golding M, Karakaya S, Kirkhus B, Le Feunteun S, Lesmes U, Macierzanka A, Mackie AR, Martins C, Marze S, McClements DJ, Menard O, Minekus M, Portmann R, Santos CN, Souchon I, Singh RP, Vegarud GE, Wickham MSJ, Weitschies W, Recio I. **INFOGEST static in vitro simulation of gastrointestinal food digestion.** Nature Protocols. 2019; 14(4): 991-1014. Epub 2019 Mar 18. *IF: 11.334 (2018)*

McDermott I, Checkland K, Moran V, Warwick-Giles L. **Achieving integrated care through commissioning of primary care services in the English NHS: a qualitative analysis.** BMJ open. 2019; 9(4): e027622. *IF: 2.376 (2018)*

Kofi Amegah A, Brahuah E, Stranges S. **Cooking with shea butter is associated with lower blood pressure in the Ghanaian population.** International Journal for Vitamin and Nutrition Research. 2019: 1-11. [Epub ahead of print]. *IF: 0.593 (2018)*

Mobarra N, Morovatdar N, Di Napoli M, Stranges S, Behrouz R, Amiri A, Farzadfard MT, Hashemy SI, Oskoii R, Khorram B, Azarpazhooh MR. **The association between inflammatory markers in the acute phase of stroke and long-term stroke outcomes: evidence from a population-based study of stroke.** Neuroepidemiology. 2019; 53(1-2): 20-26. Epub 2019 Apr 16. *IF: 2.689 (2018)*

Morovatdar N, Thrift AG, Stranges S, Kapral M, Behrouz R, Amiri A, Heshmati A, Ghahremani A, Farzadfard MT, Mokhber N, Azarpazhooh MR. **Socioeconomic status and long-term stroke mortality, recurrence and disability in Iran: The Mashhad stroke incidence study.** Neuroepidemiology. 2019; 53(1-2): 27-31. Epub 2019 Apr 16. *IF: 2.689 (2018)*

Warwick-Giles L, McDermott I, Checkland K, Moran V. **Moving towards strategic commissioning: impact on clinical commissioning groups as membership organizations.** Journal of Health Services Research & Policy. 2020; 25(1): 22-29. Epub 2019 Apr 16. *IF: 2.303 (2018)*

Makovski TT, Schmitz S, Zeegers MP, Stranges S, van den Akker M. **Multimorbidity and quality of life: systematic literature review and meta-analysis.** Ageing Research Reviews. 2019; 53: 100903. *IF: 10.390 (2018)*

Andrade R, Rebelo-Marques A, Bastos R, Zaffagnini S, Seil R, Ayeni OR, Espregueira-Mendes J. **Identification of normal and injured anterolateral ligaments of the knee: a systematic review of magnetic resonance imaging studies.** Arthroscopy. 2019; 35(5): 1594-1613 e1. Epub 2019 Apr 15. *IF: 4.433 (2018)*

Edwards J, Anderson KK, Stranges S. **Migrant mental health, Hickam's dictum, and the dangers of oversimplification.** International Journal of Public Health. 2019; 64(4): 477-478. Epub 2019 Jan 11. *IF: 2.373 (2018)*

NCD Risk Factor Collaboration (Alkerwi A as collaborator for the NCD-RisC). **Rising rural body-mass index is the main driver of the global obesity epidemic in adults.** Nature. 2019; 569(7755): 260-264. Epub 2019 May 8. *IF: 43.070 (2018)*

Huiart L, Schmitz S, Swinnen H. **Luxembourg.** In *Healthcare in Europe 2019: The finance and reimbursement systems of 11 European countries*. 4th ed. van Kemenade YW, ed. Amsterdam: EIT Health, 2019. p.97-110.

Palazzi P, Hardy EM, Appenzeller BMR. **Biomonitoring of children exposure to urban pollution and environmental tobacco smoke with hair analysis - A pilot study on children living in Paris and Yeu Island, France.** Science of The Total Environment. 2019; 665: 864-872. Epub 2019 Feb 13. *IF: 5.589 (2018)*

Hu XF, Stranges S, Chan LHM. **Circulating selenium concentration is inversely associated with the prevalence of stroke: results from the canadian health measures survey and the national health and nutrition examination survey.** Journal of the American Heart Association. 2019; 8(10): e012290. *IF: 4.660 (2018)*

Almeida JA, Motta-Santos D, Petriz BA, Gomes C, Nogueira ME, Pereira RW, Araujo RC, Prestes J, Franco OL. **High-intensity aerobic training lowers blood pressure and modulates the renal renin-angiotensin system in spontaneously hypertensive rats.** Clinical and Experimental Hypertension. 2020; 42(3): 233-238. Epub 2019 May 23. *IF: 1.522 (2018)*

Andreadou I, Cabrera-Fuentes HA, Devaux Y, Frangogiannis NG, Frantz S, Guzik T, Liehn E, Gomes CPC, Schulz R, Hausenloy DJ. **Immune cells as targets for cardioprotection: New players and novel therapeutic opportunities.** Cardiovascular Research. 2019; 115(7): 1117-1130. *IF: 7.014 (2018)*

Ardern CL, Ekås G, Grindem H, Moksnes H, Anderson A, Chotel F, Cohen M, Forssblad M, Ganley TJ, Feller JA, Karlsson J, Kocher MS, LaPrade RF, McNamee M, Mandelbaum B, Micheli L, Mohtadi NGH, Reider B, Roe JP, Seil R, Siebold R, Silvers-Granelli HJ, Soligard T, Witvrouw E, Engebretsen L. **2018 International Olympic Committee consensus statement.** Sports Orthopaedics and Traumatology. 2019; 35(2): 98-122. *IF: NA (2018)*

