LCSB in brief

The LCSB is an interdisciplinary research centre at the University of Luxembourg. It is accelerating biomedical research by closing the gap between systems biology and medical research. Collaboration between biologists, medical and computer scientists, physicists, engineers and mathematicians is offering new insights into complex systems like cells, organs and organisms. These findings are essential for understanding principal mechanisms of disease pathogenesis and for developing new tools in diagnostics and therapy.

Neurodegenerative diseases like Parkinson’s disease and description of diseases as networks are the focus of the LCSB’s research. The centre has established strategic partnerships with leading biomedical laboratories worldwide and with all major biological and medical research units in Luxembourg. The LCSB fosters collaboration with industrial partners and accelerates the translation of fundamental research results into clinical applications.
Editorial

Doing research, talking science

The Grand Duchy of Luxembourg is home to a young, lively university. The LCSB is situated at the heart of its vibrant research and study campus in Belval. The people of Luxembourg have positively welcomed science and research. One might think this is only natural and an inevitable trend. But I think there is more to it than that; I think it is due to the many excellent scientific results – and a great deal of work and dedication in science communication. Because outreach is the vehicle that brings science to the people. We want research to be there for people. I hope our Annual Report 2019 conveys this spirit.

Firstly, there was the LCSB’s tenth anniversary, which we celebrated in 2019. Large, artistically designed brain sculptures were displayed in different parts of Luxembourg City to draw attention to biomedical research. The proceeds of their sale have funded a new research project at the LCSB, looking into better diagnosis and treatment of Parkinson’s disease.

Other forms of outreach are perhaps not as artistic, but they are equally important. The Scienteens Lab raises young people’s interest with hands-on science activities. The coveted ERC (European Research Council) grant and the many awards honouring our research work are also forms of outreach, of which we are particularly proud. Finally, there is of course the transfer of scientific results into medical applications.

This will continue to be possible in the years to come thanks to the extension of funding for the National Centre of Excellence in Research on Parkinson’s Disease (NCER-PD).
Meet the LCSB team!

230 people from 49 countries all over the world. A wide range of scientific backgrounds, from biologists and clinicians to mathematicians, physicists, computer scientists and many more. Researchers, technical support and administrative staff working together to solve today’s burning questions about brain diseases. This is the LCSB team: diverse, interdisciplinary and hard-working!
Professor Balling, you founded the LCSB in the autumn of 2009. What is your most lasting impression from that time? It was clear from the beginning that the LCSB should be established on Belval campus. In 2009, Belval was just one big construction site – with no trace of a university. My wife said “You don’t want to work there, do you?” But yes, I did. And today there is a modern, lively district here, marked by research and student life. What a change in just ten years!

As the founding director of the LCSB, what overall conditions were you facing ten years ago? I had a big, blank canvas in front of me. It was wonderful. I introduced myself to the Executive Board during a rectorate meeting at the beginning of September 2009. Then, I sat down in my room in Limpertsberg and wrote plans. Of course, there was a lot at stake too. The LCSB was founded as part of a broader strategy: Luxembourg wanted to diversify and open up new economic fields to complement steel and finance. Health in a global and ageing society had been identified as one such field. The LCSB took up this responsibility. In other words, there were real expectations from the very beginning that we would achieve something for the people, for the patients.

What was important for the LCSB to gain social acceptance in Luxembourg? Open doors, active communication, reaching out to people – I immediately received many invitations and gave countless lectures. It was like that for the LCSB staff later, too. It was clear to all of us, we had to explain what we do here and how we do it. You can’t do that in one radio broadcast. You need stamina and patience.

The LCSB started off with just you as the director and a few employees. How did you choose in which direction to steer the centre? It was indeed a challenge. It is true that we started from scratch, to the extent that we hadn’t even settled on a topic yet. But it was also an opportunity. I worked with the neurologists here in Luxembourg to decide what was the right focus for us. From the discussions, one theme emerged, and that was Parkinson’s disease.

As soon as this was defined as our main focus, we began our interdisciplinary and very focused research into the mechanisms of Parkinson’s disease. On the one hand, we wanted to improve our understanding of this disease specifically and to develop better diagnostics and therapy. On the other hand, we also wanted to use Parkinson’s as a model to better understand other diseases.

So the LCSB now had a main topic and even a name in professional circles. But science thrives on publications… That’s right. The results started coming in after about two years, thanks to many young and very committed scientists. For them, Luxembourg and the LCSB were ideal places to do research: good funding, lots of freedom, not much routine. These highly productive minds with original ideas published one paper after another. Microbiome and immunity in the brain – these are just two of the research areas in which the LCSB quickly established itself and is now well-recognised.

Did things then settle down at the centre? No, and that would have been bad. I would say that the seeds started sprouting. There were some decisive steps along the way. We built up a strong bioinformatics department and became better and better at understanding complex systems such as the human body and its diseases. And last but not least, there was the connection to the patients. The scientific successes of the LCSB would not be conceivable without its close cooperation with Luxembourg’s hospitals and healthcare professionals.

And what challenges does the centre face today? The LCSB is a truly interdisciplinary centre. The basis for interdisciplinarity is cooperation and a good culture of communication – you always have to keep working on that. Above all else, there is the rightful expectation that our research will actually benefit people. This is already happening through our spin-offs and our role as coordinator of healthcare and prevention networks. In this way, we hope our research results will continue helping patients.

Last year, the LCSB had cause for celebration: its 10th anniversary. Founding Director Prof. Rudi Balling recaps the past decade and describes the secrets of the centre’s success.
10 brains for science: Mind the Brain

In 2019, the LCSB celebrated its tenth anniversary with the exhibition “Mind the Brain”. Ten Luxembourgish artists painted motifs onto ten giant fibreglass brain sculptures. In September and October, the sculptures were to be seen in various places around the City of Luxembourg. After that, they were sold, with half of the proceeds going towards funding a Parkinson’s disease research project.

Research on mechanisms of the human brain is the main focus of the LCSB. Each of the two-metre-long brain sculptures therefore related to a specific research area at the centre. Artist Joël Rollinger, for example, painted multiple faces onto one of the sculptures to depict one of the defining aspects of Alzheimer’s disease: a severe disruption of memory, after which many patients no longer recognise the faces of even their closest relatives. Eric Mangen painted another brain sculpture in fire engine red with contrasting blue and white furrows resembling electric flashes, to symbolise the neurological processes during an epileptic seizure.

The brains represented more than just research topics at the LCSB, they also stood for the combined brainpower that comes together at the interdisciplinary centre. For more than ten years, the LCSB has been attracting excellent researchers from around the world who are driving biomedical research forward. More than 200 employees from nearly 50 countries work here. Together, they aim to understand the most important mechanisms of brain diseases. Based on this knowledge, they are developing diagnostic and therapeutic tools with which doctors and healthcare professionals can help their patients.

The project funded by the sale of the sculptures illustrates well what the LCSB is all about. Combining computational and experimental expertise, it is dedicated to research on Parkinson’s biomarkers. The hope is for these substances to help in diagnosing the disease at an early stage, long before any clinical symptoms such as muscle tremors or unsteady gait appear (see p. 14).

The idea for an exhibition with brain sculptures came from the head of the Communication team at the LCSB, Dr. Sabine Schmitz, and the head of the Fundraising department of the University of Luxembourg, Dr. Philippe Lamesch, over a cup of coffee. “We wanted to share our passion for science with many people, and to do it in an unexpected way,” says Sabine Schmitz. “The artists really brought our vision to life!”
Second round for the Parkinson’s fighters

The National Centre of Excellence in Research on Parkinson’s Disease (NCER-PD) will continue its work thanks to the renewed support of the Luxembourg National Research Fund (FNR). This means the centrepiece of NCER-PD, the Luxembourg Parkinson Study, will go on for another four years, providing additional insights into the evolution of the disease.

