LCSB

University of Luxembourg

LCSB - Luxembourg Centre for Systems Biomedicine

Highlights 2024

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LCSB in brief

The LCSB is an interdisciplinary research centre at the University of Luxembourg. Its 250 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 disorders 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 mechanisms 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. ■

Cover picture:
Microglia and neurons connecting together - Electron microscopy image of a co-culture of human-derived neurons and microglia, highlighting cellular interaction between these cells, namely through tunnelling nanotubes (Mag = 392X).

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15 years of brain research

In September 2024, the LCSB celebrated 15 years of contribution to biomedical research in Luxembourg and beyond. Focusing on neurodegenerative disorders since its creation, the centre put Luxembourg on the map for its internationally recognised Parkinson's research, developed a strong expertise in bioinformatics and kept expanding its range over the years. Today, the LCSB 18 research groups bring together scientists with diverse academic backgrounds from over 50 different countries to study the brain and its diseases.

"Fifteen years ago, the LCSB started as a blank canvas. It was very exciting to have the opportunity to build something from scratch and to have a vision for the future of science in this country," recalls Dr Françoise Meisch, strategic advisor at the LCSB. "What began as a small group of motivated scientists under the leadership of Prof. Rudi Balling has now turned into a fully fledged research centre with nearly 300 members, some significant scientific results to its credit, and projects, such as the National Centre of Excellence in Research on Parkinson's disease or the Scienteens Lab, that have a direct impact on society. I think we can be proud!"

The 15-year festivities were a family affair: The LCSB team gathered to look back, look forward and enjoy some well-deserved cake. This get-together was also the opportunity to fill a time capsule with meaningful souvenirs, creating a snapshot of life at the LCSB in 2024. The capsule, to be opened in 2039, will be displayed for the next 15 years in Biotech 3, the new building being constructed on campus Belval that will soon provide additional space for biomedical research in Luxembourg. ■

Stories of a vibrant research centre

As the LCSB reaches another milestone in a troubled world, we should both celebrate our achievements over the past 15 years and plan for the future. Some of our recent successes are highlighted in this new annual report. These include the participation of NCER-PD, a national long-term research programme on Parkinson's disease, in the Parkinson's Progression Markers Initiative, a prestigious international clinical study.

Similarly, the scientific events organised by the LCSB in 2024, such as the ECDO conference, have attracted the attention of the international academic community and contributed to the attractiveness of Luxembourg as a research hub. Newly funded projects are another reason to celebrate, including additional doctoral training units that will bring several promising young scientists to our laboratories. All this consolidates the centre's position as a prominent player in the field of neuroscience and a sought-after collaboration partner.

Our aim is, of course, to continue to push the boundaries of science and you will find examples of this between these pages. As artificial intelligence and digital technologies transform biomedical research and healthcare at a rapid pace, several LCSB groups are expanding their expertise in this area. From nanoscopic connections between cells to new biomarkers, our research provides new insights into biological mechanisms relevant to health and disease. Brand-new projects launched this year are also venturing into exciting territories such as biocomputing and taking interdisciplinary research further by extending our collaborations with physicists, engineers or social scientists.

In addition to creative and high-quality research, the LCSB remains committed to having a positive impact on society, an objective that seems more relevant than ever. Our scientists are involved in outreach activities, working with a wide range of stakeholders to make this happen. From engaging with the rare disease community to launching an app for dementia prevention, from inspiring the next generation of researchers to helping navigate the post-COVID world, we aim to bring value to all layers of society.

Our world is changing at a fast pace. Some of these changes brought about by the geopolitical turmoil around us might be challenging, others linked to technological developments and new opportunities look promising. In either case, the LCSB is well-equipped for the years ahead. We will move forward thanks to our diverse interdisciplinary team which is growing in 2025, in particular with the creation of three new research groups. For our 15th anniversary, the LCSB team filled a time capsule. When we open it again in fifteen years' time, I am confident we will discover a snapshot of a vibrant research centre, ready to take on the future. This is what you will find in the stories we share with you here. ■

Michael Heneka

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Smart sensors and artificial intelligence for the benefit of patients

Predicting early and diagnosing better are two major goals of current biomedical research, because, quite often, the sooner you know about a disease, the better you can treat it. It turns out that new technologies can help address these challenges. By combining easy-to-wear sensors with artificial intelligence (AI), the AI Modelling and Prediction group at the LCSB is developing new ways to detect and monitor diseases as diverse as atrial fibrillation and sleep apnoea.

