LCSB

University of Luxembourg

LCSB - Luxembourg Centre for Systems Biomedicine

Highlights 2022

uni.lu
UNIVERSITÉ DU LUXEMBOURG

LCSB in brief

The LCSB is an interdisciplinary research centre at the University of Luxembourg. Its 270 staff members combine their expertise in a broad spectrum of disciplines - from computational biology to clinical and experimental neuroscience – to study the brain and its diseases. Research at the LCSB focuses on neurodegenerative diseases such as Alzheimer's or Parkinson's. Collaboration between biologists, medical and computer scientists, physicists, engineers as well as mathematicians offers new insights into complex biological mechanism and disease processes, with the aim of developing new tools for diagnostics, prevention and therapy.

The LCSB has established strategic partnerships with scientific partners worldwide and with all major biomedical research units in Luxembourg. The centre also carries out collaborative projects with hospitals and research-oriented companies, accelerating the translation of fundamental research results into clinical applications, for the benefit of patients. ■

Table of Contents

From left to right: Prof. Jens Kreisel, Claude Meisch, Simone Asselborn-Bintz, Prof. Iris Behrmann, Frank Wallenborn, Mauricio Bei and Prof. Michael Heneka.

A new building for biomedical research

On 29 November 2022, Claude Meisch, Minister of Research and Higher Education, and Simone Asselborn-Bintz, Mayor of Sanem, broke ground for the new Biotech 3 building (BT3) on Campus Belval, in the presence of a university delegation and the developers of the building. BT3, whose opening is scheduled for 2026, will foster interdisciplinary research and outreach activities.

It will host both laboratory and office spaces for researchers of the LCSB and the Department of Life Sciences and Medicine of the University of Luxembourg, on a total of 7400 square meters. BT3 will also include dedicated spaces to engage with society: a visitor centre, a small exhibition area and a laboratory dedicated to scientific workshops for high school students.

BT3 will be connected to the existing Biotech 2 building via a footbridge. Through this connection, all the research groups of the LCSB will be reunited under one roof. “Being interdisciplinary is a key aspect of neurodegeneration research at the LCSB, which relies on proximity and exchange,” details Prof. Michael Heneka, director of the LCSB. “I am very much looking forward to finally bringing all our groups closer together.” ■

Breaking new ground

How to best summarise my first year as the new director of the LCSB? Mentioning that we broke ground for Biotech 3 is a good start. The constructing of the new building that will host our researchers started November 2022 and it embodies well what happened in the past months. The story of the LCSB keeps unfolding: projects initiated long ago are coming to fruition and brand-new initiatives are launched. We are taking the next steps, building on the strong foundations of our centre.

Research is in full swing. We have strengthened our focus on neurodegenerative diseases, with the addition of a new research group studying neuroinflammation, the launch of a large study on risk factors and several exciting publications on Parkinson’s, Alzheimer’s, and ageing in general. Tandem projects aiming to promote interdisciplinary research and collaboration within the LCSB have been launched successfully. The centre is also part of far-reaching research initiatives involving national and European partners, such as the new centre of excellence in digital health and personalised healthcare (Clinnova).

Our infrastructure and services are evolving as well. We have developed the platforms that provide access to equipment and expertise to researchers, at the LCSB and externally. We have implemented sustainable practices in our labs and further improved animal welfare in our facilities. Lastly, a dedicated team has streamlined our publication process, to foster reproducibility and adhere to the latest scientific standards.

In many ways, research relies on human connections and exchanges. In that sense, 2022 was also marked by the LCSB team getting back together after the pandemic. This meant we could organise and participate in stimulating scientific conferences, lively internal events and exciting outreach activities. What a treat!

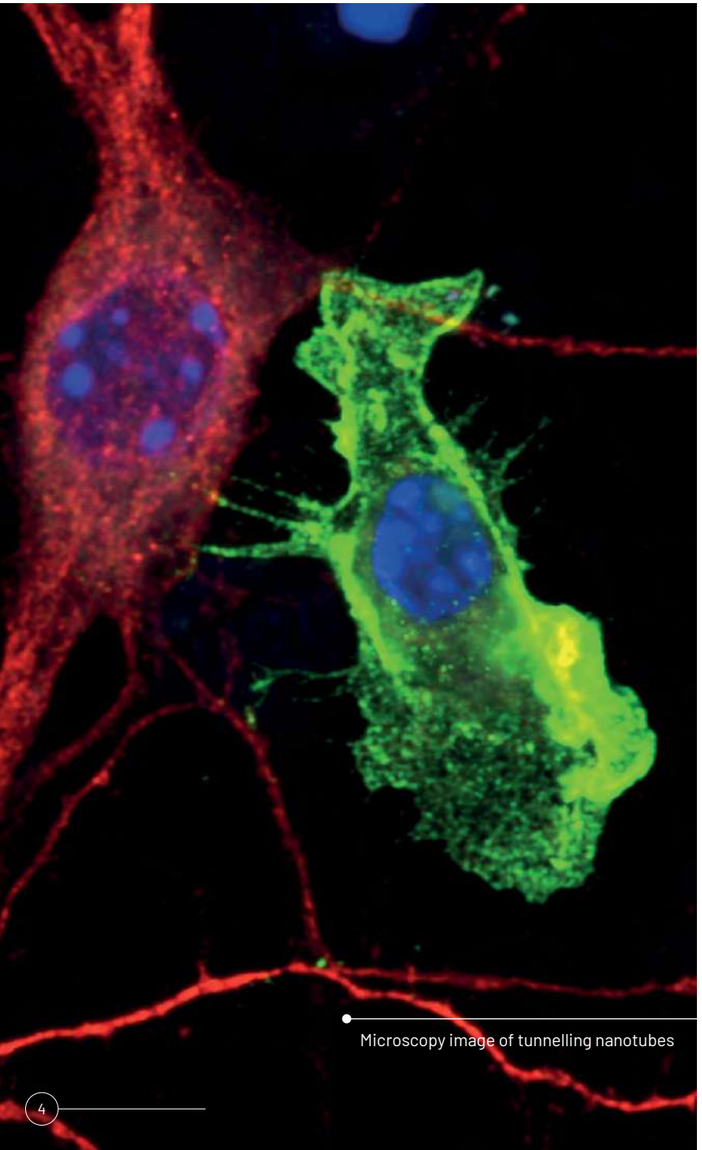
After a year of transitions, it is now time to think about the future. We have asked a group of renowned scientists to be part of the new advisory board of the LCSB. With their guidance and the contribution of our remarkable team, we will shape the LCSB strategy for the coming years. The strategy will aim to broaden current knowledge about the human brain and to break new grounds in neuroscience.

Michael Heneka

back to table of contents

Exploring neuroinflammation and its role in Alzheimer's disease

The World Health Organisation has identified dementia as a major health issue. Approximately two-thirds of all dementia patients suffer from Alzheimer's disease. To date, the mechanisms responsible for this neurodegenerative disorder remain unclear and neither preventive nor disease-modifying therapies exist.



Microscopy image of tunnelling nanotubes

At the LCSB, the new research group led by Prof. Michael Heneka studies the underlying mechanisms of Alzheimer's disease, in particular the role of the immune system and its dysregulation.

With an expected increase from currently 55 million cases to about 150 million in 2050, dementia will significantly affect healthcare systems worldwide. Alzheimer's disease is the most common cause of dementia. This neurodegenerative disorder leads to memory dysfunction, behavioural disturbances and loss of all higher cognitive functions. "It has become increasingly clear that Alzheimer's is, in fact, not a disease of the elderly but starts much earlier in life," explains Michael Heneka, director of the LCSB and head of the Neuroinflammation group. "Understanding its origins is therefore key to being able to detect and treat it before the devastating effects on the brain fully appear."

As a board-certified neurologist and clinician-scientist, Heneka has extensive experience in studying neurodegenerative diseases at experimental, preclinical and clinical levels. With the help of his group at the LCSB, he is now looking at these diseases through the lens of immune mechanisms in the central nervous system. Active since May 2022 and steadily growing, the new team focuses on early immune processes to better understand neuroinflammation, a common hallmark of neurodegenerative diseases.

The Neuroinflammation team

> From research to clinical applications to improve care for dementia patients.

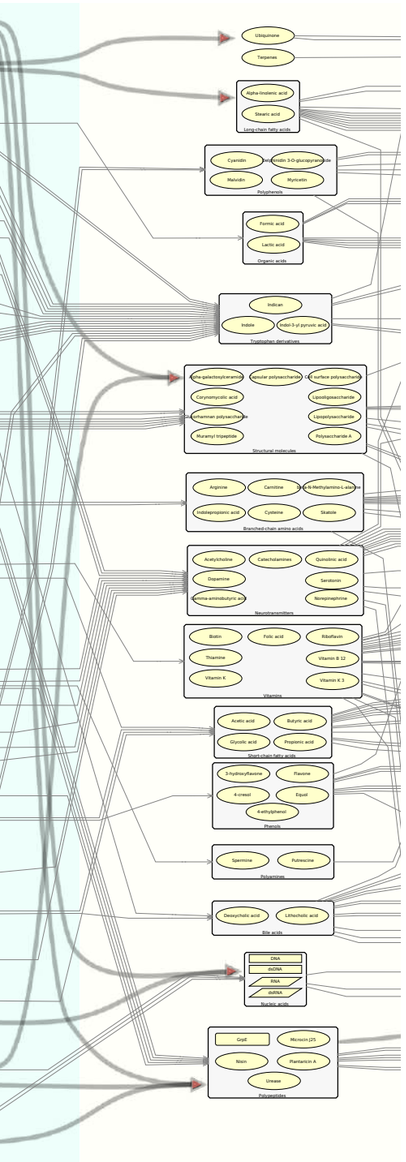
At the end of the year, the Luxembourg National Research Fund (FNR) has awarded an FNR PEARL Chair to Michael Heneka for a research project called MINIALZ. With this new project, endowed with 3.9 million euros, the Neuroinflammation group will further disentangle the role of genetic and environmental influences, such as diet and lifestyle, on the onset and progression of Alzheimer's disease. "We will study the interaction of immune cells and neurons in the brain, both in animal models and in cell cultures directly derived from blood samples given by patients," details Michael Heneka. "Our aim is to better understand what role the brain immune cells play in keeping neurons healthy and what happens if their interactions are altered."

The project will capitalise on the recent identification of a new mechanism by Michael Heneka's team: microglia, the immune cells of the brain, form connections with neighbouring neurons. These so-called tunnelling nanotubes are used to free the nerve cells from pathological proteins, ensuring their function and survival. Preliminary results suggest that the mechanisms involved are defective in microglia carrying mutations associated with Alzheimer's disease, placing this network of nanotubes at the core of neurodegeneration. This brand-new field of study is promising, opening new avenues for several brain diseases and eliciting a lot of interest in the international scientific community.

By studying the underlying mechanisms of Alzheimer's disease at the molecular level, MINIALZ will give important indications for earlier diagnosis and potential treatment options. "We want to coordinate fundamental research on dementia in Luxembourg with translational and clinical research efforts," says Michael Heneka. "Our results should help to develop new biomarkers and therapeutic measures, and support Luxembourg's ambition to provide excellent healthcare to dementia patients." ■

back to table of contents

The Expobiome Map: exploring the role of microbiome-derived molecules



https://expobiome.lcsb.uni.lu/minerva/

The human microbiome, the collection of microorganisms that live in and on our body, is intricately connected to our health. Recent studies have shown that these microbial communities are implicated in various diseases and that the molecules they produce could be drivers of many pathogenic processes, including inflammation. However, much remains to be discovered about the biology of the microbiome and its complex interactions with the human host, especially the way by which gut microbiome-derived molecules shape our immune response.

In health, the gut microbiome confers essential functions, such as digestion and synthesis of vitamins, contributes to the metabolism and plays an important role in the regulation of the immune system. In contrast, perturbations of this microbial community – called dysbiosis – have been reported in several chronic diseases associated with local or systemic inflammation, including neurodegenerative diseases. The microorganisms that inhabit our digestive tract produce a wide range of molecules. Our organs and tissues are exposed to this group of biomolecules, coined the "expobiome" by LCSB researchers. They include nucleic acids, peptides, proteins and metabolites, and impact human physiology in multiple ways. "In order to understand the causal roles of this molecular soup in the context of pathogenesis, it is therefore crucial to understand how they affect the human body, including the immune system, from a systemic perspective," explains Prof. Wilmes, head of the Systems Ecology group.

This is where the Expobiome Map, a new interactive tool developed as part of the ERC-funded project ExpoBiome led by Paul Wilmes, comes into play. It compiles the current knowledge about interactions between microbiome-derived molecules and immune pathways, allowing scientists to explore the growing body of literature on the topic and providing a basis to develop new hypotheses.

Members of the Systems Ecology group, the Bioinformatics Core and the Medical Translational Research group collaborated to integrate information from several databases and from the literature in the form of a visual display. The resulting map showcases a complex network of interactions involving numerous combinations of molecules, which contribute to many different disease processes. It can be browsed online and will help the scientific community to identify knowledge gaps or make inferences on likely links between specific microbes and diseases. "It is meant as a way to connect the dots, a basis to contextualise and expand our current understanding of the mechanistic role of the gut microbiome in human health and disease," concludes Wilmes. ■

From left to right: Prof. Stéphane Pallage, Dr Laura De Nies and Prof. Paul Wilmes

Award for excellent thesis on antimicrobial resistance

During the 2022 PhD graduation ceremony, Dr Laura de Nies, who obtained her PhD at the LCSB, received an Excellent Thesis Award for her work on "Microbiome reservoirs of antimicrobial resistance". This award presented by the University of Luxembourg recognises the exceptional quality of the research conducted by a doctoral graduate.

As a PhD student in the Systems Ecology group, Laura de Nies worked on antimicrobial resistance (AMR), which occurs when microbes evolve over time and no longer respond to antibiotic drugs, making bacterial infections harder to treat. "AMR presents a global threat to public health as emerging resistant bacteria residing within human, animal and environmental reservoirs may spread," she explains. To better understand the spread of AMR, she studied antimicrobial resistance mechanisms in different samples, from the gut microbiomes of infants and mice to microbial communities in wastewater treatment plants and glacierfed streams. The results obtained during her PhD, which have already been published in several scientific journals, improve our understanding of antimicrobial resistance and indicate possible transmission routes for its dissemination from the environment to humans. ■

Watch the Video

back to table of contents

A new survey to detect risk factors for neurodegenerative diseases

In September 2022, the National Centre of Excellence in Research on Parkinson's Disease (NCER-PD), coordinated by Prof. Rejko Krüger, launched an online survey to explore methods for risk prediction for neurodegenerative disorders. Over the course of a year, the researchers plan to reach 10,000 participants from Luxembourg and the Greater Region.

The earlier Parkinson's disease is diagnosed, the better the chances of optimally treating the symptoms and avoiding complications. In the framework of NCER-PD, researchers from the LCSB and the Luxembourg Institute of Health work together to improve the early detection of Parkinson's and develop new options for disease prevention. They focus on identifying risk factors as well as pinpointing early signs of neurodegeneration. Since 2015, the NCER-PD team has developed strong expertise in clinical research on Parkinson's, following large cohorts of participants over several years and developing the infrastructure to collect, store, share and analyse vast amounts of data in accordance with the highest scientific standards and European regulations. Taking advantage of this long-standing know-how and of a successful first survey on sleep quality and Parkinson's disease carried out in 2021, the team is now investigating risk factors for neurodegeneration more extensively.

The new study, entitled "Healthy Ageing" (HeBA), focuses on methods for risk prediction and the identification of people at risk of developing neurodegenerative diseases. Residents in Luxembourg and the Greater Region – between 50 and 80 years old and not diagnosed with Parkinson's or dementia – are invited to fill in a detailed online questionnaire covering a wide range of topics such as demographics, occupation, lifestyle, and medical history. This information will allow the researchers to calculate individual risk scores and to offer people with specific scores the possibility to benefit from further in-depth clinical assessments. "We hope to ascertain the influence of different potential risk factors and that this will help us progress towards targeted prevention for neurodegenerative diseases such as Alzheimer's and Parkinson's," details Prof. Rejko Krüger.