In 2019, an international review panel evaluated NCER-PD. The scientists and the clinical team rose splendidly to the challenge, receiving an excellent score for their research. As a result, the FNR is providing another six million euros until the middle of 2023. “With this funding, we can study the mechanisms of Parkinson’s disease in more detail and thus further improve the diagnosis and treatment of this disease,” says Prof. Rejko Krüger, coordinator of NCER-PD.

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“All those involved in NCER-PD will continue their research with the groups of volunteers with and without Parkinson’s disease. Regular comprehensive examinations will give the researchers a clear overview of how a participant’s health status develops over time, and they will be able to investigate how certain Parkinson’s treatments work in the long run,” says Krüger.

During the second funding phase of NCER-PD, participants who have already registered will continue to be studied and newly diagnosed patients will be added to the cohort. “We are also planning a new risk cohort,” says Krüger. “With this new cohort, we will be trying to identify early signs of Parkinson’s so that preventive action can be taken if necessary.”

For the risk cohort, Krüger and colleagues are looking for volunteers with so-called REM sleep behaviour disorder. People with this disorder talk or shout loudly in their sleep, kicking and punching as they act out their dreams – sometimes so harshly that even their partners suffer. People with REM sleep behaviour disorder are at greater risk of developing Parkinson’s disease later in life. The researchers will therefore be examining these people annually to monitor their condition and detect any early signs of Parkinson’s. They want to discover what factors play a role in the transition from REM sleep disorder to the onset of Parkinson’s disease.

“Furthermore, we now hope to make significant progress in the field of treatment,” Krüger emphasises. This will involve clinical trials in vitro: new active substances will be tested in the laboratory on cells from tissue samples provided by patients who have a specific genetic predisposition to Parkinson’s disease. Promising active ingredients from these experiments will then be developed further in clinical trials – and should ultimately benefit people living with Parkinson’s in Luxembourg and abroad.

The NCER-PD clinical team. From left to right: Maxime Hansen, Femke Wauters, Linda Hansen, Claire Pauly, Laura Pauly, Prof. Rejko Krüger, Dr. Guilherme Meyers, Laura Longhino, Dr. Lukas Pavelka and Dr. Lara Stute.

10 years of Parkinson’s research at the LCSB

When the LCSB was first created, its founding director Prof. Rudi Balling got together with scientists and clinicians to analyse various disease areas. He wanted to know where there was a need for action, and where there might be stimulating scientific challenges. Balling and his team chose Parkinson’s disease.

“What was special from the beginning was the systematic approach that the LCSB follows,” says Prof. Rejko Krüger, who joined the LCSB in 2014 and now heads the Clinical and Experimental Neuroscience group. They study not only occurrences inside the brain and neurons, but also the influence of the microbiome, and in particular the bacterial communities of the gut. They are modelling the disease on the computer as well, while establishing close connections with clinicians in hospitals and healthcare professionals throughout Luxembourg. “This comprehensive approach was a solid basis for building up NCER-PD together with the national partners LIH, IBBL, CHL, and LNS,” Krüger says. “NCER-PD is the leap from science to the patient – and is unique in the world as a truly nationwide study.”

“For the future, participants will remain our partners in research,” says Krüger, “but we want to be able to reduce the need for visits to the clinic, and instead employ new technologies like mobile apps and sensors to communicate remotely on a more frequent and individual basis.” In the long run, these digital health approaches will help eliminate existing barriers between research and care, so that the patients can benefit from direct therapeutic feedback and feel better equipped to fight the disease.
3D glimpse at the early stage of Parkinson’s disease

Thanks to funds raised through an exhibition, researchers at the LCSB are conducting experiments in three-dimensional cell culture models and analysing the results with new computational tools to track down the causes of this neurodegenerative disease.

For three weeks in the autumn of 2019, ten colourful, man-sized sculptures could be admired in the centre of Luxembourg City. These depictions of the human brain, created for the tenth anniversary of the LCSB, helped to promote research into the human brain – through donations and the sale of the artworks.

The funds raised are going to research into Parkinson’s disease. While scientists have a number of clues pointing to processes in the brain that favour the disease’s development, they still lack a profound understanding of the molecular mechanisms, and thus of the possibilities for treating it. “One reason for this is the difficulty of studying changes in the brain at the early stages of the disease,” says Assistant Professor Enrico Glaab, head of the Biomedical Data Science group at the LCSB. “Many key pathological changes in the brain can only be studied after a patient has died.” While signs can be found of what happened in the late stages of the disease, the researcher continues, post-mortem examination reveals very little about how the disease developed earlier.

Experiments in animal models cannot provide a complete picture and neither can research on single-layer cell culture models. “These only give a limited picture of the complex processes in the brain,” Glaab explains. In order to escape this limitation, the scientists are analysing data from new, three-dimensional cell culture models created in the LCSB laboratory of the Developmental & Cellular Biology group led by Prof. Jens Schwamborn. “These so-called organoids are models of the tissue structures that are especially affected in the brains of patients,” Schwamborn says. “They are derived from skin biopsies.” He and his team are using them to investigate various aspects of Parkinson’s disease and to find ways to detect molecular changes in the early stages.

The researchers already have their first results: “From the organoids, we have identified significant differences in gene activity between patients and control persons,” Glaab reports. His goal is to develop predictive computational models of cellular process alterations in the midbrain in order to deepen our fundamental understanding of the disease. Ultimately, this should enable the researchers to discover and computationally assess new biomarkers for early diagnosis, as well as potential targets for computational drug screening. The aim is not only to find candidate drug compounds with high affinity for a specific target, but also to investigate whether these compounds can pass biological barriers to reach their target while also having limited adverse effects. This would be a first step towards the repurposing of existing drugs or the design of new ones.
Microbiome and dietary fibre form a strong team

The human gut is rich with life. In it, microorganisms aid our digestion, produce fatty acids as well as other substances, and even affect our immune system. Through our diet, we can influence the composition of the microbial community in the gastrointestinal tract and the metabolic products they release. This in turn has repercussions not only for the prevention but also for the treatment of colorectal cancer. These were the findings of researchers led by Prof. Paul Wilmes.

For the prevention of colorectal cancer, doctors and nutritionists recommend a balanced diet with ample fibre and as little sugar as possible. “However, once colorectal cancer has been diagnosed and treatment has started, amazingly, diet is given hardly any attention at all,” says Prof. Paul Wilmes, head of the Eco-Systems Biology group at the LCSB. “But there is evidence that diet does in fact play a role not only in its onset but also in its progression. This is what we investigate: how certain nutrients and the microbiome affect cancer cells in the gut.”

To study these interactions, the microbial ecologist and his team developed the HuMiX model. It stands for “Human-Microbial X(cross)-talk” and is a unique in vitro model of the gut. PhD student Kacy Greenhalgh used this “Gut-on-a-Chip” to cultivate human colorectal cancer cells together with bacteria in nutrient solutions that reflect different diets. In one part of the experiment, this was an exemplary mixture of fibres. In another, she simulated a relatively unhealthy diet rich in simple sugars. After one to three days, Greenhalgh then studied the cells. High-throughput sequencing and additional computer simulations showed that microbes or fibres individually had no positive effect on the cancer cells. A combination of the two, however, did. Under the combined action of bacteria and fibre, the development of cancer cells falters.

“Our research was a close collaboration with the Department of Life Sciences and Medicine of the University of Luxembourg,” Wilmes explains. “The colleagues there have a great deal of experience in researching colorectal cancer and worked with us especially for the interpretation of the data. They have also assembled a collection of cancer cells from colorectal cancer patients in Luxembourg. This is an important resource for us to validate our results.” The researchers published their results in the well-known scientific journal Cell Reports. And HuMiX, the model that made the findings possible, received the Healthcare Research Award at the Luxembourg Healthcare Summit in October 2019.