Brockmeyer M, Orth P, Hofer D, Seil R, Paulsen F, Menger MD, Kohn D, Tschernig T. **The anatomy of the anterolateral structures of the knee - A histologic and macroscopic approach.** The Knee. 2019; 26(3): 636-646. Epub 2019 Mar 23. *IF: 1.762 (2018)*

Kelemen G, Gravrila-Ardelean M, Hanon C, Vasseur-Bacle S, Deloyer J, Maes C, Hustinx N, Moraitou M, Tzanakis E, Tournier I, Ernens I. **Inclusion and diversity in social work. necessary directions for the development of social networks for elderly people with mental health problems. ARPA project.** Journal Plus Education. 2019; 23(SP IS): 157-163. *IF: NA (2018)*

Boileau A, Somoza AS, Dankiewicz J, Stammet P, Gilje P, Erlinge D, Hassager C, Wise MP, Kuiper M, Friberg H, Nielsen N, Devaux Y, TTM-Trial Investigators on behalf of Cardiolinc Network. **Circulating Levels of miR-574-5p Are Associated with Neurological Outcome after Cardiac Arrest in Women: A Target Temperature Management (TTM) Trial Substudy.** Disease Markers. 2019; 2019: 1802879. *IF: 2.761 (2018)*

Rekow-Fond L, Gavrila-Ardelean M, Gavrila-Ardelean L, Fond-Harmant L. **For scientific ethics: Interview with people whose opinions are not usually taken into consideration: crossed viewpoints.** Agora Psycho-Pragmatica. 2019; 1(1): 135-146. *IF: NA (2018)*

Bohn T. **Carotenoids and markers of oxidative stress in human observational studies and intervention trials: Implications for chronic diseases.** Antioxidants. 2019; 8(6). *IF: 4.520 (2018)*

Schmitt H, Stotter C, Nehrer S, Seil R. **Autologe osteochondrate Transplantation.** In *Knorpel und Arthrose im Sport*. Nehrer S, Valderrabano V and Engelhardt M, eds. Verlag Vopelius Bernd Rolle e.K, 2019. p.77-82.

Seil R, Chiari C, Volderrabano V, Ezechieli M, Stotter C, Nehrer S. **Klinische Aspekte und Risikofaktoren des Knorpelschadens.** In *Knorpel und Arthrose im Sport*. Nehrer S, Valderrabano V and Engelhardt M, eds. Verlag Vopelius Bernd Rolle e.K, 2019. p.17-24.

Andersen V, Halekoh U, Bohn T, Tjonneland A, Vogel U, Kopp TI. **No No Interaction between polymorphisms related to vitamin A metabolism and vitamin A Intake in relation to colorectal cancer in a prospective Danish cohort.** Nutrients. 2019; 11(6). *IF: 4.171 (2018)*

Mouton C, Magosch A, Pape D, Hoffmann A, Nuhrenborger C, Seil R. **Ramp lesions of the medial meniscus are associated with a higher grade of dynamic rotatory laxity in ACL-injured patients in comparison to patients with an isolated injury.** Knee Surgery, Sports Traumatology, Arthroscopy. 2019. [Epub ahead of print]. *IF: 3.149 (2018)*

Beaney T, Burrell LM, Castillo RR, Charchar FJ, Cro S, Damasceno A, Kruger R, Nilsson PM, Prabhakaran D, Ramirez AJ, Schlaich MP, Schutte AE, Tomaszewski M, Touyz R, Wang JG, Weber MA, Poulter NR, M. M. M. Investigators (Calmes J. Alkerwi A. and Gantenbein M. as investigators). **May Measurement Month 2018: a pragmatic global screening campaign to raise awareness of blood pressure by the International Society of Hypertension.** European Heart Journal. 2019; 40(25): 2006-2017. *IF: 23.239 (2018)*

Bohn T. **Determinants and Determination of Carotenoid Bioavailability from Infant Food Formulas and Adult Nutritionals Including Liquid Dairy Products.** Journal of AOAC International. 2019; 102(4): 1044-1058. Epub 2019 Feb 20. *IF: 1.201 (2018)*

Gewandter JS, McDermott MP, He H, Gao S, Cai X, Farrar JT, Katz NP, Markman JD, Senn S, Turk DC, Dworkin RH. **Demonstrating heterogeneity of treatment effects among patients: an overlooked but important step toward precision medicine.** Clinical Pharmacology and Therapeutics. 2019; 106(1): 204-210. Epub 2019 Mar 12. *IF: 6.336 (2018)*

Olliaro PL, Vaillant M. **Designing noninferiority tuberculosis treatment trials: Identifying practical advantages for drug regimens with acceptable effectiveness.** PLoS Medicine. 2019; 16(7): e1002850. *IF: 11.048 (2018)*

Ouattara SM, Ouédraogo A, Tiono AB, Sombié B, Diarra A, Ouédraogo IN, Vaillant M, Sirima SB. **Seasonal Depiction of Malariometric Indices in Children under Five Years in a Sudanese Semi-urban Area of Burkina Faso.** International Journal of Tropical Disease & Health. 2019; 37(2): 1-12. *IF: NA (2018)*

Cucchi D, Mouton C, Dor J, Seil R. **Case 1: Pediatric ACL tear.** In *Knee arthroscopy: A case repository*. Tapasvi S and Shekhar A, eds. London: Jp Medical Ltd, 2019. p.3-11.