In a first project, the team led by Prof. Jorge Gonçalves came up with a computational model capable of predicting the transition from a normal cardiac rhythm to atrial fibrillation, the most common form of arrhythmia. Their innovative method gives early warnings on average 30 minutes before onset, with an accuracy of around 80%, meaning it could allow patients to take preventive measures to keep their cardiac rhythm stable.
"We used heart rate data to train a deep learning model that can recognise different phases – sinus rhythm, pre-atrial fibrillation and atrial fibrillation – and calculate a "probability of danger" that the patient will have an imminent episode," explains Dr Marino Gavidia who worked on this project during his PhD within the AI Modelling and Prediction group. Compared to previous work on arrhythmia prediction, this model, called WARN, is the first method to provide a warning far from onset.

In another project, the team worked on diagnosing sleep apnoea, a condition affecting millions of people worldwide. By analysing sleep study recordings, the researchers developed DRIVEN, a breakthrough method to estimate the severity of apnoea without the need for elaborate equipment and overnight stay at a clinic.
"Apnoea-Hypopnea Index (AHI) is a key metric used by doctors to divide patients into four categories: healthy, mild, moderate and severe," details Gabriela Retamales, doctoral student in the group. "Based on a single night of sleep, our model was able to place 99.3% of patients either in the correct AHI category or one class away from the true one." A level of accuracy that is expected to improve further when using data from several nights in a row, opening new avenues for apnoea diagnosis at home.

What is the common feature between these two projects? Besides their focus on diseases that are associated with several health risks and their potential to reduce the burden on healthcare systems, the two rely on a combination of easy-to-wear sensors and artificial intelligence. WARN achieves a high performance using only heart rate data that can be acquired from affordable pulse signal recorders such as smartwatches. DRIVEN analyses just a few signals, breathing patterns and oxygen levels, captured by sensors that can be used at home, from the comfort of your own bed. In both cases, wearable sensors are a game-changer.

"Traditionally, diagnosing sleep apnoea requires an overnight stay at a clinic with multiple sensors attached to the body, making it difficult for patients to sleep naturally. With DRIVEN, on the other hand, there are no cables, simply a sensor on a finger, an elastic band around the waist and a small device to store the data. We can hence offer patients a lot more comfort while still providing accurate information for doctors," describes Prof. Jorge Gonçalves. In the case of atrial fibrillation, easy-to-wear devices that can be used by patients on a daily basis open possibilities for continuous real-time monitoring which would reduce emergency interventions and improve patient outcomes.

The other innovation is of course the use of AI. In each project, the data obtained are analysed thanks to machine learning models. "These deep convolutional neural networks "learn" from large datasets and extract meaningful patterns," explains Prof. Gonçalves. "They provide fast and precise results, allow for a more prospective approach when it comes to predicting onset and their low computational cost makes them ideal for integration into wearable technologies." Additionally, the daily use of sensors by patients constantly provides new information, meaning these models can be continuously refined. Moving forward, the team will hence focus on developing personalised models trained to achieve enhanced performance for each specific patient. The potential of this approach extends beyond offering convenience, it could lead to new affordable therapeutic solutions.

"While my research group primarily focuses on fundamental questions, I am eager to collaborate with clinical and industrial partners to turn our ideas into marketable medical products," concludes Prof. Jorge Gonçalves. "Moving from theory to innovation could have a profound impact on patient care and quality of life."
As wearable health technology and artificial intelligence continue to evolve, the future of medicine may lie in the hands - or on the wrists - of patients themselves. ■

The AI Modelling and Prediction team

> As wearable technology continues to evolve, the future of medicine may lie in the hands – or on the wrists – of patients themselves.