The microbial mechanisms behind health and disease

When Paul Wilmes first arrived at the LCSB nearly ten years ago, the microbial ecologist already had a lot of experience with microbiomes in nature. At the time, he wanted to apply his skills to the microbiomes of humans. As a specialist in molecular analysis of the microbiome, he knew such analyses are not enough to understand the interactions and mechanisms between humans, microorganisms and diseases. To complement mouse models, Wilmes therefore created HuMiX, the Human–Microbial X(cross)-talk model. It allowed an in-depth look into the interactions between human and bacterial cells. In 2016, his team published the first paper on the model. Two years later, Kacy Greenhalgh used it to track down the correlation between intestinal cancer, diet and the microbiome. In the same year, Nature listed five projects from Paul Wilmes’ group among the 25 most important milestones in microbiome research. In projects on Parkinson’s and other disorders, he and his colleagues recognised that the microbiome can be involved in the onset of these diseases. Discerning the mechanisms behind this is now the main goal for the next ten years.
Modelling cell fate in degenerative diseases

The Computational Biology group at the LCSB studies cellular differentiation and reprogramming. With the help of mathematical and computational tools, this team wants to understand how complex molecular networks – for example protein-protein interactions – control the fate of human cells. The research group at the LCSB and a group at the Research Centre CIC bioGUNE in Bilbao (Spain), both led by Prof. Antonio del Sol, are jointly developing new methods to analyse such networks and model how different cell types are generated in the human body.

In 2019, the Basque foundation Ikerbasque appointed Antonio del Sol as an Ikerbasque Research Professor, a title only bestowed on internationally renowned scientists. Del Sol now works as an Ikerbasque Research Professor at the Research Centre CIC bioGUNE in Bilbao – where he is currently establishing a satellite research group – while pursuing his main activities in the group at the LCSB.

The work in the two groups focuses on stem cell research and regenerative medicine. The aim is to use mathematical and computer-assisted models to better understand how to regenerate malfunctioning cells and diseased tissue. Thanks to the toolbox they developed, the LCSB researchers have already successfully identified some molecular factors that keep stem cells quiescent in the brains of old mice and others that impair the differentiation of a specific type of cardiac cells.

At the Research Centre CIC bioGUNE, specialists are researching liver and neurological diseases, and the satellite research group will combine this expertise with the bioinformatics competence of the LCSB to explore together innovative approaches in regenerative medicine. For example, how can the growth of healthy cells be promoted in cirrhotic livers, where tissue is being destroyed? Or how can the ability of specific cells be used to boost the regeneration of damaged nerves?

In the following years, new team members will help enhance this synergy and bring together the work of experimental biologists and computational experts. Both centres also have plans in place for scientists to make guest visits to ensure intensive exchange. “These visits are an important part of the project,” says del Sol. “They will allow two-way knowledge transfer and help us answer fundamental questions for the development of new diagnostic tools and therapeutic interventions.”

Biomedical milestones and future visions

Since its creation, the LCSB seeks to model biological processes and to translate fundamental research results into novel therapies and applications. Research at the centre was strongly influenced by a groundbreaking discovery by scientists Shinya Yamanaka and Sir John Gurdon, who received the 2012 Nobel Prize in Medicine. They showed that mature cells can be reprogrammed into pluripotent stem cells. Under the right conditions, pluripotent cells can then be differentiated into other mature cells such as neurons. This discovery inspired Prof. Antonio del Sol and his team to study which molecular factors are optimal for cellular conversion. “Our research should ultimately benefit the patient,” del Sol says. “The insights of such fundamental research must culminate in translational medicine.” The researchers are, for example, currently working on reprogramming skin cells into corneal stem cells in vitro, with the hope of one day transplanting them into patients with injuries or genetic disorders. In the distant future, one can imagine that this combination of computational and experimental expertise could be used to stimulate regenerative processes and stop degeneration in various diseases like Alzheimer’s or Parkinson’s.
FNR Award: Vaginal birth strengthens the immune system

In 2019, Dr. Linda Wampach received the FNR Award for Outstanding PhD Thesis. In her thesis, she studied the intestinal microbiome of newborn babies. Wampach compared the gut flora of babies born by caesarean section with those born vaginally. The researcher in the Eco-Systems Biology group of Prof. Paul Wilmes found evidence that, during a vaginal birth, mothers not only expose their children to their first bacteria, but that those bacteria in fact have a positive influence on the newborns’ immune system. In a caesarean birth, this exposure is significantly reduced or even undetectable.

Certain diseases such as asthma and allergies occur more frequently among caesarean born children. "We believe that delayed activation of the immune system by the gut microbiome can be associated with diseases at a later age," explains Linda Wampach. Part of the study was funded by the André et Henriette Losch Foundation.

Microbiome molecules in the limelight

LCB scientist Prof. Paul Wilmes has received an elite Consolidator Grant of two million euros from the European Research Council (ERC). As part of the project “ExpoBiome”, he will research how molecules from the microbiome interact with human immune cells in patients with Parkinson’s disease and rheumatoid arthritis.

"ExpoBiome is basic research for the benefit of the patients," asserts Prof. Wilmes, head of the Eco-Systems Biology group at the LCSB. "I am confident that this novel approach will lead to the discovery of new therapeutically important molecules and will promote the development of innovative diagnostic applications.”

His optimism stems from many studies suggesting that molecules such as metabolites produced by microorganisms are strongly implicated in many chronic diseases. Scientists have, for example, long known of a relationship between the microbiome in the human gut and the development of Parkinson’s disease. For rheumatoid arthritis, it is also known that periodic fasting brings significant relief to many patients. "One hypothesis is that the activity of the gut microbiome is reduced due to the lack of nutrients and that this has a positive effect on the chronic inflammation characteristic of the disease," explains Paul Wilmes. "Until now, however, there have been no systematic studies on how microbial molecules affect chronic disease processes. The ExpoBiome project aims to close this critical knowledge gap.”

Prof. Wilmes and his team have developed a series of high-resolution experimental techniques to study the interactions between microbial molecules and human cells, which are now being deployed in the ExpoBiome project. One of these is HuMiX, a so-called “Gut-on-a-Chip” model, in which they cultivate bacterial species characteristic of the gut microbiome together with human intestinal and immune cells. With the help of this model, the LCSB researchers will, for instance, investigate whether and how the positive effects of fasting are caused by shifts in the microbial communities and the molecules they secrete. This in vitro approach will be combined with a clinical study observing the evolution of the gut microbiome of patients as they follow a fasting regimen.

"Thanks to both our HuMiX model and the clinical study, we will be able to determine which microbial molecules are formed in the gut and how they affect the course of a disease such as rheumatoid arthritis or Parkinson’s." Paul Wilmes and colleagues will be looking specifically for molecules that have anti-inflammatory properties. These could have a beneficial effect on the course of these diseases and potentially be used in future targeted therapy.

ERC Consolidator Grant

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Parkinson’s disease is extremely complex. Accordingly, thousands of scientific papers are published on the disease every year. The Parkinson’s disease map, or PD map (pdm.uni.lu) initiated by the LCSB and realised during the last ten years, makes all of the existing knowledge available in one clear overview. Today, with the LCSB’s help in establishing a European network of disease map developers, there are now maps on many different diseases.

Parkinson’s disease is characterised by the death of certain brain cells, called dopaminergic neurons. The cause of this cell death is a complex interplay between molecular processes influenced by genetic and external factors, many details of which are already known. Researchers and medical professionals are therefore interested in how the numerous factors interact and affect one another. “Our PD map sorts the scientific knowledge about Parkinson’s disease and makes logical connections between areas that influence one another. This gives rise to entirely new research hypotheses,” says Dr. Marek Ostaszewski, researcher in the Bioinformatics Core at the LCSB who coordinates the PD map project.