To participate in the study and contribute to research, go to www.heba.lu

The survey is part of a collaboration with research centres in Kassel and Göttingen (Germany), Innsbruck (Austria) and Barcelona (Spain). The objective is to have several thousand participants in each location. "As always for clinical advances, the active participation of volunteers is key," highlights Rejko Krüger. "We are very thankful to the people who dedicate their time to this important research. The information they provide is crucial to learn more about the risk factors and initial symptoms of neurodegenerative diseases, and to develop novel prevention strategies that are urgently needed." This concerted effort, leveraging the expertise of the NCER-PD team and building on an international collaboration, should lead to the creation of a European hub for risk screening for neurodegenerative diseases. The main objective is to find out how methods for risk factor assessment and early detection at the population level translate into individual risk predictions. Being able to identify people close to developing Parkinson's or dementia will indeed be crucial, once curative treatments become available.

> Exploring risk prediction to make progress in terms of prevention

HeBA is supported by the Michael J. Fox Foundation for Parkinson's Research (MJFF), a major actor in research on Parkinson's disease worldwide, whose aim is to ensure the development of improved therapies for those living with the disease. MJFF identifies and funds projects most vital to patients, and coordinates the efforts of multiple scientific teams worldwide. The foundation has taken an interest in the research conducted in Luxembourg and its support to HeBA – with one million euros over three years – is the first step towards Luxembourg joining a global MJFF initiative: the Parkinson's Progression Markers Initiative. This extensive study includes more than 50 research institutions contributing data and biological samples to one of the most robust Parkinson's databases and specimen banks worldwide. "We are very excited about the opportunity of joining this prestigious international network and can be very proud of the efforts of the NCER-PD team over the past eight years. It demonstrates that Luxembourg is highly recognised on the international stage among the key players in Parkinson's research," Krüger concludes. ■

back to table of contents

FNR Award for precision medicine

On 20 October 2022, the Luxembourg National Research Fund (FNR) presented the FNR Awards to reward exceptional contributions to science in Luxembourg. During the ceremony, Prof. Rejko Krüger, head of the Translational Neuroscience group at the LCSB and director for Transversal Translational Medicine at the Luxembourg Institute of Health (LIH), and Dr Ibrahim Boussaad, researcher at the LCSB, received the 2022 FNR Award for Outstanding Scientific Achievement.

The award was attributed to the two scientists and their team for the first proof-of-concept for precision medicine in Parkinson's disease. This long-term translational research project resulted in the publication of scientific articles in high-impact peer-reviewed journals and the registration of patents at the national and European level. It also led to the set-up of the first inter-institutional infrastructure for early drug discovery between the LCSB and the LIH. "Integrating a wide range of expertise across different disciplines over the past seven years was essential to carry out and finally succeed in this extensive project," underlines Krüger. "It is a great honour for us to receive such a prestigious award and to turn the spotlight on precision medicine for Parkinson's disease."

The project was supported by the FNR through a PEARL grant and the National Centre for Excellence in Research on Parkinson's disease (NCER-PD). ■

Watch the Video

A publication pipeline

Scientific publishing has changed dramatically over the past two decades. While the focus used to be entirely on the manuscript itself, today it is much more about the complete publication, which includes data, computer code and lab protocols. To help researchers handle the ever-growing requirements and continue publishing high-quality papers, the LCSB has established the Pre-Publication Check (PPC).

"The PPC is similar to the checklist that pilots have to go through before every flight," says Dr Laurent Heirendt, one of the initiators of the project. Researchers who want to publish, upload their manuscript to the LCSB's publication platform before submitting it to a journal. Heirendt and his colleagues then run partially automated checks and identify any missing research assets. "We do not look for scientific soundness. That is what the journal's peer review process is for," says Heirendt. Rather, the PPC team makes sure the raw material and background information – what is called research assets – are all accounted for. Ultimately, it is the data and code that enable other research groups to reproduce results and build upon them. "Research is like construction," he explains. "You lay one brick on top of another, so, if you leave gaps, others will have difficulties to build upon your work. If it is not reproducible, it cannot make a good foundation for further scientific research."

The PPC is designed to address this issue. There is more to it than just proofing data and code. Using various automated software tools, Laurent Heirendt and his colleagues also evaluate the scientific rigor, check for plagiarism, verify legal aspects and identify intellectual property. Once publications have successfully passed the PPC process, the authors can be sure that they meet the latest quality standards. They also comply with the FAIR (Findable, Accessible, Interoperable, and Reusable) principles for research assets and with the European law on data protection (GDPR).

"Studies show that the reproducibility of publications that do not go through such a process drops noticeably within five years," Heirendt mentions. "What is the use of publishing a breakthrough paper in a recognised journal if nobody cites it five years down the line because your computer code or data are not available anymore?" The PPC, he believes, is therefore far more than just the quality assurance of a publication; it is a long-term investment in public research.

After a test phase, the PPC will be implemented for all LCSB publications in a stepwise manner during 2023. Of course, the PPC team is there to accompany researchers along the way. "There is a PPC bootcamp, where we answer all questions related to this quality insurance tool," Heirendt announces. "It is accompanied with extensive documentation as well as personal advice and support for highly individual questions." ■

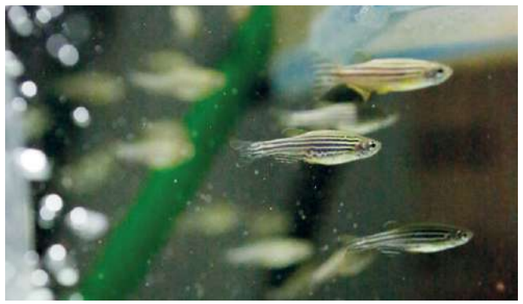
back to table of contents

Expert skills and cutting-edge facilities

Through seven platforms, the LCSB provides scientific services: access to specific equipment and expertise needed to support research in various fields.

Cutting across disciplines, from neurosciences to data science, from immunology to microbiology, the LCSB integrates different technologies and models. Platforms guarantee that important resources are easily available to all research groups. They also offer fee-based customised services to external users at national and international level. The existing facilities provide state-of-the-art equipment in the fields of sequencing and single-cell analysis, metabolomics, animal research, bioinformatics, bioimaging and high through-put screening.

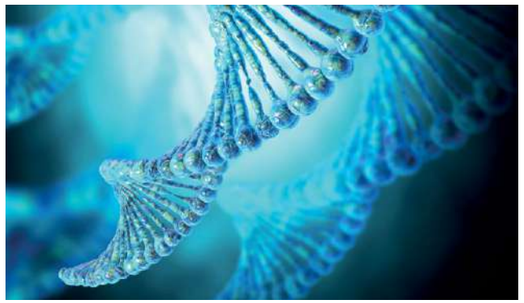
The seven platforms are run by highly skilled teams. These dedicated platform managers and technicians contribute to method development and ensure knowledge transfer. Over the coming years, the LCSB platforms will keep developing their portfolios, in close alignment with the needs of the scientific community.



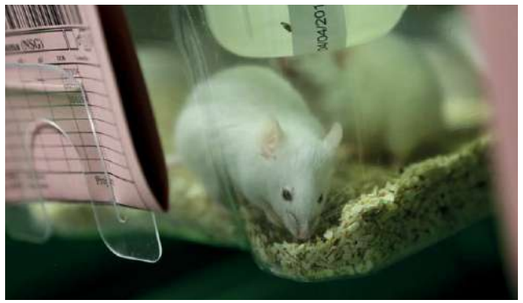
The **Aquatic platform** consists of a modern, semi-automated facility that provides husbandry and embryo production for zebrafish. Robotic feeding and maintenance of micro-environmental conditions ensure excellent conditions for research quality and animal welfare. The platform offers services such as the generation of disease models, small molecule screens and toxicological studies.

Using state-of-the-art technologies, the **Metabolomics platform** provides high quality mass spectrometry-based measurements of a wide range of small molecules in biological samples. The platform offers both gas chromatography–mass spectrometry (GC-MS) and liquid chromatography–mass spectrometry (LC-MS) services, and continuously develops new analytical methods.

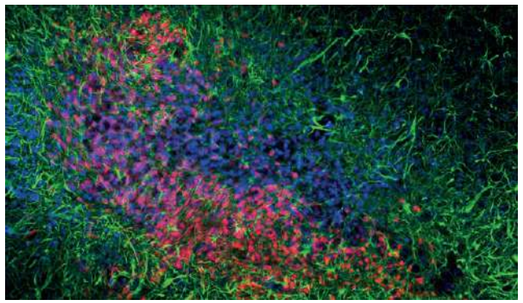
The **Bioinformatics platform** offers expertise and infrastructure for data management and large data storage. The services include workflows for data capture and analysis, assistance in the curation of clinical data and access to bioinformatics tools. The platform contributes to the integration of data across different disciplines. It also provides support for data visualisation. Lastly, it maintains web services for researchers and the IT infrastructure needed for experimental work in the lab.



The **Genomics platform** offers next-generation sequencing using a combination of instruments. Its services range from advice on experimental design, quality controls of samples and library preparation to primary data analysis. Expertise is available for single cell RNA sequencing, meta-transcriptomics, metagenomics, targeted gene sequencing and long read DNA sequencing.



The **Rodent platform** develops animal models such as humanised and germ-free mice. It comprises a breeding area and an experimental area. Scientists can run a broad range of procedures: creation of transgenic lines, stereotaxic surgery and motor behaviour studies. Work in the two animal platforms requires specific training and is done in compliance with ethical standards and animal protection laws.



The **Bioimaging platform** grants access to high-resolution microscopy and flow cytometry instruments. They are used for the observation of fixed and live samples, and for low-phototoxicity imaging of whole organs and organisms. These technologies are complemented by sophisticated image analysis of cell morphology, topology and cellular dynamics.

The **Disease modelling & screening platform** provides services related to early drug discovery and access to high-throughput screening equipment. It is a collaboration between the LCSB and the Luxembourg Institute of Health. It facilitates the translation of scientific discoveries into tangible drug candidates, helping researchers develop cellular disease models and perform phenotypic screenings.

back to table of contents

Greener life science labs

Life science research activities go through an astronomical amount of plasticware – about 5.5 million tonnes per year worldwide. Waste-sorting directly in the laboratories is part of greening the labs but is not the only eco-friendly practice that laboratories can resort to. The lab support team at the LCSB has prioritised sustainability since the beginning.

> The LCSB received a Gold certification, reflecting that we have adopted over 60% of green lab best practices.

Repairing instead of replacing and having efficient inventory software are only a few examples of initiatives already in place. “But we felt that we could do even more: for example, optimise the use of energy-intensive equipment,” explains Annegrät Daujeumont, the research support technician who oversees the Green Lab certification project at the LCSB. “We want to develop an eco-friendly attitude within the centre so that the effects on the environment are considered in every decision we make.”

To drive this behavioural change, the lab support team is implementing more structured actions, starting with a certification programme. Through a survey, “My Green Lab”, a non-profit organisation, assessed the needs of the LCSB in terms of sustainability. Their analysis provided a framework for improvements over the following months. A working group, composed of lab technicians, safety officers and scientists, was then created, allowing a collective reflection on how to best implement new eco-friendly practices.

my green lab certification.

Keeping energy consumption in check was one of the issues the LCSB team decided to tackle heads-on. “A good place to start is to identify which instruments need to be always switched on and which ones can be put on timers,” details Daujeumont. “We carried out this assessment on a case-by-case basis, in order to have the smallest possible impact on the daily organisation of the researchers and the quality of their work.”

Joining the Freezer Challenge, an international competition designed to promote best practices in cold storage management, was also a good way to motivate the LCSB team to optimise the use of fridges and freezers. Actions included defrosting, cleaning out unneeded samples and shoring up sample-tracking methods. As a result, some appliances could be turned off, extending the lifespan of the equipment while significantly reducing the energy consumption linked to cold storage.

Green chemistry was another target. The goal being to challenge the use of certain substances and propose less harmful alternatives that limit energy-consuming waste treatment. “New software enables us to easily identify dangerous chemicals and to then systemically initiate a discussion between researchers and the safety officers,” describes Annegrät Daujeumont.

Other issues can be more challenging to address, such as the limitation of plastic waste and ethical sourcing. “The whole process will take time of course, but the progress already achieved makes it all worth it,” she concludes.

Thanks to this recent team effort, the LCSB has been reassessed by My Green Lab and is now fully certified, with a Gold certification reflecting that over 60% of green lab best practices have been adopted by the centre. ■

back to table of contents

Unlocking the potential of data science in healthcare

The digital transformation of the health sector can be slow, with complex systems involving many stakeholders as well as legal and ethical questions that need to be considered. Yet, patient data and artificial intelligence are at the heart of an accelerating digital health revolution. It promises direct benefits for patients and society at large. In this context, the Luxembourg Institute of Health (LIH) and the LCSB are launching Clinnova. This new project, funded through the NCER programme of the Luxembourg National Research Fund (FNR), will support the digitalisation of healthcare. It will facilitate access, sharing and analysis of high-quality health data.

Clinnova will establish an IT-infrastructure that is interoperable, federated and secure. In Luxembourg, the Clinnova data integration centre will eventually connect hospitals, research institutions, ministries and the health insurance provider. The centre will combine clinical, biomedical and patient-generated data. It will ensure data quality and standardisation, will bridge fundamental research and healthcare, and serve as a basis for precision medicine solutions. "The focus of Clinnova to employ data science to reshape healthcare aligns well with the national priorities of Luxembourg," explains Dr Françoise Meisch, scientific strategic advisor at the LCSB, who has followed the project since the very beginning. "But Clinnova is much more than a national endeavour: It will not only connect key health players within Luxembourg but also major clinical centres in the neighbouring regions."

By partnering with digital health initiatives in France, Germany and Switzerland, Clinnova will establish a cross-border platform involving collaborators from four countries. This infrastructure will open health data exchanges between trusted public partners and set a proof-of-concept for a European integrated network. "The objective is of course to accelerate research on disease mechanisms, biomarkers and therapeutic targets," says Prof. Reinhard Schneider, head of the Bioinformatics Core at the LCSB and co-lead of Clinnova.

On the Luxembourgish side, the project will build on the long-standing expertise of the LCSB and the LIH when it comes to disease modelling, patient stratification and data curation. "We are involved in ongoing initiatives aiming to improve knowledge management and data sustainability at the European level, such as Smart4Health and HealthyCloud," details Schneider. "We also work on federating data across diseases and disciplines for various projects funded by the Innovative Medicines Initiative." Additionally, Clinnova will take advantage of the existing know-how at the LCSB in terms of artificial intelligence approaches. Patient cohorts focusing on immune diseases and managed by the different partners will generate multi-dimensional data. Researchers from the Biomedical Data Science group at the LCSB will use these real-world data to train effective algorithms that can support healthcare decision-making and enable more personalised treatments.

"By creating a federated platform to curate and combine health data, Clinnova wants to return value to the very patients and physicians who make data available," highlights Meisch. On top of backing the personalised medicine effort, this eight-year project will be a catalyst for digital health innovation. ■

Outstanding contribution to computational biology

The International Society for Computational Biology (ISCB) selected Prof. Reinhard Schneider as the winner of the 2022 Outstanding Contributions to ISCB Award. It honours a member who made beneficial and lasting contributions to the ISCB through their leadership, service and educational work.

Schneider, head of the Bioinformatics Core at the LCSB and of the ELIXIR Luxembourg Node, was recognised for his key role for both the ISCB and the broad bioinformatics community. Throughout his career, he has been involved in various national and European projects in the areas of big data, knowledge management, high performance computing and data sustainability. At the LCSB, he has for example developed the infrastructure for data integration across disciplines, such as medicine and clinical research.