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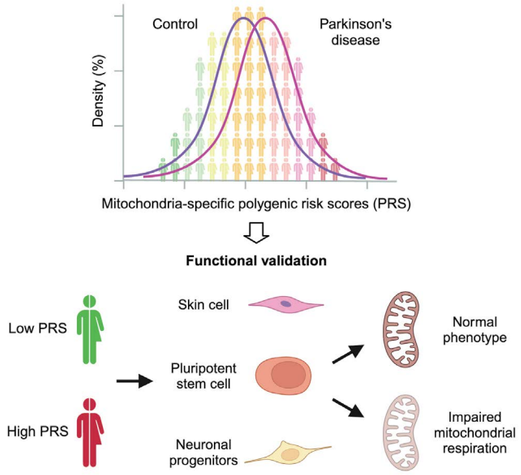
Polygenic risk scores for precision medicine



Unravelling the complex genetic architecture of Parkinson's disease remains a major challenge. While familial forms due to a single mutation account for 5 to 10% of all cases, the contribution of genetics in the remaining patients is poorly understood. Studies now suggest that a combination of common variations, called variants, in multiple genes may act as a risk factor for the disease. To explore their joint impact, polygenic risk scores have been developed by the research community in recent years.

The idea is to estimate the risk associated with the sum of the different genetic variants carried by an individual. "Most common variants have little to no effect but, when combined with several others, they can become relevant to the disease," explains Dr Patrick May, researcher in the LCSB Bioinformatics Core. He led the genetic analysis for a study on polygenic risk scores conducted by an interdisciplinary team from the LCSB. "We use statistics from large-scale genetic studies to understand if each variant is associated with the disease or with a specific trait. By adding up the estimated effects of these small changes in several genes, we can calculate a risk score and hopefully identify people with a higher likelihood of developing Parkinson's disease."

It is well-known that mitochondria, important components for human energy metabolism, play a role in Parkinson's disease. For this reason, the researchers worked on the hypothesis that some patients may harbour a combination of variants in different nuclear-encoded mitochondrial genes that contributes to neurodegeneration. They calculated mitochondria-specific polygenic risk scores for over 14.000 patients and controls, demonstrating that having multiple common mutations in genes regulating a specific mitochondrial pathway, namely oxidative phosphorylation (OXPHOS), is significantly associated with the disease. "These results indicate that polygenic risk scores provide a tool to genetically stratify patients, meaning divide them into different subgroups to enable precision medicine," details Dr Giuseppe Arena, researcher in the Translational Neuroscience group.

Next, the scientists performed functional experiments in cells donated by participants of the Luxembourg Parkinson's Study. They observed significant differences in mitochondrial respiration between the cells of patients with high and low risk scores for the OXPHOS pathway. "For the first time in this field, our study validated that the calculated risk scores match characteristics observed in cellular models derived from patients," underlines Dr Arena. Additionally, by retrospectively classifying participants from a clinical trial according to the same scores, the team showed that patients with a high risk score responded more effectively to the treatment targeting mitochondrial function, further corroborating the potential of this genetic stratification approach.

"It is exciting to see how mitochondria-specific risk scores could allow for the selection of more homogenous patient groups. These results pave the way for intelligent clinical trial design," highlights Prof. Anne Grünewald, head of the Molecular & Functional Neurobiology group. "Using polygenic risk scores to identify patients who will benefit the most from targeted therapies will have a considerable impact on precision medicine for Parkinson's disease." ■

Exposomics and brain research: A winning combination

Fifteen doctoral students graduated from the LCSB in 2024. Among them was Dr Begoña Talavera Andújar, who received the university's Excellent Thesis Award, becoming the fourth LCSB graduate in a row to receive this award reserved for the top 10% of doctoral theses defended at the University of Luxembourg.