This is of course important – and possible – for other diseases as well. During the PD map’s development, other projects have come to life at the LCSB and in many research institutions to develop maps for asthma and cancer, for example. “We all want to enable medical advancements,” Ostaszewski declares. “So, it is only natural that we are regularly sharing our knowledge and experience.”

In 2017, the community decided to meet for this purpose. Researchers from across Europe, representing seven different maps, gathered in Lyon to share their knowledge. Almost immediately after, the meeting became a regular occurrence: the second event was held in Luxembourg and the scientists have been meeting every year since. “It is important, for example to maintain common standards, so that we all construct the maps in the same way,” describes Marek Ostaszewski, pointing out one of the many challenges. The technologies used must also be compatible in terms of displaying the data, and common principles must be agreed upon as to how the implemented knowledge should be organised and graphically visualised.

“We have made enormous progress in the past three years,” the LCSB researcher is pleased to report. “This has been possible because everyone in the network is greatly interested in exchanging knowledge. We get together to solve specific problems in creating the disease maps and to take disease modelling to a new level for the benefit of the patient.”

For the current list of disease maps, see https://disease-maps.org/projects
A scientific look into the brain

What happens in the brain during Parkinson’s disease can only be indirectly studied by doctors and researchers during the patient’s lifetime. A direct view into the brain, as well as a definitive diagnosis, is only possible after death. To ensure the highest scientific level and to strengthen research activities in this line of study, a brain bank has been established in Luxembourg. Since last year, it has been open for brain donations from participants in the Luxembourg Parkinson’s Study.

“Many people are reluctant to talk about the possibility of brain donation after death,” says Prof. Michel Mittelbronn, head of the Neuropathology group at the LCSB. “But when I address fears and reservations directly, and make the benefits of such a donation clear, I often encounter an astonishing openness.” Together with several partners, Mittelbronn, who has long-standing expertise in both clinical diagnostics and research, has established a brain bank in Luxembourg – an institution that stores human brains for research purposes.

The brain bank is a cooperative project between the LCSB, the Laboratoire National de Santé (LNS), the Integrated Biobank of Luxembourg (IBBL), the Luxembourg Institute of Health (LIH), and the Centre Hospitalier de Luxembourg (CHL). “The brains will be stored there for scientific examination,” Mittelbronn says. Around 80 people so far have expressed interest in donating their brain after their death. Before the brain bank could be established, there were numerous formal questions to be clarified, as Mittelbronn explains: “There were many ethical and legal aspects of donating a brain to be considered. And of course, there have to be clear organisational rules on how the tissue donations make their way to the brain bank.”

This requires close cooperation between neuropathologists and clinicians. Prof. Mittelbronn’s partner in this field is Prof. Rejko Krüger, who heads the National Centre of Excellence in Research on Parkinson’s Disease (NCER-PD). The NCER-PD clinical team is the first point of contact for patients wishing to participate in the brain donation programme.

When death occurs, well-defined fixed procedures are in place to determine who will examine the body, remove the brain and preserve it for science. The procedures ensure compliance with ethical and scientific standards and are performed with the utmost respect for the donors and their families. Then the research begins: “We can examine the brain down to the tiniest detail using the very latest methods,” Mittelbronn says. This begins with macroscopic analysis, followed by the examination of the neurons and the cell components, and continues with the molecular and genetic examination of the brain tissue. “This allows us to collect a great deal of information about the state of the brain at the time of death,” Mittelbronn explains, “and to correlate this data with the course of the disease observed during the patient’s lifetime.”

One of Michel Mittelbronn’s goals in this pursuit is to identify biomarkers that are associated with specific forms of Parkinson’s disease. “If we examine a large number of brains whose donors had severe tremors in their hands for example, we may be able to trace this back to specific molecular changes in the brain. This will continually improve our understanding of the mechanisms of the disease,” Mittelbronn points out. Ideally, the biomarkers could later be used for diagnostic purposes or as targets for new therapeutics.

Until that stage, there is still a lot of research to be done. And this will involve good interinstitutional and interdisciplinary cooperation. “Luxembourg has ideal conditions for that,” says Mittelbronn, who has been working in the Grand Duchy for two years and has built up the Luxembourg Centre of Neuropathology. He himself has three affiliations: he directs the National Center of Pathology of the LNS and leads research groups at both the LCSB and the LIH. “While establishing the brain bank, I discovered that many research institutes are very interested in this project and are supporting it with great commitment. That makes me very confident that the brain donation programme will be a success.”

More information on brain donation:
www.parkinson.lu/brain-donation

Prof. Michel Mittelbronn
Lab Technicians at the LCSB

More than just support – an essential part of the lab

Annegrät Daujeumont works in the Eco-Systems Biology group of Prof. Paul Wilmes. Among other things, this team studies the microbial communities present in the gut of Parkinson’s patients and compares them with those of healthy volunteers. This involves analysing stool samples from both groups. Daujeumont ensures that molecules such as DNA are extracted from the samples and well-preserved so that the composition of the microbiome of the participants can be reliably determined. From quality control, to managing the stocks of all the required substances and defining the best processes with her colleagues, there is a lot to take care of. Every lab technician ensures that each experiment is carried out safely and according to the highest standards. “Guaranteeing the safety of scientists in the laboratory is especially important,” Daujeumont says, “which is why lab technicians are also trained to be able to provide critical assistance and solve problems in potentially dangerous situations.”

Every working week is different and involves different procedures. “We are never bored. I really like the variety of my job,” she says.

The tasks of the lab technicians are as diverse as the topics of the research groups they are part of. Daujeumont’s colleague Thea Van Wüllen works in the laboratory of Prof. Jens Schwamborn, who heads the Developmental & Cellular Biology group. This team also studies Parkinson’s disease, but is investigating genetic modifications that could have an influence on the disease. For this purpose, researchers and technicians are growing three-dimensional brain organoids in the laboratory. With these organoids, they are trying to recreate complex processes in the brain and to find potential therapeutic approaches.

In order to keep up with so many experiments, the scientists need support in their practical work,” Thea Van Wüllen reports: “Planning the extraction of a protein is somewhat different from actually isolating it in the lab. There is a gap between theory and practice.” This is where the hands-on skills of Van Wüllen and the LCSB technicians prove invaluable. They give advice on what would be the best protocol to address a specific scientific question and help young researchers navigate the lab. The director of the LCSB, Prof. Rudi Balling, fondly refers to the lab technicians as “secret helpers” – by assisting in the daily laboratory routine, they make an essential contribution to the high-quality research at the centre.

Laboratory technicians organise processes to keep things running smoothly in the lab and support the scientists in their practical work. Thanks to their expertise, the LCSB is able to have many complex experiments running at the same time. The two lab technicians Annegrät Daujeumont and Thea Van Wüllen are part of a large team that makes things happen in the various labs of the centre. They look after cell cultures, for example, or assist the scientists in the use of highly sensitive instruments. They also help familiarise new team members with protocols and play a key role in documentation and quality control.

Seven of the laboratory technicians at the LCSB. The full team comprises over 20 people. From left to right: Annegrät Daujeumont, Dean Cheung, Jenny Ghelfi, François Massart, Léa Grandmougin, Jean-François Conrotte, and Audrey Frachet Bour.
EU Grant

Mini-brains join the fight

As part of the EU-funded joint project CONNECT, the connections that exist between the central and the peripheral nervous system in the human body are to be modelled on what is called a Nervous-system-on-a-Chip (NoC). At the LCSB, Prof. Jens Schwamborn will help to develop this innovative technology and use it to better understand and treat neurodegenerative diseases such as Parkinson’s.