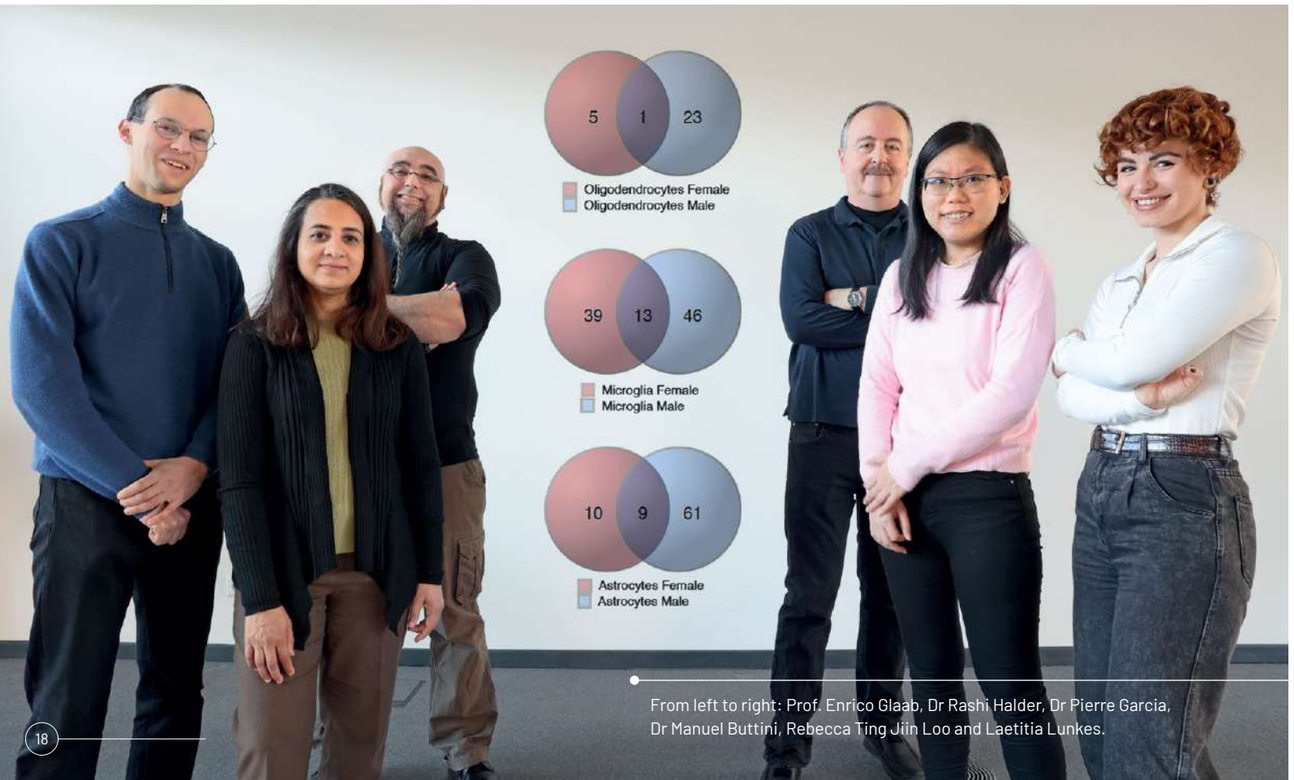
Schneider joined the ISCB board of directors in 2005 and, among other contributions, helped establish the ISCB Student Council. "I am thankful for my diverse experiences with ISCB, especially getting to invite very good students to my lab through the internship initiative and seeing the enthusiasm of these young scientists," he highlights. "I hope this programme has contributed to train a bright new generation of researchers in bioinformatics and computational biology." ■

back to table of contents

Discovering why Alzheimer's disease affects the sexes differently

It has long been recognised that biological sex seems to make a difference when it comes to Alzheimer's disease. Women are diagnosed slightly more often than men, even when accounting for differences in life expectancy, and the changes they go through are different. Assistant Prof. Enrico Glaab and the Biomedical Data Science group started an interdisciplinary project, in collaboration with several teams at the LCSB, to find out where these observed differences might show up in gene activity patterns.

Bioinformatician Assistant Prof. Enrico Glaab has been researching neurodegen-erative diseases such as Alzheimer's and Parkinson's since 2011. In the beginning, his work primarily involved examining brains post-mortem. Unfortunately, only the late stages of the disease can be studied this way. "In order to understand the early-stage mechanisms, we required dedicated disease models," he explains. In this recent project, the researchers studied a genetic mouse model for Alzheimer's, normal mice serving as a control group. "We observed, at the level of single cells, the animals' brain areas that are predominantly affected by Alzheimer's," explains Glaab. "We found out that the activity of individual genes differed significantly, not only between the Alzheimer's model and the control group as expected, but with sex-specific changes in Alzheimer's as well."



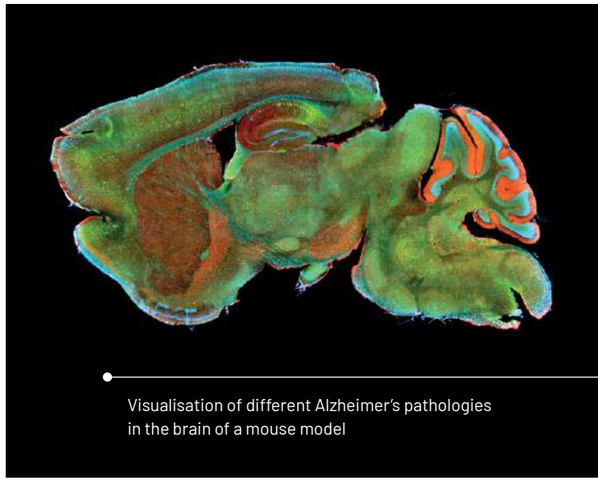
From left to right: Prof. Enrico Glaab, Dr Rashi Halder, Dr Pierre Garcia, Dr Manuel Buttini, Rebecca Ting Jiin Loo and Laetitia Lunkes.

> Understand sex-specific mechanisms to pave the way for tailored treatments.

Genes in an organism do not continuously operate at full power. Their activity can be either elevated or suppressed. A change in the activity of a protein-encoding gene can increase or decrease the production of that specific protein. Glaab and his team discovered that the activity of certain genes changed significantly in Alzheimer's mice, compared to the control mice for only one of the sexes. Moreover, they also discovered that the activity of other genes changed significantly for both sexes, but in opposite directions. "We would like to explain the mechanisms behind these differences using what we call gene regulatory networks," the researcher says. "We developed computational models of how the regulation between multiple genes takes place." This is governed by so-called transcription factor genes. In simple terms, these are master controllers that regulate the activity of several other genes. Together, those genes form a network. "If we observe coordinated and sex-specific activity changes between Alzheimer's mice and control mice in such a network, we can better understand the gene regulatory mechanisms."

Enrico Glaab's research group is specialised in bio-informatics data analysis. They combine experimental data and computational analyses using various methods, including artificial intelligence. For this study, they collaborated with other teams at the LCSB. "The Neuro-pathology group carried out the animal experiments and we jointly interpreted our results," details Glaab. Members from the rodent platform also supported the animal investigations. "One of the important principles when working with animal models is to use as few animals in the experiments as possible," he explains. "Yet, the data gained must provide a large enough basis to deliver reliable results." Combining new bioinformatics methods with the expertise of scientists and technicians familiar with animal research is of great help in this respect. "This interdisciplinary collaboration between the experimental and computational teams is essential for our work," Glaab relates. "Of course, there are challenges that arise when research groups with different backgrounds and scientific terminologies work together, but that made the project all the more exciting to me."

Now that this joint effort at the LCSB led to the discovery of changes that certain genes undergo in a common Alzheimer's model, the researchers are already taking the next step. So far, they have worked with amyloid beta mice. The protein known as amyloid beta is found as deposits in the brains of Alzheimer's patients. For the next step, they are using tau mouse models, in which a different Alzheimer-associated protein accumulates in specific brain regions. "By combining the different mouse model findings with data sets from human *post-mortem* brain tissues, we are gaining a more complete picture of the processes in Alzheimer's disease," says Enrico Glaab. "Understanding the sex-specific mechanisms behind the disease has the potential to provide more accurate diagnostics and pave the way for patient-tailored and more effective treatments," he concludes. ■



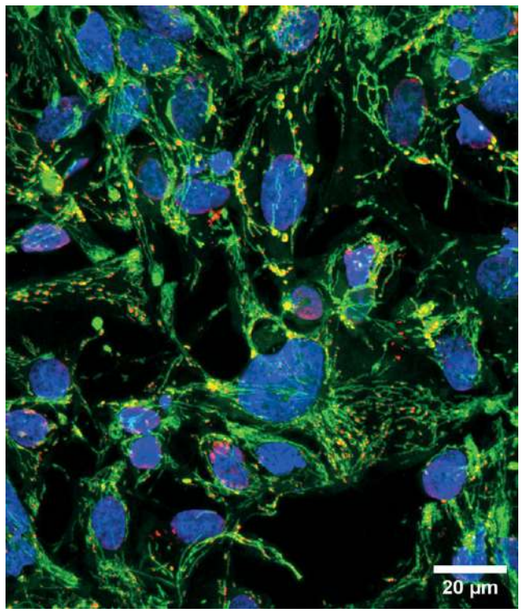
Visualisation of different Alzheimer's pathologies in the brain of a mouse model

back to table of contents

Parkin, an important multi-talent

Mitochondria are the powerhouses of human cells. When defective, they play an important role in the pathogenesis of Parkinson's disease. The Molecular and Functional Neurobiology group led by Prof. Anne Grünewald investigated the importance of a specific protein, called Parkin, in this process. Dr Kobi Wasner, who conducted his PhD in the group, was able to show what happens in the mitochondria when a genetic mutation leads to a lack of Parkin.

About ten percent of all Parkinson's disease cases are of genetic origin. Mutations in the *PRKN* gene that codes for the protein Parkin are among the genetic defects that can lead to this disease. Previous studies suggest that Parkin ensures the clearance of damaged mitochondria, but other functions of this protein remain largely unknown. To clarify Parkin's diverse roles in the cell, Dr Wasner studied neuronal cultures derived from skin biopsies of Parkinson's patients and healthy people, comparing nerve cells with and without mutations in the *PRKN* gene.



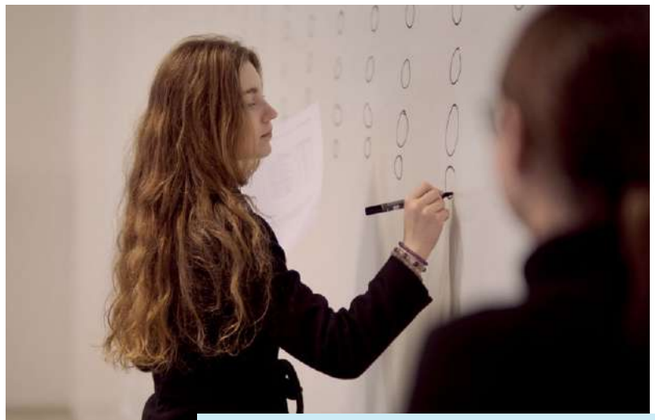
iPSC derived neurons (nuclei in blue, mitochondria in green and mitochondrial DNA in red)

Wasner discovered that beyond its role in mitochondrial removal, Parkin is also involved in the maintenance of mitochondrial DNA. As mitochondria originate from bacterial ancestors, they have their own DNA, separate from the cellular DNA in the nucleus.

The transcription and replication of this mitochondrial DNA is controlled by a complex machinery. When this machinery fails, mitochondrial DNA is released in the cell, where it may lead to an inflammatory response. "We observed that, without Parkin, mitochondrial DNA is no longer efficiently transcribed and, as a consequence, higher amounts of these DNA molecules can be found in the intracellular fluid," explains Kobi Wasner. "In addition, our research in post-mortem midbrain sections from a patient with *PRKN* mutations supported the idea that this mitochondrial DNA can cause neuroinflammation."

These results could induce a shift in research on Parkinson's disease. Scientists previously assumed that Parkin degrades an inhibitor of PGC-1 alpha, a protein that plays a central role in regulating the biogenesis of mitochondria. "By contrast, our investigations show that Parkin may in fact intervene in cellular metabolism, which in turn affects the generation of new mitochondria," says Wasner. "With so many functions linked to Parkin, it is clear that mutations in the *PRKN* gene can lead to major issues for mitochondria in nerve cells." Thus, the impact of *PRKN* mutations on mitochondrial DNA integrity and release should be kept in mind when exploring the molecular causes of genetic Parkinson's disease.

This newly acquired knowledge on the multifaceted functions of Parkin could pave the way for the development of novel therapeutic approaches for people with inherited *PRKN* mutations. "If it was possible to act at an early stage of the disease and provide patients with drugs that specifically compensate for the mitochondrial impairments caused by mutations in Parkin, this could mean a significantly longer time without the disease and thus, a considerable gain in quality of life," hopes Anne Grünewald. ■



Over 10,000 participants in growing outreach programme

In March 2022, the Scienteens Lab reached a significant milestone: Over 10,000 teenagers have participated in more than 600 workshops since the Scienteens Lab was founded in 2013! "Our team is very grateful for the support and interest of hundreds of teachers who have visited our lab with their classes," says Dr Elisabeth John, head of the Scienteens Lab. "And of course, a big thank you to all the young scientists for their enthusiasm!"

Activities in biology have been in high demand for several years, but mathematics, physics and computer science are catching up. Following in the footsteps of the Scienteens Academy in Systems Biology – a one-week interdisciplinary workshop designed for motivated high-school students – another summer school focusing on sustainability was launched in 2022. With a total of 18 different workshops available for booking, the Scienteens Lab hopes to welcome even more budding researchers in the coming years. ■

Visit the website

back to table of contents

Working in tandem to foster interdisciplinary research

Interdisciplinary collaboration and interactions between different teams are important elements that contribute to the success of a research centre like the LCSB. To encourage collaborative endeavours, the director of the LCSB launched a call for "tandem projects". The objective: to fund new collaborations in the area of neurodegenerative diseases. Five excellent projects were selected.

Several projects bringing together at least two researchers from different groups at the LCSB were submitted and assessed by external scientific experts. The main criteria for the evaluation were scientific excellence and novelty, new collaborations between teams that had never worked together being especially encouraged.

The aim was to recognise and support exploratory research ideas combining experimental, computational and clinical approaches, which could attract subsequent external funding. The five chosen proposals received 30,000 euros for a year and started at the beginning of May 2022. Discover these exciting tandem projects below.

A home monitoring system for Parkinson's patients

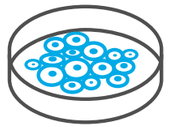
The symptoms of Parkinson's disease vary vastly from one patient to the next, so treatments must be personalised and the evolution of the symptoms monitored continuously. The project of Dr Stefano Sapienza from the Digital Medicine group and Dr Jesus Fuentes from the Systems Control group focuses on a home-monitoring platform for Parkinson's patients. Composed of wearable sensors and intelligent algorithms, this multi-modal platform monitors upper limb tremor, heart rate variability and orthostatic hypotension. The two researchers aim to assess the quality of the signals recorded, evaluate if medically relevant information can be extracted from the collected data and estimate how well this technology is received by the patients.

Environmental pollutants in midbrain organoids

The Developmental and Cellular Biology group and the Environmental Cheminformatics group initiate a new collaboration to shed light on the interaction between genetic and environmental risk factors for Parkinson's disease. They study the effects of selected environmental toxins — a fungicide, a pesticide and some persistent organic pollutants — on midbrain organoids carrying a mutation on the GBA gene. Using the groups' respective expertise in human derived midbrain organoids and in metabolomics analyses, the researchers will clarify the effect of environmental pollutants in Parkinson's disease, evaluate their impact on the brain metabolites and decipher the biological mechanisms involved.