Dr Talavera's research was supervised by Prof. Emma Schymanski in the framework of MICROH, a Doctoral Training Unit coordinated by the LCSB and funded by the Luxembourg National Research Fund (FNR). She analysed the chemical composition of various samples, such as blood, faeces and cerebrospinal fluid, from people with neurodegenerative diseases, specifically Alzheimer's and Parkinson's. She explains: "I established methods that allowed me to define chemical fingerprints that could be associated with each disease. These results show that exposomics, the study of all environmental exposures, will be an essential complementary tool for studying neurodegenerative diseases in the future."

Dr Talavera is now continuing her work on this topic as a postdoctoral researcher in the Environmental Cheminformatics group at the LCSB, building on the methods developed during her PhD. With the help of the Neuroinflammation group and their international collaborators, she aims to expand the types and numbers of samples analysed during her pilot studies, developping interdisciplinary collaborations within the LCSB and beyond. ■

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Bridges between cells for brain health

The brain contains many cell types, from neurons to microglia. The latter are integral to the brain's immune system and play a crucial role as the brain's cleanup crew. The accumulation of pathological proteins is a hallmark of several neurodegenerative disorders, including Alzheimer's disease, frontotemporal dementia and Parkinson's disease. Proteins such as alpha-synuclein and tau can abnormally aggregate inside neurons, disrupting essential cellular function. "We knew that microglia play a role in clearing these protein aggregates but we only learned recently that they can form tunnelling nanotubes, long extensions that can connect distant cells in the brain," explains Prof. Michael Heneka, FNR PEARL Chair and head of the Neuroinflammation group at the LCSB. "In a study conducted in collaboration with colleagues from France, Hungary and Germany, we looked at the transfer of cargo between neurons and microglia via these nanotubes and explored the consequences of this exchange for cellular health."

In co-cultures of neurons and microglia, the researchers observed the formation of connections between the two cell types via live cell imaging microscopy. This cutting-edge technology helped demonstrate that microglia establish contact with neurons through tunnelling nanotubes (TNTs) and alleviate them from toxic protein accumulations.

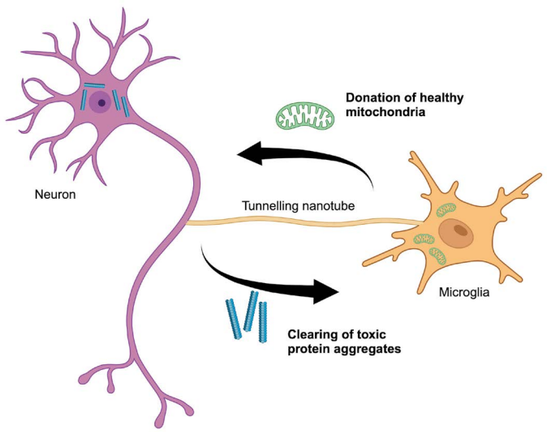
Results showed that, when toxic proteins accumulated within neurons, the number of TNTs connecting the two cell types increased and that these nanotubes contained alpha-synuclein and tau particles. The pathological proteins were transferred from neurons to microglia, where they were degraded over time. Microglia not only facilitated the clearance of toxic proteins from neurons, they also transferred mitochondria towards affected neurons via the same TNTs.

Mitochondria are important components of cells. When they don't function properly, it leads to energy deficits and oxidative stress. Both alpha-synuclein and tau can impair mitochondrial activity, contributing to the dysfunction and death of neurons in neurodegenerative diseases. Remarkably, when microglia transferred healthy mitochondria to affected neurons, the scientists noticed that it restored energy production and reduced oxidative damage, preserving neuronal functioning and survival.

Next, the researchers investigated whether known genetic mutations associated with neurodegenerative diseases influenced the formation of tunnelling nanotubes and the TNT-based rescue mechanisms. They found that mutations in different genes either reduced aggregate removal or compromised the delivery of functional mitochondria.

Altogether, these findings suggest that, by clearing protein aggregates from neurons and transferring functional mitochondria, microglial TNTs directly support neuronal health and can mitigate the progression of neurodegeneration. They also indicate new ways by which known genetic mutations may be contributing to neurodegenerative diseases. By disrupting TNT-mediated neuroprotective mechanisms, these mutations prevent microglia from supporting neurons effectively. Targeting them may provide an avenue to enhance TNT formation and activate transfer via these nanotubes, which may in turn slow down the progression of certain neurodegenerative diseases.