Within CONNECT (CONNECTing neural networks: NErvous-system-on Chip Technology), the LCSB is responsible for developing so-called brain organoids. Experts in the Developmental & Cellular Biology group led by Jens Schwamborn form these “mini-brains” from stem cells that are grown into three-dimensional masses of brain tissue. The stem cells Schwamborn’s team is using for this purpose are derived from skin cells taken from healthy volunteers and from Parkinson’s patients. The resulting organoids provide realistic representations of areas and functionalities of the human brain.

“Each organoid bears the characteristics of the respective skin cell donor,” explains Schwamborn. “If it has been grown from the skin cells of a Parkinson’s patient, for example, then processes that occur in the course of Parkinson’s can also be observed in the organoid. Furthermore, the effect certain drugs would have on that specific patient can then be tested in the lab by applying active substances in liquid form to the organoid.”

The brain belongs to the human central nervous system. “In this new device named NoC, it is represented by the brain organoids for which we are providing our expertise in CONNECT,” says Jens Schwamborn. “All parts of the nervous system that are outside the brain and the spinal cord form the peripheral nervous system (PNS). One part of the PNS is, for example, the nervous system of the gastrointestinal tract, called the enteric nervous system. Many Parkinson’s patients suffer from digestive disorders long before the typical motor dysfunctions appear, such as tremors and unsteady gait,” Schwamborn states. “The NoC must accordingly represent an individual patient’s entire nervous system.”

Therefore, all the components mentioned above are all modelled in the NoC and connected to each other by an innovative system of microtubules. According to Prof. Schwamborn, “this makes it possible to study things like the role of certain proteins that migrate throughout the nervous system and are implicated in Parkinson’s disease, which may be useful for diagnostic or therapeutic purposes.”

But he also sees another advantage of the technology: “Theoretically we can produce organoids and Nervous-systems-on-a-Chip in unlimited numbers and thus significantly reduce the need for animal testing.”

Cross-border diagnosis research for Parkinson’s patients

At the beginning of 2019, research teams from the LCSB and the University of Saarland were awarded the second prize in the competition “Excellent Networks in the Greater Region”. The prize is worth 10,000 euros, donated by SaarLB. The Saarland partner in the prizewinning project is Prof. Andreas Keller, head of the Clinical Informatics group in the Medical Faculty of the University of Saarland. His aim is to use biomarkers present in blood – so-called micro-RNAs – for diagnosing diseases at the earliest possible stage. The Luxembourg partner is a team led by Prof. Rejko Krüger, head of the Clinical & Experimental Neuroscience group at the LCSB. Thanks to the large patient and control cohort in the Luxembourg Parkinson’s Study (NCER-PD), his team was able to contribute substantially in defining the role of micro-RNAs as biomarkers for Parkinson’s disease. Keller, as a clinical bioinformatician, is able to selectively identify micro-RNAs that serve as reliable early warning signs of the disease and can therefore be of diagnostic importance. Krüger is happy to say, “The prize makes people in the Greater Region aware of the real medical advancements we are making for the patients, here and across borders.”
Exploring the intricate links between neurodegeneration and inflammation

The Molecular & Functional Neurobiology group at the LCSB, led by Associate Prof. Anne Grünewald, is investigating the role of mitochondria in premature ageing of neurons in the brain of Parkinson’s disease patients. A collaborative project with the Institute of Neurogenetics at the University of Lübeck is focusing on the link between inflammation and neurodegeneration in genetically inherited forms of the disease.

In patients suffering from a familial form of Parkinson’s disease, the first symptoms such as stiff and tense muscles in the arms and legs can already become noticeable at age 40. In this neurodegenerative disease, for which there is still no cure, neurons in the midbrain age faster and degenerate. This leads to progressive movement disorders and, ultimately, to a shortened life expectancy of the patient. Understanding the causes of this neurodegeneration is key to treating the symptoms and stopping the progression of the disease.

Anne Grünewald’s group is investigating the role of mitochondria, cell compartments that produce energy, control key metabolic processes and have their own DNA. “In Parkinson’s patients, we can see a correlation between damaged mitochondria and inflammatory processes,” Grünewald reports. The researchers are especially interested in the decomposition products of mitochondria: the components released when they deteriorate. They look for these components in the blood serum of patients and in cultures of brain cells.

The LCSB’s collaboration partner, the Institute of Neurogenetics at the University of Lübeck where Grünewald also heads a research group, provides blood serum samples from patients with mutations in one of the Parkinson’s disease-associated genes Parkin or PINK1. Blood serum is the liquid surrounding the blood cells. In healthy subjects, it usually does not contain any mitochondrial components. However, mitochondrial DNA was found in the blood serum of the patients examined. “We believe that, in Parkinson’s patients with PINK1 or Parkin mutations, the normal process of mitochondrial recycling is disrupted. The result is that impaired mitochondria are not degraded and go on to release damaged components that are detectable even outside the cells,” Grünewald says. Because there are also indications of inflammatory responses, Grünewald and her team suspect that these mitochondrial components outside the cells trigger an autoimmune response. The degradation of neurons in patients with PINK1 or Parkin mutations might be accelerated by this mechanism.

The next step in this collaborative project is to determine whether the results obtained in the blood serum can be replicated in cultures of brain cells. Since neurons cannot be taken from the patients’ brains, Prof. Grünewald’s team is growing brain cells in vitro. The neurons are differentiated from skin cells of individual patients by using induced pluripotent stem cell technology. “If our hypothesis that the degradation of neurons in the brain of Parkinson’s patients is exacerbated by the body’s own defence mechanisms is confirmed, that would be good news for the patients,” Prof. Grünewald states. “When we have a better understanding of the molecular interactions between neurodegeneration and neuroinflammation, we can try to stop the immune response that is triggered by the mitochondrial DNA. It would be conceivable to test not only anti-inflammatory substances but also treatments that eliminate mitochondrial DNA.”
Interdisciplinary interactions

Physics and biology: a dynamic duo

To deepen their understanding of complex biological systems, researchers at the LCSB use tricks of the trade from physics.

Because of the multitude of molecules involved in the inner workings of the human body, identifying the crucial mechanisms in the development of diseases is like looking for a needle in a haystack. Fortunately, biologists have valuable tools at their disposal to help in this pursuit – some of them borrowed from the toolbox of physics.

Dr. Alexander Skupin, head of the LCSB Integrative Cell Signalling group and physicist by training, makes an analogy to thermodynamic systems such as gas particles: “Physicists describe their behaviour, looking at the individual atoms and molecules,” he explains. “But ultimately, they are interested in macroscopic parameters, like pressure and temperature, that can be derived from them using statistical physics approaches.” Similarly, Skupin argues many biological systems can be described in terms of fundamental components whose properties lead to a better understanding of the global process.

Together with the group of Prof. Massimiliano Esposito at the Physics Department of the University of Luxembourg, Skupin’s team is applying the principles of thermodynamics to living organisms. The researchers are worldwide pioneers in their field. They want to find out, for example, to what extent a disruption in a certain metabolic process can cause cell degeneration – an all-important question for understanding how diseases like Parkinson’s or epilepsy occur. “The neurodegenerative mechanisms involved in such diseases are largely unexplained,” Skupin says.

“I am convinced that the bridge we are building between the two scientific disciplines will make closing such knowledge gaps much easier.” The concept was officially given the green light in 2018 during an international workshop at the LCSB titled “Physics meets Biology.” Thanks to knowledge stemming from energetics, a branch of physics focusing on energy and its transformations, the researchers have now developed a model for dying neurons in the brain of Parkinson’s patients and formed a hypothesis on how the loss of cells ought to be stoppable by intervening in certain activities inside the mitochondria, the power plants of the cells. This first success has already been confirmed in experiments with fish.