Microglia, metabolism and neurodegeneration

There is increasing evidence that oxidative stress and metabolic alterations strongly contribute to the development of neurodegenerative disorders. Recent studies also highlighted how mutations in microglia, the immune cells of the brain, can lead to damage in central nervous system neurons followed by cognitive decline. With this project, the Immunology & Genetics group and the Neuropathology group investigate metabolic alterations in a microglial-specific manner in an Alzheimer's disease mouse model. The researchers specifically study pyruvate dehydrogenase (PDH), a key enzyme regulating the energy production in cells. They will characterise the metabolic shifts induced by PDH-deficiency in microglia and explore potential treatment options targeting this enzyme.



Characterising aging effects during cell differentiation

The largest risk factor for many neurodegenerative diseases is age. To study neurodegeneration *in vitro*, induced pluripotent stem cells (iPSC) can be differentiated into brain cells, but this reprogramming deletes age-related methylation patterns. In this project, Dr Kamil Grzyb from the Integrative Cell Signalling group and Dr Rashi Halder, sequencing platform manager, address this issue by combining complementary expertise in single cell approaches and Nanopore sequencing. Their goal is to assess aging effects during the differentiation of stem cells into dopaminergic neurons in the lab, providing a complementary approach for different iPSC-based research projects.

Linking mitochondrial and microbial DNA to neuroinflammation

Recent studies highlighted the intricate role of mitochondria and the gut microbiome in eliciting inflammation in neurodegenerative diseases. With this project, researchers from the Molecular & Functional Neurobiology group and from the Systems Ecology group want to better understand these mitochondria-microbiota interactions with regard to Parkinson's disease. They study samples from patients and healthy controls through shotgun sequencing, metagenomics analysis and deep immunoprofiling. The data collected will help to ascertain the roles of mitochondrial DNA and microbial DNA in triggering neuroinflammation.

back to table of contents

Spotlight on the microbial world at the Researchers' Days

On 25-26 November 2022, the LCSB participated in the Researchers' Days with a booth dedicated to microorganisms and how scientists study them in the lab. Organised by the Systems Ecology group, the activities were a success, attracting hundreds of visitors – young and old – keen to observe microbes under a microscope, to inflate balloons with yeasts and to extract DNA from their saliva!

Organised biyearly by the Luxembourg National Research Fund (FNR), the Researchers' Days offer scientists a unique platform to present their work to a large audience. Visitors can conduct hands-on experiments and get a first insight into the world of research. In 2022, visitors of the LCSB booth were invited to discover where microscopically small organisms can be found, from the harshest environments on our planet to the inside of our gut, and how they help to keep us healthy.

A team of energetic researchers guided visitors through the different experiments and provided explanations. A big thank you for their time and enthusiasm to Amelie, Bérénice, Catherine, Charlotte, Gianfranco, Madita, Mara, Pau, Polina and Susheel! ■

How damaged cells inhibit muscle regeneration

Humans have a limited capacity for self-regeneration of tissues and organs, but they do keep a pool of stem cells throughout their life that can self-renew and differentiate into specific cell types. These stem cells are widely studied as they could enable the repair of human tissues and thus have great potential for regenerative medicine.

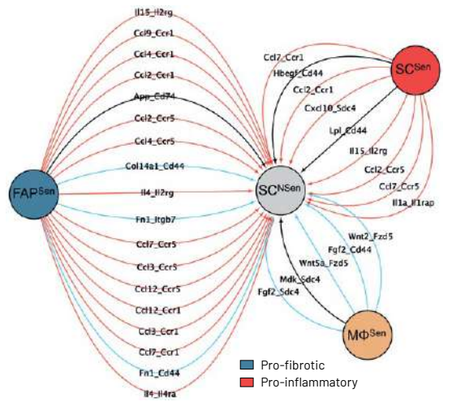
At the LCSB, Prof. Antonio Del Sol, head of the Computational Biology group, has developed several computational tools over the years to better understand the mechanisms behind stem cell differentiation and to help scientists efficiently generate various cell types in the lab. He was recently part of an international team who explored the role of cellular senescence in tissue regeneration. This group of researchers from Spain, China, Japan, USA and Luxembourg uncovered key interactions between senescent cells and stem cells, opening potential avenues towards improving muscle repair throughout life. Their findings were published in the scientific journal *Nature*.

All human cells can enter a state called senescence: they stop multiplying but do not die, lingering within the tissue. As these senescent cells accumulate throughout the body, they can impact nearby healthy cells, including stem cells. Since regenerative functions decline during ageing, while senescent cells accumulate, the researchers decided to explore the role of senescence in tissue regeneration. "Our objective was to study senescent cells *in vivo*, to understand how they emerge and how they affect the repair process of tissues throughout life," explains Antonio Del Sol. "For this purpose, we used a combination of experimental work with mice, conducted by collaborators from several institutions, and of computational methods developed by my team."

Focusing on muscle tissue in mice, the researchers first observed that senescent cells appear in muscles when they get damaged or with age. Their results show that both injury and ageing induce the accumulation of high levels of oxidative stress and DNA damage in a subset of cells, driving these cells towards senescence. In turn, the senescent cells have an impact on the stem cells present in the muscle: they repress muscle regeneration. To illustrate this effect, the scientists were able to accelerate regeneration in young mice and rejuvenate muscles of old mice by removing senescent cells from the tissue.

When looking for common traits across senescent cells, the analyses showed that they are molecularly diverse but share two major hallmarks. "By investigating closely through computational methods, we found two universal senescence markers: inflammation and fibrosis," details Antonio Del Sol. The identification of these common characteristics was key to understanding by which mechanisms senescent cells impair tissue repair. The senescent cells act through the secretion of pro-inflammatory and pro-fibrotic factors. The molecules they produce affect the stem cells nearby, inhibiting their proliferation and impairing regeneration.

Further computational analyses identified lipid-transport gene CD36 as a possible way to regulate the impact of senescent cells. As these cells accumulate in human tissue like in mice, these findings open potential avenues towards improving muscle repair throughout life. ■

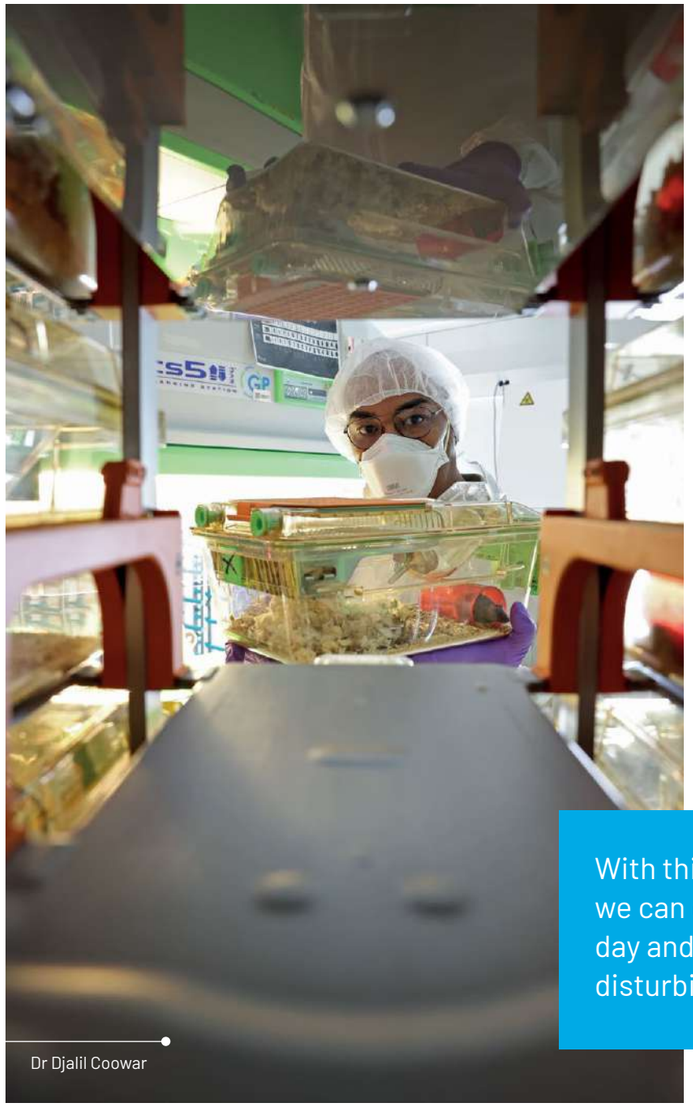


Senescent cells shape muscle regeneration by releasing pro-fibrotic and pro-inflammatory factors. (N^{Sen} = non-senescent cells / ^{Sen} = senescent cells)

back to table of contents

Watching over mice 24/7

In 2022, the rodent platform of the LCSB invested in cages with an automated monitoring system. They allow for real-time tracking of mice without any interference with the animals' routine. This new piece of equipment will contribute to research, optimise facility management and improve animal welfare.



Dr Djalil Coowar

The new cage rack installed over the summer has quite an array of functionalities. It holds 80 cages outfitted with 12 electrodes each. These sensors can monitor the animals' movement around the clock. The system also tracks key parameters such as food and water levels. "With these cages, mice don't have to be moved or require a chip, which is a huge advantage," details Prof. Evan Williams, head of the Gene Expression & Metabolism group. "This way, we can collect data 24/7 without disturbing them." The sensors use electromagnetic field technology. They detect movement based on changes in conductance as the animal passes over them. The data obtained open new possibilities for research, but this is not the only advantage of this novel system.

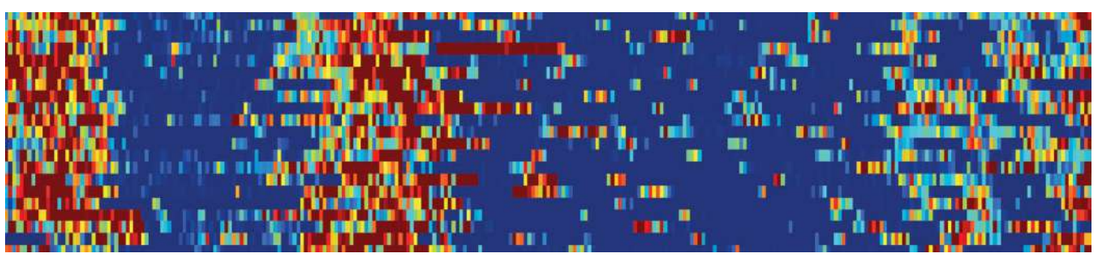
Dr Djalil Coowar, manager of the rodent platform, supervised its installation. He explains: "Any interference with the animals' routine can have a lasting impact on their behaviour. By reducing human interaction to a minimum, these cages enhance animal welfare and help our facility to optimise protocols." As an example, any anormal decrease in locomotion will be detected, allowing the technicians to identify a sick mouse faster. As the sensors measure the humidity level in each cage, they will also ensure that the bedding is only changed when needed. With no unnecessary handling, this system is beneficial for the animals. It reduces running costs as well: Less consumables are required and the workload can be streamlined.

> With this system, we can collect data day and night without disturbing the animals.

It is now possible to conduct experiments without the animals ever having to leave the security of their cage. As a result, the researchers hope to reduce experimental variability caused by stress and improve reproducibility. The automation should also help to decrease bias linked to human interventions. Of course, the technology is quite new and researchers are still figuring out how to make the most of the vast amount of data it can produce. This is what Williams and doctoral researcher Besma Boussoufa are currently working on: "We want to test every aspect of the set-up at the LCSB and refine our understanding of the system before launching longitudinal studies."

They compare data obtained in different cages and explore potential technical issues. "I am impressed with the system so far," says Evan Williams. "We can clearly see the circadian rhythm of the mice on the graphs and we have made some interesting observations." Comparisons between different mouse lines have started as well: two cohorts, comprising of normal mice and mice prone to obesity, are monitored day and night.

The results already show some distinctive patterns in their nocturnal activity and could bring new scientific insights. "Innovative hypotheses can be tested more readily from now on," highlights Williams. "It will be easy to integrate this type of measurements in a project, encouraging exploratory research." ■



Heat map representing the activity of a mouse over time for several days. Each line represents a 24h period. Each pixel corresponds to 5 minutes of data. Blue means less movement. Red means more movement.

back to table of contents

A decade after itaconic acid, here comes mesaconic acid

In 2013, LCSB researchers discovered that immune cells in the brain can produce itaconic acid, a substance that fights off bacteria and inhibits inflammation. It was the first proof of an endogenous antibiotic in the brain and, back then, their publication in the scientific journal *PNAS* won an FNR Best Publication Award. Almost ten years later, this ground-breaking result is still bearing fruit: in 2022, an international research team, including LCSB alumni and current researchers, discovered another - even more promising - anti-inflammatory substance produced by our immune cells.

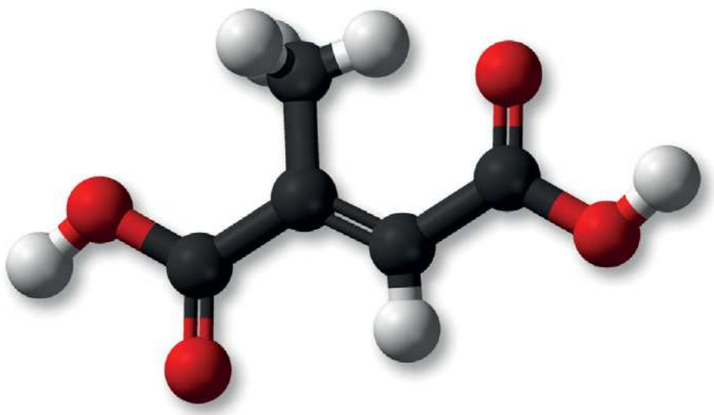
For the past decade, Prof. Karsten Hiller has conducted research on metabolic products that are involved in the human immune system. First, as the principal investigator of the Metabolomics group at the LCSB, and currently as the head of the Department of Bioinformatics and Biochemistry at the Braunschweig Integrated Centre of Systems Biology in Germany. After discovering that immune cells in the blood and brain of mammals produce itaconic acid, Karsten Hiller further investigated its mode of action and possible applications. Several of these projects were conducted within the framework of a binational research programme between Karsten Hiller and Prof. Dirk Brenner, head of the Immunology & Genetics group at the LCSB and of the Experimental and Molecular Immunology laboratory at the Luxembourg Institute of Health. In a recent study, they discovered that another metabolic product always occurs together with itaconic acid: mesaconic acid.

Mesaconic acid is a chemical compound that the body produces from itaconic acid. With the help of an international research consortium, the two researchers showed that this metabolite has an anti-inflammatory effect of similar strength to that of itaconic acid.

"Mesaconic acid can return an overactive immune system back to its normal state," explains Brenner. Interestingly, their results, published in *Nature Metabolism* in 2022, also highlighted that the two substances have a distinct impact on metabolism.

Unlike itaconic acid, mesaconic acid does not affect succinate dehydrogenase, an enzyme playing a central role in cellular metabolism. The fact that mesaconic acid has immunomodulatory properties but interferes to a lesser extent with the metabolism makes it interesting in terms of therapeutic potential. "We will now investigate further to better understand the underlying metabolic processes. We have already submitted another joint research proposal for this purpose," details Dirk Brenner. Once the researchers have precise answers, concrete pharmacological studies could be launched.

Mesaconic acid could hence become a candidate for treating diseases in which the immune system is overactive: Septic shock for example, or autoimmune diseases such as psoriasis and inflammatory bowel disease. "Given that it is a substance produced naturally by the body, it might constitute an interesting alternative to avoid side effects typically associated with anti-inflammatory drugs," concludes Dirk Brenner. ■



Prolonging the life of data

Research groups worldwide are collecting gigantic amounts of data on a daily basis. In many cases, the data are used in a single project and then end up in storage, never to be looked at again. For Prof. Reinhard Schneider, that is absurd. "If instead you share the data from different sources and aggregate them in new ways, you can gain entirely new insights from them," says the head of the LCSB Bioinformatics Core. This opinion is shared by a growing number of researchers and research funders, resulting in the broad adoption of the FAIR principles: data ought to be Findable, Accessible, Interoperable and Reusable. Following suit, Luxembourg is currently setting up a platform that will allow professional storage and access to data according to unified standards.