"This study not only deepened our understanding of intercellular communication through tunnelling nanotubes," concludes Prof. Michael Heneka. "It challenged the conventional view of microglia as contributors to neuroinflammation, highlighted a novel neuroprotective mechanism and offered insights into potential therapeutic strategies." ■



The LCSB hosts prestigious ECDO Conference

From 9 to 11 October, the LCSB hosted the 30th European Cell Death Organisation (ECDO) Conference. It was the first time this prestigious event was held in Luxembourg. Organised under the leadership of LCSB director Prof. Michael Heneka and Prof. Dirk Brenner, principal investigator of the Immunology and Genetics group, the conference brought together 250 researchers, clinicians and students around the theme "Cell death at the crossroads of neurodegeneration and cancer".

"A key focus of this year's conference was exploring cell death types beyond the canonical apoptosis, autophagy and necrosis," explains Prof. Heneka. "Understanding the factors influencing different cell death mechanisms has enhanced our insight into early cell processes in neurodegenerative diseases and cancer."

With over 100 posters and presentations, the conference provided early-career researchers a crucial platform to showcase their work and build scientific networks. As an event that rotates between different venues each year, this edition of the ECDO conference has also cemented the position of the LCSB and the University of Luxembourg as key institutions in biomedical research. "The conference was a great success, not just in terms of participation but in the quality of scientific exchanges, and we are grateful that we could hold this anniversary edition in Luxembourg," concluded Prof. Inna Lavrik, president of ECDO. ■

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Let's care for rare!
Rare disease research and outreach

Over 6,000 different rare diseases affect more than 300 million people worldwide, making them collectively as common as asthma or depression. At the LCSB, the Enzymology and Metabolism group, led by Professor Carole Linster, is studying a subset of these diseases, focusing on novel enzymes that eliminate metabolic side products and tackling key hurdles associated with rare disease research.

The group successfully identified an enzyme deficiency as the underlying cause of a severe disease in young children characterised by neurological regression, skin lesions and premature death. "Working with our collaborators in the US and Australia, we showed that NAXD deficiency leads to the accumulation of NADHX, a toxic metabolic byproduct and specific biomarker for the disease," explains Prof. Linster. "Our findings encouraged clinicians to administer niacin, better known as vitamin B3, to patients and this proved to substantially improve their symptoms."

In a recent publication, the team pursued their investigations in human cell models and discovered that NADHX accumulation inhibits an early step in the production of serine, an amino acid that serves as a precursor for numerous crucial molecules in our cells, including neurotransmission and antioxidant defence. Thanks to this deeper understanding of the molecular mechanisms involved, the team was able to identify additional therapeutic candidates including nicotinamide riboside, another form of vitamin B3, and inosine. These compounds are already available as dietary supplements and used for other indications. "Identifying beneficial nutritional interventions and repurposing approved drugs for the treatment of rare diseases helps overcome the significant economic and regulatory challenges associated with developing brand-new medications," underlines Prof. Linster.

> Beyond advancing research, we want to raise public awareness, as both are crucial steps towards enhancing the patients' quality of life.

Another difficulty in rare disease research is the availability of patient samples due to the small number of people living with a given disease. A major breakthrough in this regard has been the group's development of a new zebrafish model for Batten disease, another rare disease that primarily affects children and causes progressive vision loss, cognitive decline, behavioural changes and reduced life expectancy. By mimicking the disease, such a model facilitates research. Working with the Aquatic Platform of the LCSB, the group developed this model using CRISPR-Cas9 technology to mutate the fish equivalent of the *CLN3* gene that is linked to the disease in humans. "Zebrafish have become a widely used model for neurological diseases, mainly because of their rapid development and transparency during the larval stages, which allows direct observation of organ development under the microscope," explains Dr Ursula Heins-Marroquin, first author of this study and now a postdoctoral researcher at UMC Utrecht, who continues to work closely with the LCSB. "While the fish model did not show immediately obvious physiological changes compared to healthy control fish, detailed behavioural studies and in-depth metabolic analyses revealed that the model did indeed develop several hallmarks of Batten disease," she concludes.