The team at the LCSB also works closely together with colleagues from Great Britain and the US on the physics of cell differentiation, and the number of interdisciplinary collaborations will increase in the future. A new research group led by Prof. Anupam Sengupta at the University’s Physics Department has already joined in. These experts on the physics of living matter study, among other things, the properties of microbes and, in collaboration with the group of Prof. Paul Wilmes at the LCSB, the influence that microbes living in the gut have on the brain.

Interdisciplinarity – 10 years of back-and-forth

The LCSB defines itself as an interdisciplinary centre, for which a communication culture is essential. As Prof. Rudi Balling explains: “There is a genuine exchange going on between the disciplines at the LCSB. The scientists know that their research is progressing because they look beyond the horizon of their own field and collaborate with others. Our publications are proof of that as well.” Ten years ago, the motto of Rudi Baling was ‘Physics meets Biology’. Back then it was a vision. To make it a reality, he started discussing science with mathematicians, physicists and engineers. “I had to learn how to do that first. Then I consciously looked for people who were combining biology with other disciplines.” After that, one thing led to another and the LCSB is now studying human diseases in research groups led by physicists, engineers and computer scientists.

Interdisciplinarity will evolve in the future. Digitalisation will become increasingly important in health research. Bioinformatics and computational biology are already well represented at the LCSB, but as Prof. Balling underscores: “This means we too have to become even more involved in the development of digital tools.” Digital Health is associated with many legal and ethical issues. To address these, as well as challenging questions about social influences on health and disease, the LCSB will need people with backgrounds in law and the humanities. Only so will it be possible to make true progress in health research. “Biomedicine meets Humanities” is the new motto.
Fundraising at the LCSB

Donations keep important research moving forward

In 2013, only four years after the institute was founded, biologist Dr. Philippe Lamesch was hired at the LCSB to raise funds for research in areas such as Parkinson’s, Alzheimer’s and rare diseases. The first to donate were foundations situated in Luxembourg, such as the Fondation André Losch and the Fondation Veuve Emile Metz Tesch. Companies and private individuals soon followed suit.

“For the first few years, my work was as much about communication as raising funds,” Philippe Lamesch recalls. “At a time when the name LCSB was practically unknown in Luxembourg, we had to lay a foundation for fundraising and raise awareness of the LCSB among potential donors. Only then could we approach them directly.” Since then, various events have been established, such as Art2Cure, an art exhibition featuring local artists at the BIL’s beautiful art space Galerie l’Indépendance in Luxembourg City. Half of the proceeds go to good causes, including biomedical research at the LCSB. The LCSB is also one of the recipients of donations from the annual Espoir-en-Tête event organised by the Rotary Clubs of Luxembourg. In collaboration with major movie studios such as Disney and Fox, they show a blockbuster movie before its official release in several cinemas across the country. Funds raised go towards brain research in Luxembourg.

It is also important to keep donors informed about the projects they are supporting. Once a year, donors to the University are invited to a ‘Donor Appreciation Event’ on Campus Belval. Here they have the opportunity to meet with researchers and students. It gives the donors a great, sense of satisfaction to meet with the scientists they support and to hear about the progress that was made thanks to their financial support. “The sponsors appreciate not only this personal contact but, just as importantly, the transparency of our communication regarding the use of their donations,” Philippe Lamesch reports.

The fundraising concept at the LCSB is a success and, over time, annually raised funds have increased tenfold. Over the last decade, the fundraising activities at the University have also gradually expanded. In late 2018, a central University Fundraising Office was created. Philippe Lamesch is since then coordinating all fundraising activities with the goal of supporting students and researchers in all faculties and centres. At the LCSB, Dr. Lisa Smits was recently hired to fundraise specifically for the centre, to maintain the strong bond with the long-time donors and develop new fruitful partnerships.

FNR Award: A computer model for cell conversion

In 2019, Prof. Antonio del Sol, head of the Computational Biology group at the LCSB, and Dr. Satoshi Okawa, a member of del Sol’s team, received an FNR Award in the category “Outstanding Scientific Publication”. The prize honoured a scientific article co-authored by del Sol and Okawa that was published in the journal Nature Communications. It presents a computational platform, named “TransSyn”, that can accurately predict how one subtype of cells can be converted into a different subtype. The predictions obtained thanks to the platform have been successfully applied to reprogram stem cells into dopaminergic neurons, the brain cells affected in Parkinson’s disease.

The jury praised the distinguished publication as an important contribution to an area of research that requires better predictive tools. “I think we were successful because we were able to prove with experimental data that our model’s predictions are correct,” says del Sol. “We are honoured by FNR’s acknowledgement of our work.”
A team at the LCSB has managed to improve the diagnostic distinction between Parkinson’s patients and people without the disease – by combining data from different examination methods and using artificial intelligence.

Confirming whether a person with certain characteristic symptoms has Parkinson’s disease is a challenge for medical practitioners. Definitive proof of Parkinson’s-specific changes in the brain can currently only be obtained through a pathological autopsy.

Clinical examinations only provide indirect evidence for these changes and need in some cases to be supported by imaging techniques such as positron emission tomography (PET scan). As part of this method, patients are injected with a tiny and harmless amount of a gamma-emitting radioactive substance that disperses throughout the brain. The radiation pattern from this radioactive marker reveals whether the brain has been affected by the disease.

“Additionally, in recent years, there is a new focus on comprehensively analysing disease-related molecular changes that can be detected outside the brain in living patients,” says Assistant Professor Enrico Glaab, head of the Biomedical Data Science group at the LCSB. “Specifically, we study molecular changes in the patient’s blood.” This got the scientist and his team wondering whether combining the information from two methods – PET imaging and a branch of molecular analysis known as metabolomics – using new machine learning approaches might yield better results.

“We hoped this would allow us to distinguish Parkinson’s patients from unaffected subjects more accurately and robustly, as a step towards a more reliable diagnostic approach,” Glaab says. He and his team conducted a research project to investigate this approach.

“A large number of different metabolites – small molecules produced by the body – were studied in blood analyses,” Glaab relates. The researchers integrated the measurement data from those studies with PET scans of the brain. To evaluate all the datasets together, they employed machine learning: an artificial intelligence algorithm independently learned to read out the typical characteristics of Parkinson’s disease from the data of sixty Parkinson’s patients and fifteen healthy people in a control group.

The LCSB researchers successfully concluded this project: “We were able to show that if we integrate both types of data and use artificial intelligence for the analysis, then we achieve significantly higher accuracy in the distinction between patients and unaffected subjects,” Enrico Glaab reports. Furthermore, using this method, the bioinformatician and his team at the LCSB were the first to confirm that metabolomics can provide added value for the detection of Parkinson’s disease. “The advantage of a combined analysis had not been statistically confirmed before,” says Glaab.

“The method is currently mainly a research tool,” he remarks, “but we hope we can further develop it towards clinical applications.”

The aims of this research, which Glaab and collaborators published in the journal *Neurobiology of Disease* in 2019, extend beyond the improved diagnosis of Parkinson’s disease: “Our goal is to understand Parkinson’s better and to gain more detailed insights into the molecular alterations associated with the disease,” the scientist emphasises. Also, more accurate early diagnosis is an important prerequisite for the development of new treatments that could one day halt the disease process.
Alumni Day

Wisdom from the previous generations

In September 2019, to celebrate its 10th anniversary, the LCSB invited its alumni to join the current team members for a day of presentations and discussions. It was an opportunity to meet up with old friends but also to learn what career paths one can embark on after leaving the LCSB. From forging a future as a scientist in academia or as part of a research support team to switching to a brand-new job in the private or public sector, five former colleagues told their very diverse stories. In the short interviews below, they give a glimpse of what they did at the LCSB, what they remember from their time at the centre and where it has led them since.