Andrade R, Rebelo-Marques A, Bastos R, Zaffagnini S, Seil R, Ayeni OR, Espregueira-Mendes J. **Author Reply to "Regarding 'Identification of Normal and Injured Anterolateral Ligaments of the Knee: A Systematic Review of Magnetic Resonance Imaging Studies".** Arthroscopy. 2019; 35(8): 2258-2260. *IF: 4.433 (2018)*

Lalem T, Devaux Y. **Circulating microRNAs to predict heart failure after acute myocardial infarction in women.** Clinical Biochemistry. 2019; 70: 1-7. Epub 2019 May 24. *IF: 2.430 (2018)*

Lion A, Vuillemin A, Thornton JS, Theisen D, Stranges S, Ward M. **Physical activity promotion in primary care: a Utopian quest?** Health Promotion International. 2019; 34(4): 877-886. *IF: 1.913 (2018)*

Seil R, Cucchi D, Ninulescu C, Dor J, Mouton C. **Anatomic anterior cruciate ligament reconstruction for adolescent patients with open physis.** Annals of Joint. 2019; 4: 31-31. *IF: NA (2018)*

Boileau A, Lino Cardenas CL, Courtois A, Zhang L, Rodosthenous RS, Das S, Sakalihasan N, Michel JB, Lindsay ME, Devaux Y. **MiR-574-5p: A Circulating Marker of Thoracic Aortic Aneurysm.** International Journal of Molecular Sciences. 2019; 20(16). *IF: 4.183 (2018)*

Ruiz-Castell M, Makovski TT, Bocquet V, Stranges S. **Sleep duration and multimorbidity in Luxembourg: results from the European Health Examination Survey in Luxembourg, 2013-2015.** BMJ Open. 2019; 9(8): e026942. *IF: 2.376 (2018)*

Lugano G, Gianola S, Castellini G, Banfi G, Seil R, Denti M, de Girolamo L. **Evidence-Based Medicine (EBM) is properly perceived but its application is still limited in the orthopedic clinical practice: an online survey among the European Society of Sports Traumatology, Knee Surgery and Arthroscopy (ESSKA) members.** Knee Surgery, Sports Traumatology, Arthroscopy. 2019. [Epub ahead of print]. *IF: 3.149 (2018)*

Seil R, Mouton C, Schuster P, Raoulis VA, Hoffmann A, Pape D, Ollivier M. **[Solutions for complications after knee osteotomies].** Arthroskopie. 2019; 32(5): 345-352. *IF: NA (2018)*

Dumas G, Tan H, Dumas L, Perrin P, Lion A, Schmerber S. **Skull vibration induced nystagmus in patients with superior semicircular canal dehiscence.** European Annals of Otorhinolaryngology, Head and Neck Diseases. 2019; (4): 263-272. Epub 2019 Apr 25. *IF: 1.318 (2018)*

Edwards J, Hu M, Thind A, Stranges S, Chiu M, Anderson KK. **Gaps in understanding of the epidemiology of mood and anxiety disorders among migrant groups in Canada: A systematic review.** The Canadian Journal of Psychiatry. 2019; 64(9): 595-606. Epub 2019 May 26. *IF: 4.080 (2018)*

Iddir M, Degerli C, Dingeo G, Desmarchelier C, Schleeh T, Borel P, Larondelle Y, Bohn T. **Whey protein isolate modulates beta-carotene bioaccessibility depending on gastro-intestinal digestion conditions.** Food Chemistry. 2019; 291: 157-166. Epub 2019 Apr 1. *IF: 5.399 (2018)*

Jusic A, Devaux Y, EU-CardioRNA COST Action (CA17129). **Noncoding RNAs in hypertension.** Hypertension. 2019; 74(3): 477-492. Epub 2019 Jul 29. *IF: 7.017 (2018)*

Macovei M, Schritz A, Majery N, RADERMECKER R, Rusu D. **Occupational medicine type 2 diabetes screening in Luxembourg.** Diabetes Updates. 2019; 5(3): 1-5. *IF: NA (2018)*

Nicholson K, Makovski TT, Stranges S. **The integration of primary care and public health to improve population health: tackling the complex issue of multimorbidity.** International Journal of Public Health. 2019; 64(7): 983-984. Epub 2019 Jul 4. *IF: 2.373 (2018)*

Seil R, Hirschmann MT. **[Better Results through open and honest Handling of Complications].** Arthroskopie. 2019; 32(5): 307-307. *IF: NA (2018)*

Naudin G, Bastien P, Mezzache S, Trehu E, Bourokba N, Appenzeller BMR, Soeur J, Bornschlogl T. **Human pollution exposure correlates with accelerated ultrastructural degradation of hair fibers.** Proceedings of the National Academy of Sciences of the United States of America. 2019; 116(37): 18410-18415. Epub 2019 Aug 26. *IF: 9.580 (2018)*

Cortes J, Gonzalez JA, Medina MN, Vogler M, Vilaro M, Elmore M, Senn SJ, Campbell M, Cobo E. **Does evidence support the high expectations placed in precision medicine? A bibliographic review.** F1000 Research. 2019; 7: 30. [Epub ahead of print]. *IF: NA (2018)*

Aguayo GA, Hulman A, Vaillant MT, Donneau AF, Schritz A, Stranges S, Malisoux L, Huiart L, Guillaume M, Sabia S, Witte DR. **Prospective association among diabetes diagnosis, HbA1c, glycemia and frailty trajectories in an elderly population.** Diabetes Care. 2019; 42(10): 1903-1911. Epub 2019 Aug 26. *IF: 15.270 (2018)*

Chata C, Palazzi P, Grova N, Haan S, Emond C, Vaillant M, Appenzeller BMR. **Blood pharmacokinetic of 17 common pesticides in mixture following a single oral exposure in rats: implications for human biomonitoring and exposure assessment.** Archives of Toxicology. 2019; 93(10): 2849-2862. Epub 2019 Aug 19. *IF: 5.741 (2018)*

Seil R, Chotel F, Robert H. **Collaborative efforts are needed to gain new knowledge on pediatric and adolescent Anterior Cruciate Ligament (ACL) injuries.** Orthopaedics & Traumatology: Surgery & Research. 2019; 105(6): 1033-1035. Epub 2019 Jul 30. *IF: 1.572 (2018)*