The Luxembourg National Data Service (LNDS) is developed in collaboration with the LCSB. "We have gained a great deal of experience for a project of this nature through the ELIXIR programme," Schneider says. "The LCSB has hosted the national Node for this European infrastructure since 2017 and we have set up a platform dedicated to biomedical data." The LNDS will build on this expertise and expand the scope of activities with an interdisciplinary approach at the national level. The new service infrastructure will in fact benefit multiple areas including finance, materials research, physics and social sciences. "It will be a true added value for interdisciplinary topics," says Schneider.

The LNDS was launched in 2022, with the support of six ministries and under the leadership of the Ministry of Research, giving the project a strong tailwind. Thanks to the expertise of the Bioinformatics Core and a good amount of strategic planning, the platform is becoming a reality. "We started by asking potential users what it is that they need, so that we could develop a concept relevant for all the national players," explains Schneider. This includes the private sector, as the plan is to offer a variety of services for companies in addition to managing scientific data. The LNDS team also did some benchmarking, learning from infrastructures existing in other European countries such as Finland. Researchers

will now focus on what is needed for data from their respective disciplines, ensuring that specialist expertise is present across the entire thematic range of the LNDS.

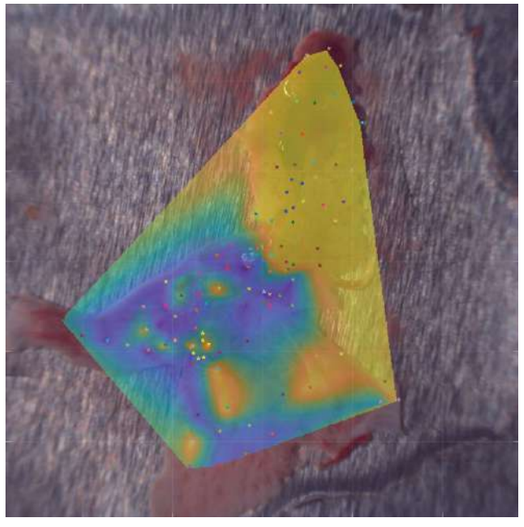
Indeed, it is not enough to be good at handling electronically stored information. "Only specialised scientists know how data are collected during an actual experiment and how they have to be prepared to be valuable for further use," Schneider says. "Only they can properly curate the data and thus assure their quality." Many legal aspects are to be taken into consideration as well. Medical data from drug development are for example subject to strict privacy regulations. They may only be reused for further research questions under very specific conditions. There, as well, the experience of the members of the Bioinformatics Core will be useful, as they have previously worked on ethical, legal and social implications linked to data sharing. "We have to respect all of these issues in establishing and operating the LNDS – so that the secondary use of data does indeed confer a true scientific benefit and an added value for Luxembourg as a whole," concludes Schneider. ■

back to table of contents

Innovative spectroscopy for rapid diagnosis of brain tumours

Being able to distinguish between healthy tissue and a tumour during surgery is key to ensure maximal tumour excision with minimal damage. In a project supported by the Fondation Cancer, the National Department of Neurosurgery at the Centre Hospitalier du Luxembourg (CHL) collaborated with the Luxembourg Centre for Neuropathology (LIH/LCSB/LNS) and the Interventional Neuroscience group at the LCSB to explore the potential of Raman Spectroscopy as a non-invasive technique for diagnosis in neuro-oncology.

Timely discrimination between different types of tumours of the central nervous system, such as lymphoma and glioblastoma, is an important part of diagnosis. "Glioblastoma for example is the most common and aggressive brain tumour in adults," details Prof. Frank Hertel, director of the neurosurgery department at CHL and head of the Interventional Neuroscience group at the LCSB. "The rapid and reliable identification of the tumour as well as its total resection are crucial for proper treatment and prognosis." In this context, Hertel's team worked together with researchers at the Laboratoire National de Santé (LNS) and the Luxembourg Institute of Health (LIH) to investigate the clinical suitability of using Raman Spectroscopy to categorise tumours and discriminate cancerous tissue from healthy tissue during surgery.



Histological verification of the meningioma-dura mater-classifier. Classifier heat map with colour scale ranging from blue (healthy tissue) to yellow (meningioma).

Raman Spectroscopy is a non-destructive method that can provide detailed information about the chemical structure of a material. It is a light scattering technique: the samples are exposed to a laser beam and the light is, in a small part, reflected in a different wavelength depending on the composition of the analysed material. "Raman spectroscopy enables a fast and observer-independent examination of biological tissue," explains Dr Andreas Husch, researcher in the Interventional Neuroscience group at the LCSB. "It generates an individual spectroscopic fingerprint which can be used to determine biological properties and potentially reveal the tumour type."

Fresh fragments of resected tumours were analysed by Raman Spectroscopy in the operating room, then fixed and assessed by a neuropathologist. Additional Raman measurements were also acquired on fixed tissue of the same tumours in the pathology department at LNS. The measurements and pathological findings were used in combination to train a machine-learning classifier, an algorithm that automatically categorises data into different groups. This classifier was then tested on independent tumour samples. "The algorithm we developed can now distinguish between meningioma and healthy tissue, between lymphoma and glioblastoma, and is being investigated to discriminate glioma and carcinoma," highlights Husch. "It is very accurate as well, for example it separates meningioma and dura mater – the surrounding tissue – with a sensitivity of 96%."

From left to right: Dr Felix Kleine Borgmann, Prof. Frank Hertel and Dr Andreas Husch.

> A promising method for fast tumour discrimination and guided surgery.

These results show that, combined with machine learning, Raman Spectroscopy can be used as a quick and reliable complementary tool for neuro-oncology. It has potential to accelerate the diagnostic workflow and facilitate immediate treatment decisions. This promising optical method could also contribute to guided surgery, helping the surgeon to identify tumour borders and assisting in resection control. Dr Felix Kleine Borgmann, researcher at LIH, explains: "Since modern minimally invasive neurosurgery is already based entirely on computer-assisted optical instruments, Raman spectroscopy could easily be integrated into the surgical workflow." Its utilisation could revolutionise the clinical routine.

While Raman Spectroscopy proved to be an efficient way to examine fresh tissue samples, the researchers also wanted to investigate its suitability for analysis of formalin-fixed and paraffin-embedded surgical specimen. "Our trained algorithm could precisely distinguish between normal and pathologic brain tissue, based on the spectral properties of fixed glioblastoma samples, independent of the chemical fixation process used," says Andreas Husch. "This non-invasive method is not only suitable as a tool for fast tumour discrimination, which may help to choose the proper treatment option," concludes Frank Hertel. "It can also serve as an additional method in the pathological toolbox." ■

back to table of contents

Alzheimer's research at Art2Cure closing event

On 20 September 2022, Prof. Michael Heneka gave a lecture during the closing event for Art2Cure, a fundraising initiative where Luxembourg-based artists contribute their work to help fund local biomedical research. It was an opportunity to meet donors who have generously supported the LCSB and the University of Luxembourg over the years. Heneka, who took up the position of LCSB director at the beginning of 2022, recapitulated key findings on dementia and Alzheimer's disease, the main focus of his work. He also highlighted the importance of conducting interdisciplinary research and developing a national healthcare strategy to tackle the disease.

The funds raised during this ninth edition of Art2Cure will go towards the Alzheimer's fund at the LCSB. It will support several research initiatives, including a project led by Michael Heneka to explore the pivotal role played by immune mechanisms in the initiation and progression of the disease. ■

Artworks by Colm Mac Athlaoich (1-2), Liz Van Zeeland (3) and Chiara Dahlem (4)

Safety in the lab: One for all and all for one

While handling hazardous chemicals or biological agents is often an integral part of working in the lab, it should not affect the health of scientists. This is where biosafety officers come in. They are experts at assessing risks in a laboratory and they can help researchers stay safe while doing experiments. "Every research institution must have safety procedures to deal with risks," explains Marie Fosséprè, biosafety officer at the LCSB since 2018. "Our role is to systematically develop mitigation strategies so that everyone is protected at any time or location."

The job of a biosafety officer takes many forms, from fulfilling legal requirements to approving chemical purchase for example. "Providing protective equipment goes hand in hand with implementing best practices in the lab and thinking about sustainability in the long run. The outcome of all these measures put together is a good work environment coupled with high quality results." says Marie Fosséprè.

At the LCSB, the biosafety officers raise awareness among researchers right from the start: they organise trainings for newcomers, provide essential information to staff members working in the lab and help them to adopt the correct habits early on. "We are here to facilitate research and ensure that it is done in a safe way, but safety is everyone's responsibility," Marie Fosséprè points out. "Following the safety measures is compulsory to protect both yourself and your colleagues."

After the first trainings, the collaboration between scientific staff and the biosafety officers goes on. The latter rely on the feedback from researchers and lab technicians to pinpoint safety issues. Someone is not comfortable with handling a specific substance: The biosafety officers will study the safety data sheet, which comes with every hazardous material, and implement the relevant safety precautions. A research team would like to start a novel experiment: Marie Fosséprè and her colleagues will perform a risk assessment before it starts and introduce new safety processes if needed. They also organise collaborative exercises called "safety mapping" on a regular basis to review the activities of a given research group and identify areas of improvement. And what if – despite all the precautions – there is an incident, a chemical spill for example? Of course, the biosafety officers will be there to assist.

They visit the labs as often as possible to ensure that the protective equipment is working properly or that rules are being upheld. "But we are not a sort of police," assures Marie Fosséprè. "We are partners who can provide expertise, advise the researchers and contribute to everybody's safety at the LCSB." Everyone has a role to play, it is a joint effort: working together to build a common and sustainable safety culture. ■

← back to table of contents

LCSB short stories

Carole Linster becomes Associate Professor

The principal investigator of the Enzymology & Metabolism group was promoted to Associate Professor through the internal competitive promotion process of the university. Carole Linster started to work at the LCSB as a post-doctoral researcher in 2012 before creating her own research group just a year later. She has been successfully leading research on enzyme function, metabolite repair and rare diseases since then. Congratulations!

Digital Medicine Conference

On 26-27 October, the LCSB organised the "European Digital Medicine Conference Luxembourg". It brought together 160 participants from academia, industry, patient organisations as well as policymakers. The programme featured talks by international experts and various health ministries on data-driven healthcare, digital medicine innovation and translation into European markets. It highlighted how interdisciplinary this new field is, encompassing healthcare as well as the legal, technical and societal aspects of digital transformation. In addition, European Institute of Innovation and Technology (EIT) Health hosted a matchmaking event prior to the conference to present their flagship and support EIT Health Business Plan proposal submissions.

3R Symposium

On 20 October, LCSB researchers and technicians participated in the second edition of the Luxembourg 3R Symposium. This conference organised by local research institutes and ministries was an opportunity to discuss progress in the field of animal research as well as best practices to improve quality and ethics. In Luxembourg, scientists follow the 3Rs principle: Reduce, Replace and Refine. They strive to minimise the number of laboratory animals and to design protocols ensuring their welfare.

Four inaugural lectures

Between 2020 and 2022, four new principal investigators joined the LCSB: Evan Williams, Dirk Brenner, Jochen Klucken and Michael Heneka. As on-site events were limited for a while, the corresponding inaugural lectures were all organised in 2022. These talks covered a wide range of topics, from Alzheimer's research to digital medicine, from immunology to genetics and metabolism, allowing the new LCSB professors to present their work to the academic community.

Annual team retreat

On 1 June, the whole LCSB team was invited to gather all together for the first time since the pandemic. Around 160 staff members participated in various activities, from tandem discussions to get to know colleagues to riddle solving in teams and a retro train ride through the Luxembourgish landscape. A barbecue brought this very enjoyable day to a close. It was the perfect combination of good weather, good times and good people!

New SAB

In 2022, with the arrival of a new director, the LCSB established a new scientific advisory board. The new SAB is composed of nine researchers: experts in their respective fields, from neuroscience to data science, working in leading research institutions from all over the world. They will help the centre shape its long-term scientific strategy and international positioning.

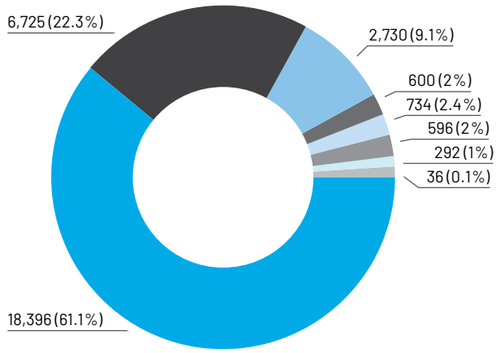
Visitors from Bonn

In August, scientists from the University of Bonn came to Luxembourg to discover campus Belval and meet researchers from the LCSB and the LIH. Initiated by Prof. Heneka, this three-day meeting was designed to promote collaborations as part of a new internationalisation strategy, aiming to build bridges between the LCSB and other research centres in neuroscience.

back to table of contents

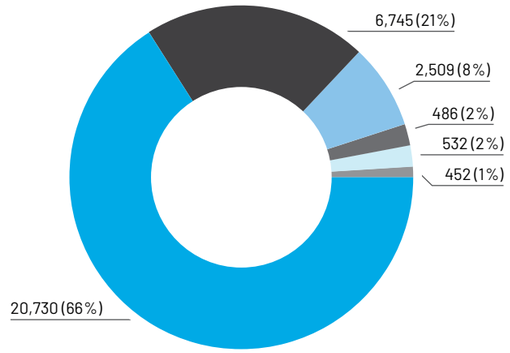
Facts & Figures

2022 LCSB income (in kEUR)



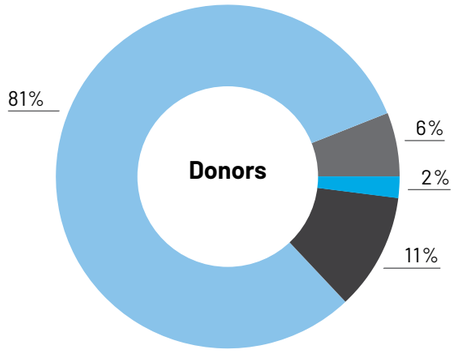
- University of Luxembourg
- Luxembourg National Research Fund (FNR)
- EU programmes
- Further grants
- Fundraising
- Ministries
- Funds for knowledge transfer
- Industry cooperation

2022 LCSB expenses (in kEUR)

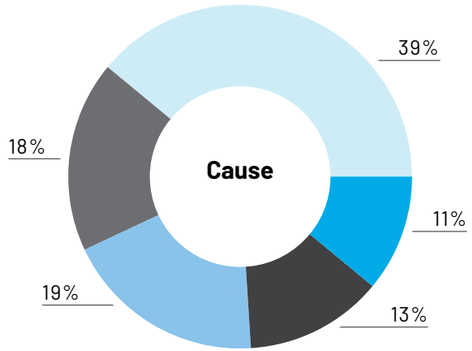


- Wages
- Operating expenses
- Investments
- Representation and registration
- Sub-contracting
- Travel

Fundraising



- Associations
- Corporate
- Foundations
- Private individuals



- Alzheimer's research
- Parkinson's research
- Rare disease research
- Education
- Other topics

LCSB organigram

Director's office
- Personal assistant
- Scientific officer

LCSB Director (M. Heneka)

Research Strategy (F. Meisch)

Research groups

Bioinformatics Core (R. Schneider)	**Biomedical Data Science** (E. Glaab)	**Computational Biology** (A. del Sol)
Developmental & Cellular Biology (J. Schwamborn)	**Digital Medicine** (J. Klucken*)	**Systems Ecology** (P. Wilmes)
Environmental Cheminformatics (E. Schymanski)	**Enzymology & Metabolism** (C. Linster)	**Gene Expression & Metabolism** (E. Williams)
Immunology & Genetics (D. Brenner**)	**Integrative Cell Signalling** (A. Skupin)	**Interventional Neuroscience** (F. Hertel***)
Medical Translational Research (J. Schneider)	**Molecular and Functional Neurobiology** (A. Grünewald)	**Neuropathology** (M. Mittelbronn****)
Neuroinflammation (M. Heneka)	**Systems Control** (J. Goncalves)	**Translational Neuroscience** (R. Krüger*)