Dr. Maike Aurich
I worked at the LCSB as a research associate in the Molecular Systems Physiology group between 2013 and 2017. I developed approaches to use what we call "omics data" to better understand human metabolism and study what cells do in the case of disease. For example, I explored what metabolic pathways can be found in cancer cells and what are the molecular and cellular processes specific to Parkinson's patients.

I am now a Research and Education manager in the Hopitaux Robert Schuman hospital group. I use my experience as a researcher to facilitate scientific activities and training within the hospital.

An event that made a lasting impression on me was when the participants from the Luxembourg Parkinson's Study came to the LCSB. Meeting patients and discussing our work with them was a valuable reality check. We must never forget the people behind the data. Plus, it was a typical Luxembourgish experience, where we had to switch between German and French to communicate with everybody!

Dr. Anna-Lena Hiljie
While I was a post-doctoral researcher in the Developmental & Cellular Biology group between 2013 and 2016, I saw the LCSB in its early stages. Setting up a new lab after the group's move from Münster and later on moving this lab from BT1 to BT2 were very important experiences. I also had the chance to implement a new module for Master's students at the University of Luxembourg. All of this was crucial when deciding in which direction my professional career should go.

It is also helpful for my current job as Site Coordinator of the German Center for Neurodegenerative Diseases in Tübingen. Here, I am responsible for administrative tasks such as personnel and budget management, communication and technology transfer. I am also coordinating various scientific seminar series, organising an international Summer School and teaching at the Graduate School for Neuroscience.

During my time at the LCSB, I came to realise that we all have a lot more expertise than we think, especially the amount that we gain from work and life experience. I still remember standing at the coffee machine, chatting with people I had never talked to before. The concept of having a single common coffee machine was a great idea! From the perspective of a coordinator, I can now tell how hard – and how important – it is to get people from different groups and different fields in contact with each other.

Dr. Thanneer Malai Perumal
I was a research associate at the LCSB between 2012 and 2015. I was part of the Computational Biology group and my work focused on stem cell research applied to cancer and brain diseases.

Afterwards, I joined the Maastricht Centre for Systems Biology in the Netherlands until 2018 and finally moved to the Flemish Institute for Technological Research in Belgium as a Principal Investigator. I now conduct applied research to translate state-of-the-art techniques and methodologies into daily clinical practice.

I joined the LCSB at an early stage in my career and I experienced it as a very inspiring environment where the pursuit of knowledge was always the main focus. Being in close proximity to many high-level researchers allowed me to learn, in a relatively short amount of time, different skills that are key to becoming a successful academic. My time at the LCSB also helped me realise what I value most in science and the areas in which I needed to develop to mature as a scientist.

I attended the 2014 Lindau Nobel Laureate Meeting as a representative of Luxembourg after being presented as a candidate from the LCSB. It was truly a fantastic event! For me, it is a perfect example of the opportunities offered to LCSB researchers. I think the spirit of the LCSB and its focus on scientific excellence has not changed since then, and is still its driving force.

Dr. Gökhan Ertaylan
I was a post-doctoral researcher in the Developmental & Cellular Biology group between 2013 and 2016. It was a stressful time, moving all the lab equipment and our offices. But I remember it especially fondly because we all kept the LCSB team spirit alive. We made it by sticking together!

Jill Bohler
I was a lab technician at the LCSB until April 2018. I worked within the Clinical & Experimental Neuroscience group for almost four years, and that was an opportunity to gain a great deal of professional experience. I learned a lot, both in terms of scientific knowledge and project management. This experience made it possible to take on a position with more responsibilities afterwards. I am now working for the police forensic department of Police Lëtzeburg - Service de Police judicair - Section Police scientifique.

I remember the move from Biotech 1 (BT1) – our first building on Campus Belval – to the brand-new BT2 in September 2015. It was a stressful time, moving all the lab equipment and our offices. But I remember it especially fondly because we all kept the LCSB team spirit alive. We made it by sticking together!

Dr. Thanneer Malai Perumal
From 2012 to 2014, I was a research associate in the Computational Biology group, where I studied biological networks and developed algorithms with applications in different collaborative projects at the LCSB, such as the Parkinson's Disease map and research on cellular reprogramming.

I then worked as a senior researcher at Sage Bionetworks, a non-profit organisation promoting open science and collaborations to accelerate biomedical research. There, I coordinated consortia on Alzheimer’s, schizophrenia and sepsis, and studied data collected from remote patient monitoring applications. I have now joined the healthcare company F. Hoffman-La-Roche, where I focus on digital biomarkers.

The diversity at the LCSB, both in terms of nationalities and scientific fields, taught me a lot. Having these diverse groups under one roof, you learn from one another and solve problems in a collaborative manner. It also helped me to adapt the way I interact with people from different backgrounds. To this day, this is still very useful in my career. Another skill that I learned through my stay at the LCSB is how to be able to re-invent yourself in the ever-changing scientific landscape.

One of my favourite memories is the LCSB team retreat in 2013. The scientific discussions that day sparked my interest in the lack of phenotypes in neurodegeneration and led me to where I am today. And the team-building activities were great fun!
Short stories from the LCSB

Events 2019

1 When the labs open their doors
On 23 March, the LCSB participated in the annual Open Day organised by the University of Luxembourg. Future students, parents and the general public, who came to learn more about the study programmes and visit the campus, were invited to have a look behind the scenes of biomedical research. During four guided tours through the LCSB labs, visitors discovered how scientists work together to better understand the mechanisms of diseases. Some researchers explained how they can turn skin cells into nerve cells to study the effects of Parkinson’s disease, and showed samples of brain organoids, small 3D cell cultures developed at the LCSB. Meanwhile their colleagues explored how they investigate the interactions between human cells and the microbes that live inside the human gut with HuMiX, an artificial gut model.

2 RIKEN Outpost Labs in Luxembourg
In July, the link between Luxembourg’s and Japan’s research was strengthened by the signature of a Memorandum of Understanding between the University of Luxembourg, the Luxembourg Institute for Health and the Japanese institute RIKEN. As a result, senior scientists from RIKEN will carry out research projects in Luxembourg in collaboration with local researchers, within so-called joint RIKEN Outpost Labs.

3 Fourth edition of the NCER-PD social event
At the beginning of the summer, the NCER-PD team invited all participants of the Luxembourg Parkinson’s Study to join the annual get-together and celebrate the study’s excellent international evaluation results. Around 120 participants and their families discovered how neurons are reprogrammed from donated skin samples, what impact the environment can have on Parkinson’s, how wearable sensors can help to collect data on patients’ gait and how brain donation after death can contribute to advances in Parkinson’s research.

4 Bridging the scales of the brain
The yearly LCSB symposium addressed the complexity of the human brain by bringing together world-wide leading experts from experimental and computational neuroscience in an interdisciplinary framework. The programme focused on the integration of the different biological scales ranging from molecules to the whole brain. Speakers and participants discussed their work, illustrating how cutting-edge approaches, such as single cell biology, neuroimaging and connectomics, can generate insights on the dynamics of the brain in health and disease.

5 Fun science for all!
With their interactive workshops about genetics and dynamic systems, the LCSB and the Scienteens Lab entertained hundreds of visitors during the Science Festival. This four-day event, held from 7 to 10 November in Luxembourg City, promoted science education in Luxembourg and aimed at connecting science and society. The LCSB offered a playful approach to genetics with DNA extraction from saliva and small tests to illustrate heritability. Meanwhile the Scienteens Lab interested young and old alike in a “fox and rabbit” game to understand the relation between predators and their preys. Experiments and demonstrations drew a crowd from start to finish!

6 Spotlight on quality
The second edition of the LCSB Quality Day took place on 28 November, focusing on data protection, FAIR data (findable, accessible, interoperable, and reusable) and study design. Reflecting on how we work, the team identified best practices and areas for improvement, opening plenty of projects for 2020.