Berkan O, Arslan S, Lalem T, Zhang L, Sahin NO, Aydemir EI, Korkmaz O, Egilmez HR, Cekin N, Devaux Y. **Regulation of microRNAs in coronary atherosclerotic plaque.** Epigenomics. 2019; 11(12): 1387-1397. Epub 2019 Oct 9. *IF: 4.404 (2018)*

Collignon O, Schritz A, Senn SJ, Spezia R. **Clustered allocation as a way of understanding historical controls: Components of variation and regulatory considerations.** Statistical Methods in Medical Research. 2019: 962280219880213. [Epub ahead of print]. *IF: 2.388 (2018)*

Avan A, Digaleh H, Di Napoli M, Stranges S, Behrouz R, Shojaeianbabaei G, Amiri A, Tabrizi R, Mokhber N, Spence JD, Azarpazhooh MR. **Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: an ecological analysis from the Global Burden of Disease Study 2017.** BMC Medicine. 2019; 17(1): 191. *IF: 8.285 (2018)*

Tournier I, Hanon C, Vasseur-Bacle S, Deloyer J, Moraitou M, Tzanakis E, Gravrila-ardelean M, Kelemen G, Fond-Harmant L. **Mental health care networks in older adults: A narrative review.** Journal Plus Education. 2019; 25(2): 179-187. *IF: NA (2018)*

Bernatz S, Ilina EI, Devraj K, Harter PN, Mueller K, Kleber S, Braun Y, Penski C, Renner C, Halder R, Jennewein L, Solbach C, Thorsen F, Pestalozzi BC, Mischo A, Mittelbronn M. **Impact of Docetaxel on blood-brain barrier function and formation of breast cancer brain metastases.** Journal of Experimental & Clinical Cancer Research. 2019; 38(1): 434. *IF: 6.309 (2018)*

Brown P, RELISH Consortium (Vaillant M. as collaborator for the RELISH Consortium), Zhou Y. **Large expert-curated database for benchmarking document similarity detection in biomedical literature search.** Database. 2019; 2019. In press. *IF: 3.683 (2018)*

Jacobs R, Chalkley M, Bohnke JR, Clark M, Moran V, Aragon MJ. **Measuring the activity of mental health services in England: Variation in categorising activity for payment purposes.** Administration and Policy in Mental Health and Mental Health Services Research. 2019; 46(6): 847-857. *IF: 2.681 (2018)*

Stranges S, Takeda A, Martin N, Rees K. **Cochrane corner: does the Mediterranean-style diet help in the prevention of cardiovascular disease?** Heart. 2019; 105(22): 1691-1694. Epub 2019 Aug 22. *IF: 5.082 (2018)*

Diffo Kaze A, Maas S, Belsey J, Hoffmann A, Seil R, van Heerwaarden R, Pape D. **Mechanical strength of a new plate compared to six previously tested opening wedge high tibial osteotomy implants.** Journal of Experimental Orthopaedics. 2019; 6(1): 43. *IF: NA (2018)*

Makhani LA, Moran V, Sadique Z, Singh NS, Revill P, Roberts B. **Examining the use of economic evaluations in health-related humanitarian programmes in low- and middle-income countries: a systematic review.** Health Policy and Planning. 2019. [Epub ahead of print]. *IF: 2.717 (2018)*

European Centre for Disease Prevention and Control, WHO Regional Office for Europe, Fischer A. (as contributor for HIV/AIDS surveillance at Luxembourg). **HIV/AIDS surveillance in Europe 2019 – 2018 data.** Stockholm: ECDC, 2019. 95 p.

Cimino J. **Insights of the Journal of Clinical Oncology and Therapeutics.** Journal of Clinical Oncology and Therapeutics. 2019; 1(1). *IF: NA (2018)*

Laouali N, Mancini FR, Hajji-Louati M, El Fatouhi D, Balkau B, Boutron-Ruault MC, Bonnet F, Fagherazzi G. **Dietary inflammatory index and type 2 diabetes risk in a prospective cohort of 70,991 women followed for 20 years: the mediating role of BMI.** Diabetologia. 2019; 62(12): 2222-2232. Epub 2019 Aug 9. *IF: 7.113 (2018)*

Vanhaverbeke M, Vausort M, Veltman D, Zhang L, Wu M, Laenen G, Gillijns H, Moreau Y, Bartunek J, Van De Werf F, Devaux Y, Janssens S, Sinnaeve PR, E. U-CardioRNA COST Action CA. **Peripheral blood RNA levels of QSOX1 and PLBD1 are new Independent predictors of left ventricular dysfunction after acute myocardial Infarction.** Circulation. Genomic and Precision Medicine. 2019; 12(12): e002656. Epub 2019 Nov 22. *IF: NA (2018)*

Anaya-Loyola MA, Brito A, Vergara-Castaneda H, Sosa C, Rosado JL, Allen LH. **Low serum B12 concentrations are associated with low B12 dietary intake but not with Helicobacter pylori infection or abnormal gastric function in rural mexican women.** Nutrients. 2019; 11(12): 2922. *IF: 4.171 (2018)*

Guihard B, Chollet-Xemard C, Lakhnati P, Vivien B, Broche C, Savary D, Ricard-Hibon A, Marianne Dit Cassou PJ, Adnet F, Wiel E, Deutsch J, Tissier C, Loeb T, Bounes V, Rousseau E, Jabre P, Huiart L, Ferdynus C, Combes X. **Effect of rocuronium vs succinylcholine on endotracheal intubation success rate among patients undergoing out-of-hospital rapid sequence intubation: A randomized clinical trial.** JAMA Cardiol. 2019; 322(23): 2303-2312. *IF: 51.273 (2018)*