Scientific central services

Aquatic and Rodent platforms	**Bioinformatics platform & ELIXIR-LU**	**Disease modelling & screening platform****
Bioimaging	**Metabolomics**	**Genomics**

Infrastructure (N. Bonjean)

Safety
- Safety & biosafety
- Quality assurance & SOPs

Equipment
- Instrument care & purchase
- Technology platforms

Logistics
- Laboratory supplies
- Sample shipment
- Technical support

Infrastructure
- Facility management & development
- Lab coordination

Operations (A. Vogler)

Communication & Fundraising
- External & internal communication
- Event management
- Donor acquisitions & management
- Charity events

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

Innovation & Partnering
- Business development & legal
- Technology transfer

Management & Strategy
- Secretariat
- Process management
- Strategic planning

Scienteens Lab
- Curriculum development
- Outreach to schools

* in cooperation with LIH & CHL ** in cooperation with LIH *** in cooperation with CHL **** in cooperation with LNS & LIH

back to table of contents

National grants in 2022

Project acronym	Programme	LCSB responsible(s)	Project coordinator (if applicable)
CLINNOVA	FNR NCER (INITIATE)	Reinhard Schneider, Venkata Satagopam, Enrico Glaab	Ulf Nehrbass (LIH)
MINIALZ	FNR PEARL	Michael Heneka	
NEXTIMMUNE-2	FNR PRIDE	Anne Grünewald, Michael Heneka, Jens Schwamborn, Evan Williams	Dirk Brenner (LIH)
PREVENE	FNR Industrial Fellowship	Patricia Martins Conde	
DigiBio	FNR RESCOM Lecture Series	Enrico Glaab	
2022 DigiMed Conference	FNR RESCOM	Jochen Klucken	
PEAQ_MP	FNR INTERMOBILITY	Benoît Kunath	
QuLuPEX	FNR AFR bilateral	Carole Linster	
One Earth	FNR RESCOM Lecture Series	Paul Wilmes	
FullGenomeNet	FNR AFR	Gabriela Baraona	
NAXDivo	FNR CORE	Carole Linster	
VMNeuro7	FNR RESCOM	Michael Heneka	
AMINF	UL IAS Audacity 2022	Michael Heneka	Josh Berryman (FSTM)
Precision Medicine in PD	FNR RESCOM 2022	Rejko Krüger	
Living in a microbial world	FNR Science in Society	Charlotte De Rudder	
#Post it!	FNR Science in Society	Maren Krüger	
CoVaLux	Haut Commissariat pour la Protection Nationale (HCPN)	Paul Wilmes, Venkata Sagatopam, Alexander Skupin, Jorge Goncalves	LIH
MidStriPD	FNR CORE	Jens Schwamborn	

European grants in 2022

Project acronym	Programme	LCSB responsible(s)	Project coordinator
IMMUPARKNET	COST	Jens Schwamborn	University of Piemonte Orientale, Italy
BE READY	Horizon Europe	Paul Wilmes	INSERM, France
SIMPATHIC	Horizon Europe	Rejko Krüger	Radboudumc, The Netherlands
Can.Heal	EU4Health	Adrian Thorogood	Sciensano, Belgium
EHDS2 Pilot	EU4Health	Regina Becker	Health Data Hub, France
PARC	HORIZON Programme Cofund Actions	Emma Schymanski	ANSES, France
GDI	Digital Europe	Christophe Trefois	European Molecular Biology Laboratory, Germany
IDERHA	JU-IHI	Venkata Satagopam	Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V., Germany
NLRP3 tau pathology	EMBO Postdoctoral Fellowship	Bora Taştan	
Treat-ION 2	BMBF	Patrick May	University of Tübingen, Germany
Gut-Brain-PD	FNR INTER NWO	Rejko Krüger	
PreDYT	FNR INTER EJP-RD	Enrico Glaab	Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Italy
GENOMIT	FNR INTER EJP RD	Carole Linster	Klinikum Rechts der Isar, TU München, Germany
DEEPEN-iRBD	FNR INTER ERA PerMed	Rejko Krüger	UNIVERSITA DEGLI STUDI DI MILANO, Italy
RECAST	FNR INTER JPND	Enrico Glaab	University of Tübingen, Germany
REBALANCE	FNR INTER JPND	Michael Heneka	University of Eastern Finland
IFUNEC	FNRS	Paul Wilmes	Elisabeth Letellier (FSTM)
KWF	Foundation, European	Patrick May	Amsterdam UMC, The Netherlands

International grants in 2022

Project acronym	Programme	LCSB responsible(s)	Project coordinator
HeBA	Michael J. Fox Foundation	Rejko Krüger	LIH
PreMedPD	Parkinson Foundation	Rejko Krüger	

back to table of contents

Key performance indicators

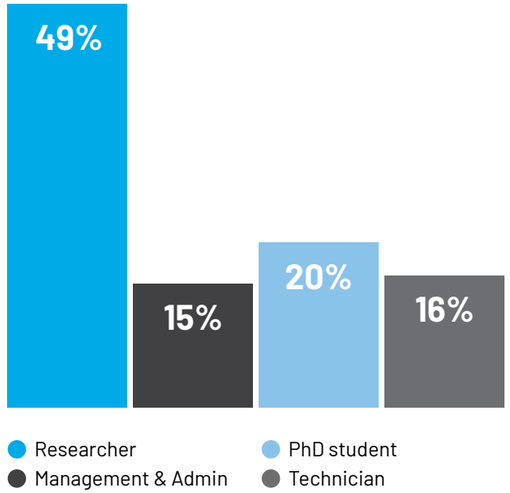
Personnel	
Research groups:	18
PEARL (active):	2
ATTRACT (active):	1
ERC (active):	1
Total staff:	273
Externally funded staff:	122
PhD students:	59
Nationalities:	41
External competitive funding °	
Total:	131 M EUR
Fundraising °	
Total:	6.9 M EUR
Collaborations	
Collaborative projects active in 2022:	610
Industrial partners in active projects:	77

Publications	
Total publications:	149
Publications IF>10:	31
Publications in 25% best of field*:	67%
Open Access (OA) Publications:	86%
Publications in OA journals:	49%
Cumulative number of publications°:	1390
Innovation	
Patents°:	37
Proof of concept°: (total 4.1 M EUR)	9
Spin-offs active:	3

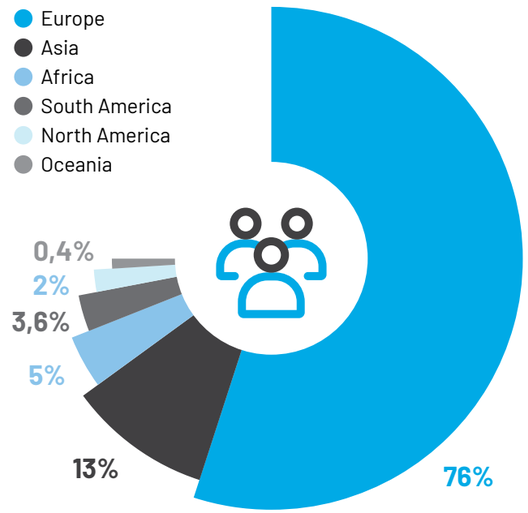
* based on Web of Science

° cumulative (2009-2022)

Staff categories 2022



Staff origins



Scientific Advisory Board

Members	
Maria Grazia Spillantini	Professor of Molecular Neurology, University of Cambridge
Li-Huei Tsai	Professor of Neuroscience, MIT
Hermona Soreq	Professor of Molecular Neuroscience, Hebrew University of Jerusalem
Natasa Przulj	Professor of Biomedical Data Science, Barcelona Supercomputing Center
David Holtzman	Professor of Neurology, Washington University
Lennart Mucke	Professor of Neuroscience, University of California
Hans-Christian Pape	Professor of Physiology, Westfälische Wilhelms-University
Etienne Hirsch	Professor of Neuroscience, Paris Brain Institute
Andreas Beyer	Professor for Systems Biology, University Cologne

back to table of contents

Publications 2022

Book

1. Muhammad Ali et al., Computational Methods to Identify Cell-Fate Determinants, Identity Transcription Factors, and Niche-Induced Signaling Pathways for Stem Cell Research. *Methods In Molecular Biology* (Clifton, N.J.), 2471–83-109, 10.1007/978-1-0716-2193-6_4

Book Series

1. Carlos Vega et al., Translational Challenges of Biomedical Machine Learning Solutions in Clinical and Laboratory Settings, Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics), 13347 LNBI - 353–358, 10.1007/978-3-031-07802-6_30

Case Reports

1. Sergio Castro-Gomez et al., CNS Superficial Siderosis Mimicking a Motor Neuron Disease. *Brain Sciences*, 12 - (11) - 1558, 10.3390/brainsci12111558

2. Gabriela Novak et al., Generation of two human induced pluripotent stem cell lines from fibroblasts of Parkinson's disease patients carrying the ILE368ASN mutation in PINK1 (LCSBi002) and the R275W mutation in Parkin (LCSBI004). *Stem Cell Research*, 61–102765, 10.1016/j.scr.2022.102765

Editorial

1. Jochen G Schneider et al., Editorial: Mitochondrial Biology and Its Role in Metabolic Diseases. *Frontiers In Endocrinology*, 13 - 944728, 10.3389/fendo.2022.944728

2. Wei Gu et al., Editorial: Digital Innovation and Data-Driven Research in Neurodegenerative Diseases. *Frontiers In Neurology*, 13 – 961847, 10.3389/fneur.2022.961847

Journal

1. Melissa Schepers et al., Selective PDE4 subtype inhibition provides new opportunities to intervene in neuroinflammatory versus myelin damaging hallmarks of multiple sclerosis. *Brain Behavior And Immunity*, 109 – 1–22, 10.1016/j.bbi.2022.12.020

2. B J Kunath et al., Alterations of oral microbiota and impact on the gut microbiome in type 1 diabetes mellitus revealed by integrated multi-omic analyses. *Microbiome*, 10 - (1) - 243, 10.1186/s40168-022-01435-4

3. Dietlind L Gerloff et al., Prediction and verification of glycosyltransferase activity by bioinformatics analysis and protein engineering. *Star Protocols*, 4 - (1) - 101905, 10.1016/j.xpro.2022.101905

4. Marie Macnee et al., Data-driven historical characterization of epilepsy-associated genes. *European Journal Of Paediatric Neurology*, 42 – 82–87, 10.1016/j.ejpn.2022.12.005

5. Dilek Mercan et al., The Contribution of the Locus Coeruleus-Noradrenaline System Degeneration during the Progression of Alzheimer's Disease. *Biology*, 11–(12) - 1822, 10.3390/biology11121822

6. Stanislav Iakhno et al., Longitudinal analysis of the faecal microbiome in pigs fed Cyberlindnera jadinii yeast as a protein source during the weanling period followed by a rapeseed- and faba bean-based grower-finisher diet. *Animal Microbiome*, 4 - (1) - 62, 10.1186/s42523-022-00217-5

7. Joanne Trinh et al., Mitochondrial DNA heteroplasmy distinguishes disease manifestation in PINK1/PRKN-linked Parkinson's disease. *Brain*, 10.1093/brain/awac464

8. Kyra Geyer et al., Multiple Functions of the Type II Thioesterase Associated with the Phoslactomycin Polyketide Synthase. *Biochemistry*, 61 - (23) – 2662–71, 10.1021/acs.biochem.2c00234

9. Maria Pires Pacheco et al., scFASTCORMICS: A Contextualization Algorithm to Reconstruct Metabolic Multi-Cell Population Models from Single-Cell RNAseq Data. *Metabolites*, 12 - (12) - 1211, 10.3390/ metabo12121211

10. S. Reif et al., Supporting patients with heart failure with digital therapeutics—A pilot study in Germany. *Digital Health*, 8 - 20552076221143899, 10.1177/20552076221143899

11. Eric Bach et al., Joint structural annotation of small molecules using liquid chromatography retention order and tandem mass spectrometry data. *Nature Machine Intelligence*, 4 - (12) - 1224–1237, 10.1038/s42256-022-00577-2

12. Irina Balaur et al., GraphML-SBGN bidirectional converter for metabolic networks. *Journal Of Integrative Bioinformatics*, 19 - (4) - 20220030, 10.1515/jib-2022-0030

13. Aurélie Fischer et al., Long COVID Classification: Findings from a Clustering Analysis in the Predi-COVID Cohort Study. International *Journal Of Environmental Research And Public Health*, 19 - (23), 10.3390/ijerph192316018

14. Maria G. Balta et al., RvD1n-3 DPA Downregulates the Transcription of Pro-Inflammatory Genes in Oral Epithelial Cells and Reverses Nuclear Translocation of Transcription Factor p65 after TNF-a Stimulation. *International Journal Of Molecular Sciences*, 23 - (23), 10.3390/ijms232314878

15. Fubo Cheng et al., Intronic enhancers of the human SNCA gene predominantly regulate its expression in brain in vivo. *Science Advances*, 8 - (47) - eabq6324, 10.1126/sciadv.abq6324

16. Heiko Gassner et al., The Effects of an Individualized Smartphone-Based Exercise Program on Self-defined Motor Tasks in Parkinson Disease: Pilot Interventional Study. *Jmir Rehabilitation And Assistive Technologies*, 9 - (4) - e38994, 10.2196/38994

17. Menglin Zheng et al., A single cell-based computational platform to identify chemical compounds targeting desired sets of transcription factors for cellular conversion. *Stem Cell Reports*, 18 - (1) - 131–44, 10.1016/j.stemcr.2022.10.013

18. Rosa C Paolicelli et al., Microglia states and nomenclature: A field at its crossroads. *Neuron*, 110 - (21) - 3458–3483, 10.1016/j.neuron.2022.10.020

19. Oskar Hickl et al., binny: an automated binning algorithm to recover high-quality genomes from complex metagenomic datasets. *Briefings In Bioinformatics*, 23 - (6) - bbac431, 10.1093/bib/bbac431

20. Remi Stevelink et al., Individualised prediction of drug resistance and seizure recurrence after medication withdrawal in people with juvenile myoclonic epilepsy: A systematic review and individual participant data meta-analysis. *Eclinicalmedicine*, 53 - 101732, 10.1016/j.eclinm.2022.101732

21. Holger R Roth et al., Rapid artificial intelligence solutions in a pandemic-The COVID-19-20 Lung CT Lesion Segmentation Challenge. *Medical Image Analysis*, 82 - 102605, 10.1016/j.media.2022.102605

22. Corrado Ameli et al., PaFSe: A Parameter-Free Segmentation Approach for 3D Fluorescent Images. *Sn Computer Science*, 3 - (6), 10.1007/s42979-022-01265-z

23. Sumaiya Iqbal et al., Delineation of functionally essential protein regions for 242 neurodevelopmental disorders. *Brain*, 146 - (2) - 519–533, 10.1093/brain/awac381

24. Bob Biewer et al., Effects of Low Intensity Pulsed Ultrasound Stimulation on the Temporal Dynamics of Irradiated Bone Tissue Healing: A Histomorphometric Study in Rabbits. *International Journal Of Molecular Sciences*, 23 - (20), 10.3390/ijms232012426

25. Mehri Baniasadi, et al., DBSegment: Fast and robust segmentation of deep brain structures considering domain generalization. *Human Brain Mapping*, 44 - (2) – 762–78, 10.1002/hbm.26097

26. Frank Menger et al., Enhancing spectral quality in complex environmental matrices: Supporting suspect and non-target screening in zebra mussels with ion mobility. *Environment International*, 170 –107585, 10.1016/j.envint.2022.107585

27. Lukas et al., Body-First Subtype of Parkinson's Disease with Probable REM-Sleep Behavior Disorder Is Associated with Non-Motor Dominant Phenotype. *Journal Of Parkinsons Disease*, 12 - (8) – 2561–2573, 10.3233/JPD-223511