7 Team life
At the beginning of July, the LCSB members had the opportunity to escape from the usual routine and interact with their colleagues in a new way. A team retreat paired each participant with an “alien” from another group. They had two hours to get to know each other and understand their respective work. In short, computer scientists stepped into the lab while biologists dived into code, administrative staff ventured into science while researchers discovered the support machinery. If the perspective had some break out in cold sweat, the result was indisputable: learning about your colleagues’ work is enjoyable – especially when it ends with a barbecue – and always useful!

8 A festive thank you
As donations are a very important part of research funding, the LCSB welcomed around 60 of its beneficiaries on 27 November to thank them for their contribution and show what was made possible by their involvement. The evening started with a meet-and-greet followed by lab tours. It ended with a reception in the Hall des Poches with all the sponsors of the university, to celebrate the creation of a central fundraising office at the university. All year long, the LCSB also welcomed long-term donors and prospective new ones for presentations and lab tours. These visits are crucial to raise both awareness and funds.
Facts and figures

2019 LCSB income (in kEUR)

- **University of Luxembourg**
- **Luxembourg National Research Fund (FNR)**
- **EU programmes**
- **Funds for knowledge transfer**
- **Further grants**
- **Wages**
- **Investigations**
- **Travel**
- **Representation and registration**
- **Sub-contracting**

2019 LCSB expenses (in kEUR)

- **University of Luxembourg**
- **Luxembourg National Research Fund (FNR)**
- **EU programmes**
- **Funds for knowledge transfer**
- **Further grants**
- **Wages**
- **Operating expenses**
- **Investigations**
- **Travel**
- **Representation and registration**
- **Sub-contracting**

Fundraising

- **Donors**
- **Corporate**
- **Associations**

European grants in 2019

- **Project acronym**
- **Programme**
- **LCSB responsible**
- **Project coordinator (if applicable)**

National grants in 2019

- **Project acronym**
- **Programme**
- **LCSB responsible**
- **Project coordinator (if applicable)**
### Key performance indicators

| Personnel | Research groups: 16  
|           | PEARL (active): 2 (2*)  
|           | ATTRACT (active): 5 (2)  
|           | Total staff: 230  
|           | Externally funded staff: 119  
|           | PhD students: 52  
| Nationalities: 69 |

| Innovation | Patents: 29 *  
|            | Proof of concept: 8 (total 3.5 M EUR) *  
|            | Spin-offs: active: 5  

| Collaborations | Collaborative projects active in 2019: >480  
|                | Industrial partners in active projects: 65  

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<th>External competitive funding °</th>
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| Publications | Total publications: 132  
|             | Publications IF > 10: 22  
|             | Publications in 25% best of field: 83%**  
|             | Cumulative number of publications°: 883  

* one jointly with other national partners  
° cumulative (2009–2019)  
** based on WoS

### Scientific advisory board

<table>
<thead>
<tr>
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<tr>
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### LCSB organigram

#### Director’s office
- Personal assistant
- Scientific officer

#### LCSB Director (R. Balling)

#### Research Strategy (P. Meisch)
- Bioinformatics Core (R. Schneider)
- Developmental & Cellular Biology (J. Schiemann)
- Enzymology & Metabolism (C. Linster)
- Molecular & Functional Neurobiology (A. Grünewald)
- Clinical & Experimental Neuroscience (K. Krüger***)
- Interventional Neuroscience (P. Wilmes)
- Neuropathology (M. Mittelbronn)**
- Integrative Cell Signalling (A. Skupin)
- Systems Control (J. Gonçalves)
- Clinical & Experimental Neuroscience (R. Krüger***)
- Environmental Chemoinformatics (E. Schymanski)
- Medical Translational Research (J. Schneider)

#### Animal facilities Aquatics & Rodents (R. Balling)

#### Bioinformatics services (R. Schneider)

#### Imaging (A. Skupin)

#### Metabolomics (C. Linster)

#### Sequencing (P. Wilmes)

#### Scientific central services
- Infrastructure (N. Bonjean)
- Operations (A. Vogler)
- Shared UL Functions °
  - HR, IP, DPO, etc.

#### Safety
- Safety & Biosafety
- Quality assurance & SOPs

#### Equipment
- Instrument care & purchase
- Technology platforms

#### Communication
- External & Internal communication
- Event management

#### Finance & Grants
- Budget planning, reporting & control
- Grants services

#### Innovation & Partnering
- Business Development & Legal
- Technology transfer

#### Management & Strategy
- Strategic planning
- Process management

#### Scienteens Lab
- Curriculum development
- Outreach to schools

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#### Experimentation groups
- in cooperation with CHL

#### Medical groups
- in cooperation with LNS & LIH

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LCSB collaborations

USA: 55 projects (5*)
Canada: 6 projects (1*)
Argentina: 2 projects (1*)
Brazil: 3 projects (1*)
Portugal: 5 projects (1*)
France: 2 projects (1*)
Spain: 5 projects (1*)

Collaboration partners

337 (78%)
15 (3%)
3 (1%)

* Project within a multinational consortium

Staff categories 2019

Researcher: 36 (16%)
Management & Admin: 52 (22%)
PhD student: 108 (47%)
Technician: 34 (15%)

Staff origins

Europe: 76% Africa: 3%
North America: 4%
South America: 4%
Asia: 1%
Oceania: 1%

Awards 2019

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<td>FNR Award - Outstanding scientific publication</td>
<td>Antonio Del Sol</td>
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<td>FNR Award - Outstanding PhD thesis</td>
<td>Linda Wampach</td>
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<td>Competition “Excellent Networks in the Greater Region” - Second prize</td>
<td>Rejko Krüger (LCSB) and Andreas Keller (University of Saarland)</td>
</tr>
<tr>
<td>Falling Walls Luxembourg 2019 - Second prize</td>
<td>Kacy Greenhalgh</td>
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<td>Falling Walls Luxembourg 2019 - Audience prize</td>
<td>Ursula Heins-Marroquin</td>
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<td>European Bioinformatics Institute (EMBL-EBI) Metagenomics Bioinformatics training course - Best poster prize</td>
<td>Laure De Ners</td>
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<tr>
<td>India-EMBO Symposium on the human microbiome - Poster prize</td>
<td>Sushil Buni</td>
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<tr>
<td>Activ Motif - Epigenetic Services Grant Competition - Winning abstract</td>
<td>Biomedical Data Science group (LCSB) and Epigenetics group (LSRU)</td>
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<tr>
<td>Luxembourg Healthcare Summit - 2019 Healthcare Research Award</td>
<td>HubAX - Paul Wilmes, Kacy Greenhalgh and Kris Ver Donck</td>
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Publications 2019

Books
1. Jake Powell, Martin Falkie, Alexander Skopoullis, Werner Brack, Cyrus Eng, Rutger Tho "A Statistical View on Calcium Oscillations". Calcium Signaling: Advances in Experimental Medicine and Biology 1333 - 799-826, 10.1007/978-3-030-02657-3_32
2. Sael Quresumwet, Ameur Fauquier "Hernia in a Human Cerebral Organoid: A Specialized Method to Resolve Fine 3D Features of Astrocytes in Nonhuman Primate (Macaca fascicularis) and Human Fixed Brain Samples." Astrocytes: Methods and Protocols, Methods in Molecular Biology (Clifton, N.J.), 1938 - 85-95, 10.1007/978-1-64231-968-5_5

Conference Proceedings
5. Johannes Coudray, Daan Caljouw "Kinship driven multiscale modeling reveals the role of the striatal stabilizing system.". Journal of Neuroscience, 39 - 10.1523/JNEUROSCI.8122-18.2019

Peer-reviewed articles