Devaux Y, Nossent AY, E. U-CardioRNA COST Action CA. **A role for m6A RNA methylation in heart failure development?** European Journal of Heart Failure. 2019: 10.1002/ejhf.1714. *IF: 12.129 (2018)*

Edwards J, Thind A, Stranges S, Chiu M, Anderson KK. **Concordance between health administrative data and survey-derived diagnoses for mood and anxiety disorders.** Acta Psychiatrica Scandinavica. 2019: 10.1111/acps.13143. [Online ahead of print]. *IF: 4.694 (2018)*

Beranger R, Hardy EM, Binter AC, Charles MA, Zaros C, Appenzeller BMR, Chevrier C. **Multiple pesticides in mothers' hair samples and children's measurements at birth: Results from the French national birth cohort (ELFE).** International Journal of Hygiene and Environmental Health. 2020; 223(1): 22-33. Epub 2019 Nov 8. *IF: 4.379 (2018)*

Iglesias-Gonzalez A, Hardy EM, Appenzeller BMR. **Cumulative exposure to organic pollutants of French children assessed by hair analysis.** Environment International. 2020; 134: 105332. Epub 2019 Nov 27. *IF: 7.943 (2018)*

Nielsen RO, Bertelsen ML, Ramskov D, Damsted C, Verhagen E, Bredeweg SW, Theisen D, Malisoux L. **Randomised controlled trials (RCTs) in sports injury research: authors-please report the compliance with the intervention.** British journal of sports medicine. 2020; 54(1): 51-57. Epub 2019 Sep 11. *IF: 11.645 (2018)*

Spennacchio P, Meyer C, Karlsson J, Seil R, Mouton C, Senorski EH. **Evaluation modalities for the anatomical repair of chronic ankle instability.** Knee Surgery, Sports Traumatology, Arthroscopy. 2020; 28(1): 163-176. Epub 2019 Oct 23. *IF: 3.149 (2018)*

Sun R, Pan C, Li QX, Peng F, Mai B. **Occurrence and congener profiles of polybrominated diphenyl ethers in green mussels (Perna viridis) collected from northern South China Sea and the associated potential health risk.** The Science of the total environment. 2020; 698: 134276. Epub 2019 Sep 3. *IF: 5.589 (2018)*

Wiley ER, Seabrook JA, Gilliland JA, Anderson KK, Stranges S. **Green space and substance use and addiction: A new frontier.** Addictive Behaviors. 2020; 100: 106155. Epub 2019 Oct 15. *IF: 2.963 (2018)*

Malisoux L, Delattre N, Urhausen A, Theisen D. **Shoe cushioning influences the running injury risk according to body mass: a randomized controlled trial involving 848 recreational runners.** The American Journal of Sports Medicine. 2020; 48(2): 473-480. Epub 2019 Dec 26. *IF: 6.093 (2018)*

Smith LK, Blondel B, Zeitlin J, Euro-Peristat Scientific Committee (Billy A. as representative for Luxembourg). **Producing valid statistics when legislation, culture and medical practices differ for births at or before the threshold of survival: Report of a European workshop.** British Journal of Obstetrics and Gynaecology. 2020; 127(3): 314-318. Epub 2019 Nov 6. *IF: 5.193 (2018)*

Grova N, Wang X, Hardy EM, Palazzi P, Chata C, Appenzeller BMR. **Ultra performance liquid chromatography - tandem mass spectrometer method applied to the analysis of both thyroid and steroid hormones in human hair.** Journal of Chromatography A. 2020; 1612: 460648. Epub 2019 Oct 26. *IF: 3.858 (2018)*

Magnitskaya N, Mouton C, Gokeler A, Nuehrenboerger C, Pape D, Seil R. **Younger age and hamstring tendon graft are associated with higher IKDC 2000 and KOOS scores during the first year after ACL reconstruction.** Knee Surgery, Sports Traumatology, Arthroscopy. 2020; 28(3): 823-832. Epub 2019 May 22. *IF: 3.149 (2018)*

TRANSVERSAL ACTIVITIES

Ullmann P, Nurmik M, Schmitz M, Rodriguez F, Weiler J, Qureshi-Baig K, Felten P, Nazarov PV, Nicot N, Zuegel N, Haan S, Letellier E. **Tumor suppressor miR-215 counteracts hypoxia-induced colon cancer stem cell activity.** Cancer Letters. 2019; 450: 32-41. Epub 2019 Feb 18. *IF: 6.508 (2018)*

Azuaje F. **Artificial intelligence for precision oncology: beyond patient stratification.** NPJ Precision Oncology. 2019; 3: 6. *IF: NA (2018)*

Jochner MCE, An J, Lattig-Tunnemann G, Kirchner M, Dagane A, Dittmar G, Dirnagl U, Eickholt BJ, Harms C. **Unique properties of PTEN-L contribute to neuroprotection in response to ischemic-like stress.** Scientific Reports. 2019; 9(1): 3183. *IF: 4.011 (2018)*

Azuaje F, Kaoma T, Jeanty C, Nazarov PV, Muller A, Kim SY, Dittmar G, Golebiewska A, Niclou SP. **Hub genes in a pan-cancer co-expression network show potential for predicting drug responses.** F1000 Research. 2019; 7: 1906. *IF: NA (2018)*

Malik AR, Szydlowska K, Nizinska K, Asaro A, van Vliet EA, Popp O, Dittmar G, Fritsche-Guenther R, Kirwan JA, Nykjaer A, Lukasiuk K, Aronica E, Willnow TE. **SorCS2 controls functional expression of amino acid transporter EAAT3 and protects neurons from oxidative stress and epilepsy-induced pathology.** Cell Reports. 2019; 26(10): 2792-2804 e6. *IF: 7.815 (2018)*