28. Menglin Zheng et al., ChemPert: mapping between chemical perturbation and transcriptional response for non-cancer cells. *Nucleic Acids Research*, 51 - (D1) - D877–89, 10.1093/nar/gkac862

29. Makoto Kiyose et al., MR imaging profile and histopathological characteristics of tumour vasculature, cell density and proliferation rate define two distinct growth patterns of human brain metastases from lung cancer. *Neuroradiology*, 65 - (2) - 275–85, 10.1007/s00234-022-03060-2

30. Arthur N. Montanari et al., Functional observability and subspace reconstruction in nonlinear systems. *Physical Review Research*, 4 - (4), 10.1103/PhysRevResearch.4.043195

31. Sonia Sabate-Soler et al., Immunocompetent brain organoids—microglia enter the stage. *Progress In Biomedical Engineering*, 4 - (4), 10.1088/2516-1091/ac8dcf

32. St Elmo Wilken et al., Interrogating the effect of enzyme kinetics on metabolism using differentiable constraint-based models. *Metabolic Engineering*, 74 – 72–82, 10.1016/j.ymben.2022.09.002

33. Laura de Nies et al., Mobilome-driven segregation of the resistome in biological wastewater treatment. *Elife*, 11, 10.7554/eLife.81196

34. Velma T E Aho et al., SnapShot: The Expobiome Map. *Cell Host & Microbe*, 30 - (9) – 1340–1340.e1, 10.1016/j.chom.2022.08.015

35. Paul Wilmes et al., The gut microbiome molecular complex in human health and disease. *Cell Host & Microbe*, 30 - (9) – 1201–1206, 10.1016/j.chom.2022.08.016

36. Daniel Weiss et al., Genetic stratification of motor and QoL outcomes in Parkinson's disease in the EARLYSTIM study. *Parkinsonism & Related Disorders*, 103 – 169–174, 10.1016/j.parkreldis.2022.08.025

37. Johanna Kruger et al., Loss-of-function variants in the KCNQ5 gene are implicated in genetic generalized epilepsies. *Ebiomedicine*, 84 - 104244, 10.1016/j.ebiom.2022.104244

38. Gabriela Novak et al., Dopamine, Psychosis, and Symptom Fluctuation: A Narrative Review. *Healthcare*, 10 - (9) - 1713, 10.3390/healthcare10091713

39. Daniele Proverbio et al., Buffering variability in cell regulation motifs close to criticality. *Physical Review E*, 106 - (3) - L032402, 10.1103/PhysRevE.106.L032402

40. Oluyomi M Adesoji et al., Benchmarking of univariate pleiotropy detection methods applied to epilepsy. *Human Mutation*, 43 - (9) - 1314–1332, 10.1002/humu.24417

41. Tobias Brunger et al., Conserved patterns across ion channels correlate with variant pathogenicity and clinical phenotypes. *Brain*, 146 - (3) - 923–934, 10.1093/brain/awac305

42. Alexander Heinz et al., Itaconate controls its own synthesis via feedback-inhibition of reverse TCA cycle activity at IDH2. *Biochimica Et Biophysica Acta-Molecular Basis Of Disease*, 1868 - (12) - 166530, 10.1016/j.bbadis.2022.166530

43. Laura Mahoney-Sanchez et al., Alpha synuclein determines ferroptosis sensitivity in dopaminergic neurons via modulation of ether-phospholipid membrane composition. *Cell Reports*, 40 - (8) - 111231, 10.1016/j.celrep.2022.111231

44. Muhammad Ali et al., Single-Cell Transcriptional Profiling and Gene Regulatory Network Modeling in Tg2576 Mice Reveal Gender-Dependent Molecular Features Preceding Alzheimer-Like Pathologies. *Molecular Neurobiology*, 10.1007/s12035-022-02985-2

45. Sandeep Grover et al., Genome-wide Association and Meta-analysis of Age at Onset in Parkinson Disease: Evidence From the COURAGE-PD Consortium. *Neurology*, 99 - (7) - e698-710, 10.1212/WNL.0000000000200699

46. Jesus Fuentes et al., Renyi Entropy in Statistical Mechanics. *Entropy*, 24 - (8), 10.3390/e24081080

47. Alexandra Leer et al., Design of an experimental platform for gait analysis with ActiSense and StereoPi. *Current Directions In Biomedical Engineering*, 8 - (2) – 572–575, 10.1515/cdbme-2022-1146

48. Aurélie Fischer et al., Long COVID Symptomatology After 12 Months and Its Impact on Quality of Life According to Initial Coronavirus Disease 2019 Disease Severity. *Open Forum Infectious Diseases*, 9 - (8) - ofac397, 10.1093/ofid/ofac397

49. Ramon Diaz-Uriarte et al., Ten quick tips for biomarker discovery and validation analyses using machine learning. *Plos Computational Biology*, 18 - (8) - e1010357, 10.1371/journal.pcbi.1010357

50. Tony Heurtaux et al., Normal and Pathological NRF2 Signalling in the Central Nervous System. *Antioxidants*, 11 - (8), 10.3390/antiox11081426

51. Ebtisam Alharbi et al., Selection of data sets for FAIRification in drug discovery and development: Which, why, and how? *Drug Discovery Today*, 27 - (8) - 2080–2085, 10.1016/j.drudis.2022.05.010

52. Melanie Vausort et al., Regulation of N6-Methyladenosine after Myocardial Infarction. *Cells*, 11 - (15), 10.3390/cells11152271

53. Nicole J et al., Clinical and biochemical distinctions for a metabolite repair disorder caused by NAXD or NAXE deficiency. *Journal Of Inherited Metabolic Disease*, 45 - (6) – 1028–38, 10.1002/jimd.12541

54. Emma L. Schymanski, Global Challenges: Opening up Chemistry, Pandemics, and Air Pollution. *Acs Environmental Au*, 2 - (4) - 287–289, 10.1021/acsenvironau.2c00032

55. Yolanda Pires-Afonso et al., Elucidating tumour-associated microglia/macrophage diversity along glioblastoma progression and under ACOD1 deficiency. *Molecular Oncology*, 16 - (17) – 3167–3191, 10.1002/1878-0261.13287

back to table of contents

56. Begona Talavera Andujar et al., Studying the Parkinson's disease metabolome and exposome in biological samples through different analytical and cheminformatics approaches: a pilot study. *Analytical And Bioanalytical Chemistry*, 414 - (25) – 7399–419, 10.1007/s00216-022-04207-z

57. Cloe Domenighetti et al., The Interaction between HLA-DRB1 and Smoking in Parkinson's Disease Revisited. *Movement Disorders*, 37 - (9) – 1929–1937, 10.1002/mds.29133

58. Maria G Balta et al., Expression and function of resolvin RvD1n-3 DPA receptors in oral epithelial cells. *European Journal Of Oral Sciences*, 130 - (4) - e12883, 10.1111/eos.12883

59. Atte Aalto et al., Linear system identifiability from single-cell data. *Systems & Control Letters*, 165 - (ARTN 105287) - 105287, 10.1016/j. sysconle.2022.10528

60. Carlos Vega et al., Smart Scheduling (SMASCH): multi-appointment scheduling system for longitudinal clinical research studies. *Jamia Open*, 5 - (2) - ooac038, 10.1093/jamiaopen/ooac038

61. Pauline Mencke et al., Generation of isogenic control DJ-1-delP GC13 for the genetic Parkinson's disease-patient derived iPSC line DJ-1-delP (LCSBi008-A-1). *Stem Cell Research*, 62 - 102815, 10.1016/j. scr.2022.102815

62. Leila Ezzat et al., Benthic Biofilms in Glacier-Fed Streams from Scandinavia to the Himalayas Host Distinct Bacterial Communities Compared with the Streamwater. *Applied And Environmental Microbiology*, 88 - (12) - e0042122, 10.1128/aem.00421-22

63. Daniele Proverbio et al., Model-based assessment of COVID-19 epidemic dynamics by wastewater analysis. *Science Of The Total Environment*, 827 - 154235, 10.1016/j. scitotenv.2022.154235

64. Varun S Sharma et al., PCfun: a hybrid computational framework for systematic characterization of protein complex function. *Briefings In Bioinformatics*, 23 - (4), 10.1093/bib/bbac239

65. Joseph A Charbonnet et al., Communicating Confidence of Per- and Polyfluoroalkyl Substance Identification via High-Resolution Mass Spectrometry. *Environmental Science & Technology Letters*, 9 - (6) - 473–81, 10.1021/acs.estlett.2c00206

66. Yizhou Hu et al., Neural network learning defines glioblastoma features to be of neural crest perivascular or radial glia lineages. *Science Advances*, 8 - (23) - eabm6340, 10.1126/sciadv.abm6340

67. G Arena et al., Neurodegeneration and Neuroinflammation in Parkinson's Disease: a Self-Sustained Loop. *Current Neurology And Neuroscience Reports*, 22 - (8) – 427–40, 10.1007/s11910-022-01207-5

68. Massimo Bourquin et al., The microbiome of cryospheric ecosystems. *Nature Communications*, 13 - (1) - 3087, 10.1038/s41467-022-30816-4

69. Joanne Trinh, et al., Molecular mechanisms defining penetrance of LRRK2-associated Parkinson's disease, *Medizinische Genetik*, 34 - (2) - 103-116, 10.1515/medgen-2022-2127

70. Francesca Bowring et al., Exploration of whether socioeconomic factors affect the results of priority setting partnerships: updating the top 10 research priorities for the management of Parkinson's in an international setting. *Bmj Open*, 12 - (6) - 10.1136/bmjopen-2021-049530

71. Tyler J Kohler et al., Glacier shrinkage will accelerate downstream decomposition of organic matter and alters microbiome structure and function. *Global Change Biology*, 28 - (12) – 3846–3859, 10.1111/gcb.16169

72. Gunter Hoglinger et al., GBA-associated PD: chances and obstacles for targeted treatment strategies. *Journal Of Neural Transmission*, 129 - (9) - 1219-33, 10.1007/s00702-022-02511-7

73. Mark Corbett et al., Biomarkers of systemic treatment response in people with psoriasis: a scoping review. *British Journal Of Dermatology*, 187 - (4) – 494–506, 10.1111/bjd.21677

74. Niklas Schwarz et al., Spectrum of Phenotypic, Genetic, and Functional Characteristics in Patients With Epilepsy With KCNC2 Pathogenic Variants. *Neurology*, 98 - (20) - e2046–e2059, 10.1212/WNL.0000000000200660

75. Adelene Lai et al., The Next Frontier of Environmental Unknowns: Substances of Unknown or Variable Composition, Complex Reaction Products, or Biological Materials (UVCBs). *Environmental Science & Technology*, 56 - (12) – 7448–66, 10.1021/acs.est.2c00321

76. Martin Lang et al., A genome on shaky ground: exploring the impact of mitochondrial DNA integrity on Parkinson's disease by highlighting the use of cybrid models. *Cellular And Molecular Life Sciences*, 79 - (5) - 283, 10.1007/s00018-022-04304-3

77. Takumi Kobayashi et al., A FAsT contribution: Adipocytes rewire their metabolism to acquire immune functions. *Cell Metabolism*, 34 - (5) - 656–657, 10.1016/j. cmet.2022.04.007

78. Wei He et al., Mesaconate is synthesized from itaconate and exerts immunomodulatory effects in macrophages. *Nature Metabolism*, 4 - (5) - 524–533, 10.1038/s42255-022-00565-1

79. F Chen et al., Citraconate inhibits ACOD1 (IRG1) catalysis, reduces interferon responses and oxidative stress, and modulates inflammation and cell metabolism. *Nature Metabolism*, 4 - (5) - 534–546, 10.1038/s42255-022-00577-x

80. Egle Danileviciute et al., PARK7/DJ-1 promotes pyruvate dehydrogenase activity and maintains Treg homeostasis during ageing. *Nature Metabolism*, 4 - (5) – 589–607, 10.1038/s42255-022-00576-y

81. Ravi Ramessur et al., Biomarkers of disease progression in people with psoriasis: a scoping review. *British Journal Of Dermatology*, 187 - (4) – 481–493, 10.1111/bjd.21627

82. Pauline Mencke et al., Generation and characterization of a genetic Parkinson's disease-patient derived iPSC line DJ-1-delP (LCSBi008-A). *Stem Cell Research*, 62 - 102792, 10.1016/j.scr.2022.102792

83. Kobi Wasner et al., Parkin Deficiency Impairs Mitochondrial DNA Dynamics and Propagates Inflammation. *Movement Disorders*, 37 - (7) – 1405–1415, 10.1002/mds.29025

84. Susheel Bhanu Busi et al., Genomic and metabolic adaptations of biofilms to ecological windows of opportunity in glacier-fed streams. *Nature Communications*, 13 - (1) - 2168, 10.1038/s41467-022-29914-0

85. Christophe M. Capelle et al., Combinatorial analysis reveals highly coordinated early-stage immune reactions that predict later antiviral immunity in mild COVID-19 patients. *Cell Reports Medicine*, 3 - (4) - 100600, 10.1016/j.xcrm.2022.100600

86. Lars Tonges et al., Blood-based biomarker in Parkinson's disease: potential for future applications in clinical research and practice. *Journal Of Neural Transmission*, 129 - (9) - 1201–17, 10.1007/s00702-022-02498-1

87. Gianfranco Frigerio et al., Development and Application of an LC-MS/MS Untargeted Exposomics Method with a Separated Pooled Quality Control Strategy. *Molecules*, 27 - (8) - 2580, 10.3390/molecules27082580

88. Hana Brunhoferova et al., Bioremediation of 27 Micropollutants by Symbiotic Microorganisms of Wetland Macrophytes. *Sustainability*, 14 - (7) - 3944, 10.3390/su14073944

89. Anna Schleimer et al., Introgressive hybridisation between domestic pigs (Sus scrofa domesticus) and endemic Corsican wild boars (S. s. meridionalis): effects of human-mediated interventions. *Heredity*, 128 - (4) - 279-90, 10.1038/s41437-022-00517-1

90. Christophe M Capelle et al., Stress hormone signalling inhibits Th1 polarization in a CD4 T-cell-intrinsic manner via mTORC1 and the circadian gene PER1. *Immunology*, 165 - (4) - 428–44, 10.1111/imm.13448

91. Fikile Mhlongo et al., Evaluation of the wound healing properties of South African medicinal plants using zebrafish and in vitro bioassays. *Journal Of Ethnopharmacology*, 286 - 114867, 10.1016/j.jep.2021.114867

92. Ciaran Campbell et al., A pharmacogenomic assessment of psychiatric adverse drug reactions to levetiracetam. *Epilepsia*, 63 - (6) – 1563–1570, 10.1111/epi.17228

93. Sonja Fixemer et al., Microglia phenotypes are associated with subregional patterns of concomitant tau, amyloid-beta and alpha-synuclein pathologies in the hippocampus of patients with Alzheimer's disease and dementia with Lewy bodies. *Acta Neuropathologica Communications*, 10 - (1) - 36, 10.1186/s40478-022-01342-7

94. Nicolas Malvaux et al., In Vitro Comparative Study of Platelets Treated with Two Pathogen-Inactivation Methods to Extend Shelf Life to 7 Days. *Pathogens*, 11 - (3) - 343, 10.3390/pathogens11030343

95. Sonia Sabate-Soler et al., Microglia integration into human midbrain organoids leads to increased neuronal maturation and functionality. *Glia*, 70 - (7) - 1267–88, 10.1002/glia.24167

96. Carolin Gabbert et al., Coffee, smoking and aspirin are associated with age at onset in idiopathic Parkinson's disease. *Journal Of Neurology*, 269 - (8) - 4195–4203, 10.1007/s00415-022-11041-x

97. Daniele Proverbio et al., Performance of early warning signals for disease re-emergence: A case study on COVID-19 data. *Plos Computational Biology*, 18 - (3) - e1009958, 10.1371/journal.pcbi.1009958

98. Alexandra Sipol et al., MondoA drives malignancy in B-ALL through enhanced adaptation to metabolic stress. *Blood*, 139 - (8) – 1184–1197, 10.1182/blood.2020007932

99. Elena I. Ilina et al., Enzymatic activity of glycosyltransferase GLT8D1 promotes human glioblastoma cell migration. *Iscience*, 25 - (2) - 103842, 10.1016/j.isci.2022.103842

100. Francesco Brunelli et al., PINK1 Protects against Staurosporine-Induced Apoptosis by Interacting with Beclin1 and Impairing Its Pro-Apoptotic Cleavage. *Cells*, 11 - (4) - 678, 10.3390/cells11040678

101. Gregory C Addicks et al., GCN5 maintains muscle integrity by acetylating YY1 to promote dystrophin expression. *Journal Of Cell Biology*, 221 - (2) - e202104022, 10.1083/ jcb.202104022

102. Richard Milne et al., Return of genomic results does not motivate intent to participate in research for all: Perspectives across 22 countries. *Genetics In Medicine*, 24 - (5) – 1120–1129, 10.1016/j.gim.2022.01.002

103. Jean-David Morel et al., The mouse metallomic landscape of aging and metabolism. *Nature Communications*, 13 - (1) - 607, 10.1038/s41467-022-28060-x

104. Pierre Garcia et al., Neurodegeneration and neuroinflammation are linked, but independent of alpha-synuclein inclusions, in a seeding/spreading mouse model of Parkinson's disease. *Glia*, 70 - (5) – 935–60, 10.1002/glia.24149

105. Catherine Sedrani et al., Toward hypothesis-driven, personalized microbiome screening. *Cell Reports Methods*, 2 - (1) - 100139, 10.1016/j.crmeth.2021.100139

106. Alise Zagare et al., Midbrain organoids mimic early embryonic neurodevelopment and recapitulate LRRK2-p.Gly2019Ser-associated gene expression. *American Journal Of Human Genetics*, 109 - (2) – 311–27, 10.1016/j.ajhg.2021.12.009

107. Veronica Mutti et al., Structural Plasticity of Dopaminergic Neurons Requires the Activation of the D3R-nAChR Heteromer and the PI3K-ERK1/2/Akt-Induced Expression of c-Fos and p70S6K Signaling Pathway. *Molecular Neurobiology*, 59 - (4) – 2129–49, 10.1007/s12035-022-02748-z

108. Ni Zeng et al., DJ-1 depletion prevents immunoaging in T-cell compartments. *Embo Reports*, 23 - (3) - e53302, 10.15252/embr.202153302

109. Susanne Schmitz et al., Prevalence and Cost of Care for Parkinson's Disease in Luxembourg: An Analysis of National Healthcare Insurance Data. *Pharmacoeconomics - Open*, 6 - (3) – 405–14, 10.1007/s41669-021-00321-3

110. Mahmoud Koko et al., Association of ultra-rare coding variants with genetic generalized epilepsy: A case-control whole exome sequencing study. *Epilepsia*, 63 - (3) – 723–735, 10.1111/epi.17166

111. Gabriela Novak et al., Single-cell transcriptomics of human iPSC differentiation dynamics reveal a core molecular network of Parkinson's disease. *Communications Biology*, 5 - (1) - 49, 10.1038/s42003-021-02973-7

112. Aaqib Sohail et al., Itaconate and derivatives reduce interferon responses and inflammation in influenza A virus infection. *Plos Pathogens*, 18 - (1) - e1010219, 10.1371/journal.ppat.1010219

113. Greta Del Mistro et al., Focal adhesion kinase plays a dual role in TRAIL resistance and metastatic outgrowth of malignant melanoma. *Cell Death & Disease*, 13 - (1) - 54, 10.1038/s41419-022-04502-8

114. Cloe Domenighetti et al., Dairy Intake and Parkinson's Disease: A Mendelian Randomization Study. *Movement Disorders*, 37 - (4) - 857–864, 10.1002/mds.28902

115. Fubo Cheng et al., DYT6 mutated THAP1 is a cell type dependent regulator of the SP1 family. *Brain*, 145 - (11) – 3968–3984, 10.1093/brain/awac001

116. Arthur N Montanari et al., Functional observability and target state estimation in large-scale networks. *Proceedings Of The National Academy Of Sciences Of The United States Of America*, 119 - (1) - e2113750119, 10.1073/pnas.2113750119

117. Adelene Lai et al., An algorithm to classify homologous series within compound datasets. *Journal Of Cheminformatics*, 14 - (1) - 85, 10.1186/s13321-022-00663-y

back to table of contents

118. Stefania Vetrano et al., ImmUniverse Consortium: Multi-omics integrative approach in personalized medicine for immune-mediated inflammatory diseases. *Frontiers In Immunology*, 13 - 1002629, 10.3389/fimmu.2022.1002629

119. Kenza Nedara et al., Relevance of the TRIAP1/p53 axis in colon cancer cell proliferation and adaptation to glutamine deprivation. *Frontiers In Oncology*, 12 - 958155, 10.3389/fonc.2022.958155

120. Hiba Mohammed Taha et al., The NORMAN Suspect List Exchange (NORMAN-SLE): facilitating European and worldwide collaboration on suspect screening in high resolution mass spectrometry. *Environmental Sciences Europe*, 34 - (1) - 104, 10.1186/s12302-022-00680-6

121. Yasen Wang et al., Data-Driven Discovery of Stochastic Differential Equations. *Engineering*, 17 - 244–252, 10.1016/j.eng.2022.02.007

122. Max Meyrath et al., Nanoluciferase-based cell fusion assay for rapid and high-throughput assessment of SARS-CoV-2-neutralizing antibodies in patient samples. *Methods in Enzymology*, 675 - 351–381, 10.1016/bs.mie.2022.07.015

123. Regina Becker et al., Secondary Use of Personal Health Data: When Is It "further Processing" under the GDPR, and What Are the Implications for Data Controllers? *European Journal Of Health Law*, 1–29, 10.1163/15718093-bja10094

124. Jade Brandani et al., Spatial patterns of benthic biofilm diversity among streams draining proglacial floodplains. *Frontiers In Microbiology*, 13 - 948165, 10.3389/fmicb.2022.948165

125. L. Pavelka et al., Age at onset as stratifier in idiopathic Parkinson's disease – effect of ageing and polygenic risk score on clinical phenotypes. *Npj Parkinson's Disease*, 8 - (1) - 102, 10.1038/s41531-022-00342-7

126. Norberto Sánchez-Cruz et al., Paths to Cheminformatics: Q&A with Norberto Sánchez-Cruz and Emma Schymanski. *Journal Of Cheminformatics*, 14 - (1) - 51, 10.1186/s13321-022-00628-1

127. Ekaterina Mavrina et al., Multi-Omics Interdisciplinary Research Integration to Accelerate Dementia Biomarker Development (MIRIADE). *Frontiers In Neurology*, 13 - 890638, 10.3389/fneur.2022.890638

128. Beatriz Garcia Santa Cruz et al., Generalising from conventional pipelines using deep learning in high-throughput screening workflows. *Scientific Reports*, 12 - (1) - 11465, 10.1038/s41598-022-15623-7

129. Ahmed Abdelmonem Hemedan et al., Boolean modelling as a logic-based dynamic approach in systems medicine. *Computational And Structural Biotechnology Journal*, 20 – 3161–72, 10.1016/j.csbj.2022.06.035

130. Theresa Luth et al., Benchmarking Low-Frequency Variant Calling With Long-Read Data on Mitochondrial DNA. *Frontiers In Genetics*, 13 - 887644, 10.3389/fgene.2022.887644

131. Christina Wolf et al., GDAP1 loss of function inhibits the mitochondrial pyruvate dehydrogenase complex by altering the actin cytoskeleton. *Communications Biology*, 5 - (1) - 541, 10.1038/s42003-022-03487-6

132. Nicole Kiweler et al., Mitochondria preserve an autarkic one-carbon cycle to confer growth-independent cancer cell migration and metastasis. *Nature Communications*, 13 - (1) - 2699, 10.1038/s41467-022-30363-y

133. Laura de Nies et al., Evolution of the murine gut resistome following broad-spectrum antibiotic treatment. *Nature Communications*, 13 - (1) - 2296, 10.1038/s41467-022-29919-9

134. Dominik Ternes et al., The gut microbial metabolite formate exacerbates colorectal cancer progression. *Nature Metabolism*, 4 - (4) – 458–75, 10.1038/s42255-022-00558-0

135. Maria C.P. et al., Defense response-like reaction associated with an anomaly in Eucalyptus grandis. Trees-Structure And Function, 36 - (4) - 1285–1302, 10.1007/s00468-022-02288-y

136. Davide G. et al. Glutathione-dependent redox balance characterizes the distinct metabolic properties of follicular and marginal zone B cells. *Nature Communications*, 13 - (1) - 1789, 10.1038/s41467-022-29426-x

137. David S. Bouvier et al., The Multifaceted Neurotoxicity of Astrocytes in Ageing and Age-Related Neurodegenerative Diseases: A Translational Perspective. *Frontiers In Physiology*, 13 - 814889, 10.3389/fphys.2022.814889

138. Wenjuan Yang et al., Unspecific CTL Killing Is Enhanced by High Glucose via TNF-Related Apoptosis-Inducing Ligand. *Frontiers In Immunology*, 13 - 831680, 10.3389/fimmu.2022.831680

139. Agnes Langer et al., Additive Effect of Dopaminergic Medication on Gait Under Single and Dual-Tasking Is Greater Than of Deep Brain Stimulation in Advanced Parkinson Disease With Long-duration Deep Brain Stimulation, *Neuromodulation*, 26 - (2) - 364-373, 10.1016/j.neurom.2022.01.015

140. Laure Pauly et al., Retrograde Procedural Memory in Parkinson's Disease: A Cross-Sectional, Case-Control Study. *Journal Of Parkinsons Disease*, 12 - (3) - 1013–1022, 10.3233/JPD-213081

141. Szilvia Veszelka et al., A Triple Combination of Targeting Ligands Increases the Penetration of Nanoparticles across a Blood-Brain Barrier Culture Model. *Pharmaceutics*, 14 - (1) - 86, 10.3390/pharmaceutics14010086

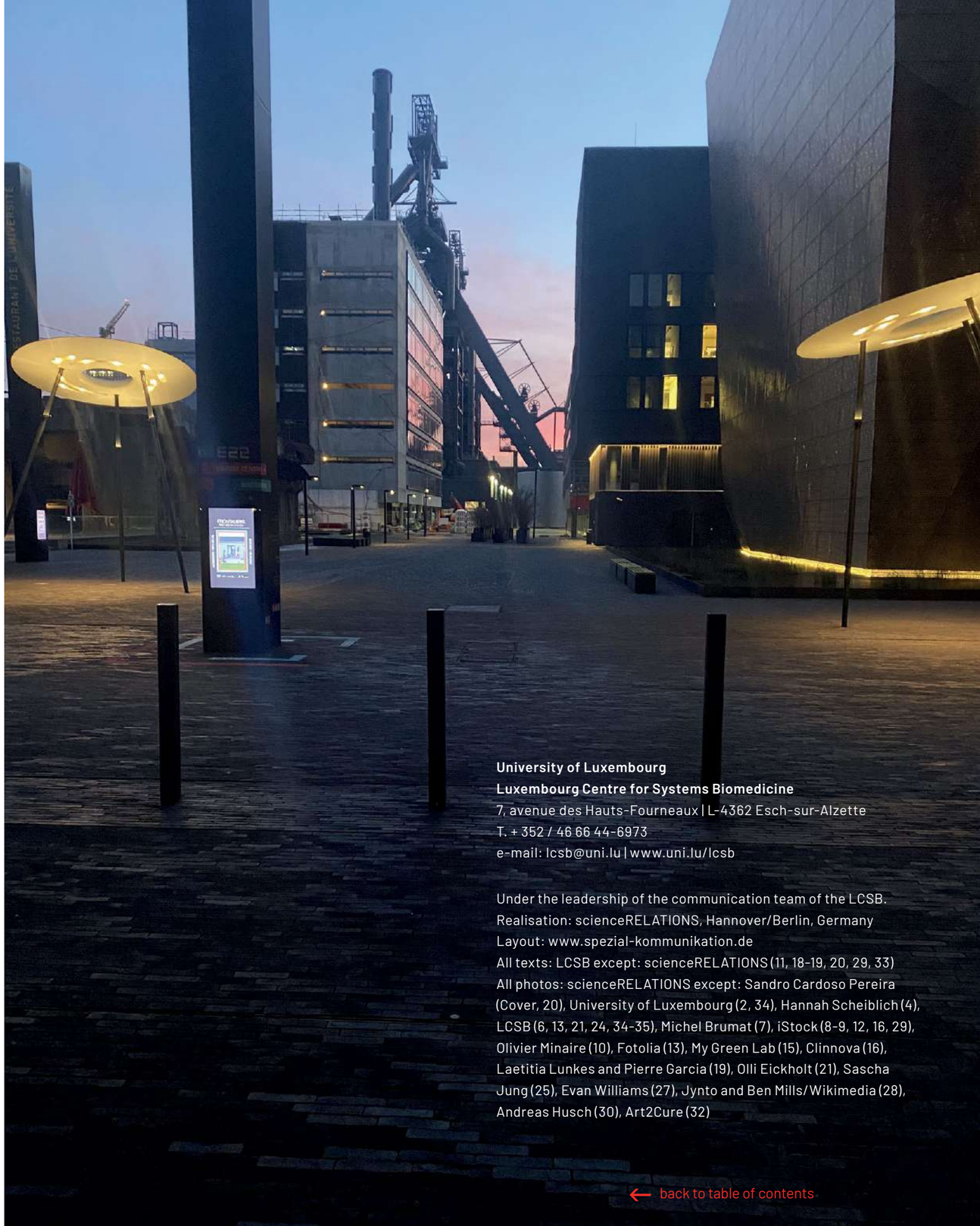
142 . Odette Fründt et al., Impact of COVID-19 Pandemic on (Health) Care Situation of People with Parkinson's Disease in Germany (Care4PD). *Brain Sciences*, 12 - (1) - 62, 10.3390/brainsci12010062

143. Cioé Domenighetti et al., Mendelian Randomisation Study of Smoking, Alcohol, and Coffee Drinking in Relation to Parkinson's Disease. *Journal Of Parkinsons Disease*, 12 - (1) – 267–82, 10.3233/JPD-212851

Letter

1. Claire Pauly et al., Disease Progression, Resilience, and Inflammation Markers During the Coronavirus Disease 2019 Pandemic in Parkinson's Disease. *Movement Disorders*, 37 - (11) – 2315–2317, 10.1002/mds.29212

2. Gabriel Sigmund et al., Broaden chemicals scope in biodiversity targets. *Science*, 376 - (6599) - 1280, 10.1126/science.add3070



University of Luxembourg
Luxembourg Centre for Systems Biomedicine
7, avenue des Hauts-Fourneaux | L-4362 Esch-sur-Alzette
T. + 352 / 46 66 44-6973
e-mail: lcsb@uni.lu | www.uni.lu/lcsb

Under the leadership of the communication team of the LCSB.
Realisation: scienceRELATIONS, Hannover/Berlin, Germany
Layout: www.spezial-kommunikation.de
All texts: LCSB except: scienceRELATIONS (11, 18-19, 20, 29, 33)
All photos: scienceRELATIONS except: Sandro Cardoso Pereira (Cover, 20), University of Luxembourg (2, 34), Hannah Scheiblich (4), LCSB (6, 13, 21, 24, 34-35), Michel Brumat (7), iStock (8-9, 12, 16, 29), Olivier Minaire (10), Fotolia (13), My Green Lab (15), Clinnova (16), Laetitia Lunkes and Pierre Garcia (19), Olli Eickholt (21), Sascha Jung (25), Evan Williams (27), Jynto and Ben Mills/Wikimedia (28), Andreas Husch (30), Art2Cure (32)

back to table of contents


LCSB