Theorin L, Faxen K, Sorensen DM, Migotti R, Dittmar G, Schiller J, Daleke DL, Palmgren M, Lopez-Marques RL, Gunther Pomorski T. **The lipid head group is the key element for substrate recognition by the P4 ATPase ALA2, a phosphatidylserine flippase.** The Biochemical Journal. 2019; 476(5): 783-794. *IF: 4.331 (2018)*

Dittmar G, Hernandez DP, Kowenz-Leutz E, Kirchner M, Kahlert G, Wesolowski R, Baum K, Knoblich M, Hofstatter M, Muller A, Wolf J, Reimer U, Leutz A. **PRISMA: Protein Interaction Screen on Peptide Matrix Reveals Interaction Footprints and Modifications- Dependent Interactome of Intrinsically Disordered C/EBPbeta.** iScience. 2019; 13: 351-370. Epub 2019 Mar 1. *IF: NA (2018)*

Hossain JA, Latif MA, Ystaas LAR, Ninzima S, Riecken K, Muller A, Azuaje F, Joseph JV, Talasila KM, Ghimire J, Fehse B, Bjerkvig R, Miletic H. **Long-term treatment with valganciclovir improves lentiviral suicide gene therapy of glioblastoma.** Neuro-Oncology. 2019; 21(7): 890–900. *IF: 10.091(2018)*

Longworth J, Dittmar G. **Assessment of ubiquitin chain topology by targeted mass spectrometry.** Methods in Molecular Biology. 2019; 1977: 25-34. *IF: NA (2018)*

Schilling J, Broemer M, Atanassov I, Duernberger Y, Vorberg I, Dieterich C, Dagane A, Dittmar G, Wanker E, van Roon-Mom W, Winter J, Krauss S. **Deregulated splicing is a major mechanism of RNA-Induced toxicity in Huntington's disease.** Journal of Molecular Biology. 2019; 431(9): 1869-1877. Epub 2019 Jan 31. *IF: 5.067 (2018)*

Fontrodona N, Aube F, Claude JB, Polveche H, Lemaire S, Tranchevent LC, Modolo L, Mortreux F, Bourgeois CF, Auboeuf D. **Interplay between coding and exonic splicing regulatory sequences.** Genome Research. 2019; 29(5): 711-722. Epub 2019 Apr 8. *IF: 9.944 (2018)*

van Well EM, Bader V, Patra M, Sanchez-Vicente A, Meschede J, Furthmann N, Schnack C, Blusch A, Longworth J, Petrasch-Parwez E, Mori K, Arzberger T, Trumbach D, Angersbach L, Showkat C, Sehr DA, Berlemann LA, Goldmann P, Clement AM, Behl C, Woerner AC, Saft C, Wurst W, Haass C, Ellrichmann G, Gold R, Dittmar G, Hipp MS, Hartl FU, Tatzelt J, Winklhofer KF. **A protein quality control pathway regulated by linear ubiquitination.** The EMBO Journal. 2019; 38(9). Epub 2019 Mar 18. *IF: 11.227 (2018)*

Larrue C, Heydt Q, Saland E, Boutzen H, Kaoma T, Sarry JE, Joffre C, Recher C. **Oncogenic KIT mutations induce STAT3-dependent autophagy to support cell proliferation in acute myeloid leukemia.** Oncogenesis. 2019; 8(8): 39. *IF: 5.995 (2018)*

Lazareth H, Henique C, Lenoir O, Puelles VG, Flamant M, Bollee G, Fligny C, Camus M, Guyonnet L, Millien C, Gaillard F, Chipont A, Robin B, Fabrega S, Dhaun N, Camerer E, Kretz O, Grahammer F, Braun F, Huber TB, Nochy D, Mandet C, Bruneval P, Mesnard L, Thervet E, Karras A, Le Naour F, Rubinstein E, Boucheix C, Alexandrou A, Moeller MJ, Bouzigues C, Tharaux PL. **The tetraspanin CD9 controls migration and proliferation of parietal epithelial cells and glomerular disease progression.** Nature Communications. 2019; 10(1): 3303. *IF: 11.878 (2018)*

Baum K, Rajapakse J, Azuaje F. **Analysis of correlation-based biomolecular networks from different omics data by fitting stochastic block models.** F1000 Research. 2019; 8(465). *IF: NA (2018)*

Grinev VV, Nazarov PV, Klimov EA. **Power-law behavior of the alternative splicing of exons in human transcriptome.** Annual Research & Review in Biology. 2019; 32(6): 1-13. *IF: NA (2018)*

Nowak M, Suenkel B, Porras P, Migotti R, Schmidt F, Kny M, Zhu X, Wanker EE, Dittmar G, Fielitz J, Sommer T. **DCAF8, a novel MuRF1 interaction partner, promotes muscle atrophy.** Journal of Cell Science. 2019; 132(17). *IF: 4.517 (2018)*

Sompairac N, Nazarov PV, Czerwinska U, Cantini L, Biton A, Molkenov A, Zhumadilov Z, Barillot E, Radvanyi F, Gorban A, Kairov U, Zinovyev A. **Independent component analysis for unraveling the complexity of cancer omics datasets.** International Journal of Molecular Sciences. 2019; 20(18). *IF: 4.183 (2018)*

Nazarov PV, Wienecke-Baldacchino AK, Zinovyev A, Czerwinska U, Muller A, Nashan D, Dittmar G, Azuaje F, Kreis S. **Deconvolution of transcriptomes and miRNomes by independent component analysis provides insights into biological processes and clinical outcomes of melanoma patients.** BMC Medical Genomics. 2019; 12(1): 132. *IF: 2.568 (2018)*

Azuaje F, Kim SY, Perez Hernandez D, Dittmar G. **Connecting histopathology imaging and proteomics in kidney cancer through machine learning.** Journal of Clinical Medicine. 2019; 8(10). *IF: 5.688 (2018)*

Zhao X, Nedvetsky P, Stanchi F, Vion AC, Popp O, Zuhlke K, Dittmar G, Klussmann E, Gerhardt H. **Endothelial PKA activity regulates angiogenesis by limiting autophagy through phosphorylation of ATG16L1.** eLife. 2019; 8. *IF: 7.551 (2018)*

Simons JA, Vaillant M, Hipp G, Pavelka L, Stute L, Pauly C, Kruger R. **Multilingual validation of the first French version of Munich Dysphagia Test–Parkinson's Disease (MDT-PD) in the Luxembourg Parkinson's Study.** Frontiers in Neurology. 2019; 10: 1180. *IF: 2.635 (2018)*

Aasen SN, Espedal H, Holte CF, Keunen O, Karlsen TV, Tenstad O, Maherally Z, Miletic H, Hoang T, Eikeland AV, Baghirov H, Olberg DE, Pilkington GJ, Sarkar G, Jenkins RB, Sundstrom T, Bjerkvig R, Thorsen F. **Improved drug delivery to brain metastases by peptide-mediated permeabilization of the blood-brain barrier.** Molecular Cancer Therapeutics. 2019; 18(11): 2171-2181. Epub 2019 Aug 29. *IF: 4.856 (2018)*

Cosma A. **The nightmare of a single cell: Being a doublet.** Cytometry Part A. 2019: 10.1002/cyto.a.23929. [Online ahead of print]. *IF: 3.433 (2018)*

Kolber P, Kruger R. **Gene-environment interaction and Mendelian randomisation.** Revue Neurologique. 2019; 175(10): 597-603. Epub 2019 Sep 19. *IF: 2.177 (2018)*

Richez U, De Castilla H, Guerin CL, Gendron N, Luraghi G, Grimme M, Wu W, Taverna M, Jansen P, Latremouille C, Migliavacca F, Dubini G, Capel A, Carpentier A, Smadja DM. **Hemocompatibility and safety of the Carmat Total Artifical Heart hybrid membrane.** Heliyon. 2019; 5(12): e02914. *IF: NA (2018)*

Berenguer-Escuder C, Grossmann D, Massart F, Antony P, Burbulla LF, Glaab E, Imhoff S, Trinh J, Seibler P, Grunewald A, Kruger R. **Variants in Miro1 cause alterations of ER-Mitochondria contact sites in fibroblasts from Parkinson's disease patients.** Journal of Clinical Medicine. 2019; 8(12): 2226. *IF: 5.688 (2018)*

Baum K, Schuchhardt J, Wolf J, Busse D. **Of gene expression and cell division time: A mathematical framework for advanced differential gene expression and data analysis.** Cell systems. 2019; 9(6): 569-579 e7. Epub 2019 Sep 11. *IF: 8.640 (2018)*

Tranchevent LC, Azuaje F, Rajapakse JC. **A deep neural network approach to predicting clinical outcomes of neuroblastoma patients.** BMC Medical Genomics. 2019; 12(Suppl 8): 178. *IF: 2.568 (2018)*

Kofanova O, Bellora C, Garcia Frasquilho S, Antunes L, Hamot G, Mathay C, Mommaerts K, Muller A, DeWitt B, Betsou F. **Standardization of the preanalytical phase of DNA extraction from fixed tissue for next-generation sequencing analyses.** New Biotechnology. 2020; 54: 52-61. Epub 2019 Aug 6. *IF: 3.739 (2018)*

INTEGRATED BIOBANK OF LUXEMBOURG

Glaab E, Trezzi JP, Greuel A, Jager C, Hodak Z, Drzezga A, Timmermann L, Tittgemeyer M, Diederich NJ, Eggers C. **Integrative analysis of blood metabolomics and PET brain neuroimaging data for Parkinson's disease.** Neurobiology of Disease. 2019; 124: 555-562. Epub 2019 Jan 9. *IF: 5.160 (2018)*

Okawa S, Del Sol A. **A general computational approach to predicting synergistic transcriptional cores that determine cell subpopulation identities.** Nucleic Acids Research. 2019; 47(7): 3333-3343. *IF: 11.147 (2018)*

Schlicker L, Boers HM, Dudek CA, Zhao G, Barua A, Trezzi JP, Meyer-Hermann M, Jacobs DM, Hiller K. **Metabolic effects of fiber mixes revealed by in vivo stable isotope labeling in humans.** Metabolites. 2019; 9(5). *IF: 3.303 (2018)*

Schlicker L, Boers HM, Dudek CA, Zhao G, Barua A, Trezzi JP, Meyer-Hermann M, Jacobs DM, Hiller K. **Postprandial metabolic effects of fiber mixes revealed by in vivo stable isotope labeling in humans.** Metabolites. 2019; 9(5). *IF: 3.303 (2018)*

Ammerlaan W, Betsou F. **Biospecimen science of blood for cfDNA genetic analyses.** Current Pathobiology Reports. 2019; 7(2): 9-15. *IF: NA (2018)*

Betsou F, Gaignaux A, Ammerlaan W, Norris PJ, Stone M. **Biospecimen science of blood for Peripheral Blood Mononuclear Cell (PBMC) functional applications.** Current Pathobiology Reports. 2019; 7(2): 17-27. *IF: NA (2018)*

Mathieson W, Thomas G. **Using FFPE tissue in genomic analyses: Advantages, disadvantages and the role of biospecimen science.** Current Pathobiology Reports. 2019; 7(3): 35-40. *IF: NA (2018)*

Lippi G, Betsou F, Cadamuro J, Cornes M, Fleischhacker M, Fruekilde P, Neumaier M, Nybo M, Padoan A, Plebani M, Sciacovelli L, Vermeersch P, von Meyer A, Simunic AM, Working Group for Preanalytical Phase, European Federation of Clinical Chemistry Laboratory M. **Preanalytical challenges - time for solutions.** Clinical Chemistry and Laboratory Medicine. 2019; 57(7): 974-981. *IF: 3.638 (2018)*

Zaffaroni G, Okawa S, Morales-Ruiz M, Del Sol A. **An integrative method to predict signalling perturbations for cellular transitions.** Nucleic Acids Research. 2019; 47(12): e72. *IF: 11.147 (2018)*

de Soysa TY, Ranade SS, Okawa S, Ravichandran S, Huang Y, Salunga HT, Schricker A, Del Sol A, Gifford CA, Srivastava D. **Single-cell analysis of cardiogenesis reveals basis for organ-level developmental defects.** Nature. 2019; 572(7767): 120-124. Epub 2019 Jul 24. *IF: 43.070 (2018)*

Kloten V, Neumann MHD, Di Pasquale F, Sprenger-Haussels M, Shaffer JM, Schlumpberger M, Herdean A, Betsou F, Ammerlaan W, Af Hallstrom T, Serkkola E, Forsman T, Lianidou E, Sjoback R, Kubista M, Bender S, Lampignano R, Krahn T, Schlange T, Cancer-Id consortium. **Multicentric evaluation of circulating plasma MicroRNA extraction technologies for the development of clinically feasible reverse transcription quantitative PCR and next-generation sequencing analytical work flows.** Clinical Chemistry. 2019; 65(9): 1132-1140. Epub 2019 Jun 24. *IF: 6.891 (2018)*

Schwarz N, Knutti N, Rose M, Neugebauer S, Geiger J, Jahns R, Klopp N, Illig T, Mathay C, Betsou F, Scherag A, Kiehntopf M. **Quality assessment of the preanalytical workflow in liquid biobanking: Taurine as a serum-specific quality indicator for preanalytical process variations.** . Biopreservation and Biobanking. 2019; 17(5): 458-467. Epub 2019 Jul 24. *IF: 1.362(2018)*

Schymanski EL, Baker NC, Williams AJ, Singh RR, Trezzi JP, Wilmes P, Kolber PL, Kruger R, Paczia N, Linster CL, Balling R. **Connecting environmental exposure and neurodegeneration using cheminformatics and high resolution mass spectrometry: potential and challenges.** Environmental Science Processes & Impacts. 2019; 21(9): 1426-1445. *IF: 2.688 (2018)*

Stellino C, Hamot G, Bellora C, Trouet J, Betsou F. **Preanalytical robustness of blood collection tubes with RNA stabilizers.** Clinical Chemistry and Laboratory Medicine. 2019; 57(10): 1522-1529. *IF: 3.638 (2018)*

Nickels SL, Walter J, Bolognin S, Gerard D, Jaeger C, Qing X, Tisserand J, Jarazo J, Hemmer K, Harms A, Halder R, Lucarelli P, Berger E, Antony PMA, Glaab E, Hankemeier T, Klein C, Sauter T, Sinkkonen L, Schwamborn JC. **Impaired serine metabolism complements LRRK2-G2019S pathogenicity in PD patients.** Parkinsonism & Related Disorders. 2019; 67: 48-55. Epub 2019 Sep 19. *IF: 4.360 (2018)*

Lampignano R, Neumann MHD, Weber S, Kloten V, Herdean A, Voss T, Groelz D, Babayan A, Tibbesma M, Schlumpberger M, Chemi F, Rothwell DG, Wikman H, Galizzi JP, Bergheim IR, Russnes H, Mussolin B, Bonin S, Voigt C, Musa H, Pinzani P, Lianidou E, Brady G, Speicher MR, Pantel K, Betsou F, Schuuring E, Kubista M, Ammerlaan W, Sprenger-Haussels M, Schlange T, Heitzer E, Innovative Medicines Initiative C-IDC. **Multicenter evaluation of circulating cell-free dna extraction and downstream analyses for the development of standardized (pre)analytical work flows.** Clinical Chemistry. 2019. [Epub ahead of print]. *IF: 6.891 (2018)*

Benakis C, Martin-Gallausiaux C, Trezzi JP, Melton P, Liesz A, Wilmes P. **The microbiome-gut-brain axis in acute and chronic brain diseases.** Current Opinion in Neurobiology. 2019; 61: 1-9. *IF: 6.014 (2018)*

Dufresne J, Bowden P, Thavarajah T, Florentinus-Mefailoski A, Chen ZZ, Tucholska M, Norzin T, Ho MT, Phan M, Mohamed N, Ravandi A, Stanton E, Slutsky AS, Dos Santos CC, Romaschin A, Marshall JC, Addison C, Malone S, Heyland D, Scheltens P, Killestein J, Teunissen C, Diamandis EP, Siu KWM, Marshall JG. **The plasma peptides of breast versus ovarian cancer.** Clinical proteomics. 2019; 16: 43. *IF: 2.892 (2018)*

Kofanova O, Bellora C, Garcia Frasquilho S, Antunes L, Hamot G, Mathay C, Mommaerts K, Muller A, DeWitt B, Betsou F. **Standardization of the preanalytical phase of DNA extraction from fixed tissue for next-generation sequencing analyses.** New Biotechnology. 2020; 54: 52-61. Epub 2019 Aug 6. *IF: 3.739 (2018)*

Dries R, Stryjewska A, Coddens K, Okawa S, Notelaers T, Birkhoff J, Dekker M, Verfaillie CM, Del Sol A, Mulugeta E, Conidi A, Grosveld FG, Huylebroeck D. **Integrative and perturbation-based analysis of the transcriptional dynamics of TGFbeta/BMP system components in transition from embryonic stem cells to neural progenitors.** Stem Cells. 2020; 38(2): 202-217. Epub 2019 Dec 13. *IF: 5.614 (2018)*

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