Importantly, through this work, carried out in collaboration with the Environmental Cheminformatics group and the Metabolomics and Lipidomics platform, the team identified biomarker candidates for Batten disease that may be detected very early in patients, before the first neurological symptoms arise. In the fish larvae with the *CLN3* mutation, compounds called glycerophosphodiester accumulate to high levels. Other scientists independently found that this metabolic

change can also be detected in the blood of patients with *CLN3* Batten disease, enabling early diagnosis.

In addition to expanding its research into other rare diseases, the group led by Prof. Linster aims to strengthen its position in the rare disease community through further international collaborations and outreach activities. In 2024, the group had the pleasure of hosting Prof. Abdellah Tebani from Rouen University Hospital for an eight-week research stay, which culminated in a public lecture on Rare Disease Day, co-hosted with ALAN, the association for rare diseases in Luxembourg. The event highlighted the challenges faced by people with rare diseases, including lengthy diagnostic processes and limited availability of treatments. To further raise awareness on this topic, the team participated in the Researchers' Days, alongside several LCSB volunteers, showcasing to hundreds of visitors how their research helps to address these challenges. ■

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Inspiring the next generation of female scientists

Gabriela Retamales is not only a PhD student in the LCSB's AI Modelling and Prediction group, she is also a mother, a friend and a dedicated hockey player. Originally from Chile, her journey to Luxembourg has been marked by courage, determination and a willingness to seize new opportunities. For all these qualities, she was featured as one of the female role models highlighted in the *Women [& Girls] in Science* video series created by the Ministry for Gender Equality and Diversity, and Research Luxembourg.

"I am happy to be able to inspire the next generation of female researchers and to show them that by embracing their uniqueness they can achieve great things in the scientific field," explains Gabriela Retamales, who works on developing mathematical models of the complex networks of gene interactions in neurodegenerative disorders. "When you work hard, exciting opportunities will present themselves. You just have to be brave enough to take them," she concludes. ■

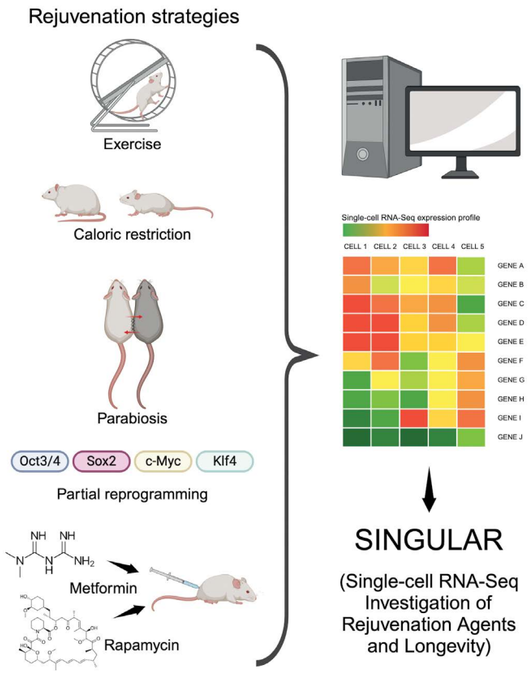
Watch the video

The cell rejuvenation atlas

There is a growing interest in rejuvenation interventions for their potential to mitigate the effects of ageing in humans. These interventions – ranging from lifestyle changes, such as calorie restriction and exercising, to gene therapies and surgical procedures – have been shown to increase the average lifespan in model organisms but have significant limitations. None of them achieves a global improvement across organs and tissues. Additionally, some of the procedures are either not transferable to humans or bear safety concerns. To provide an overview of the existing strategies and of their effects on different cell types, researchers from the Computational Biology groups at the LCSB and at the Center for Cooperative Research in Biosciences – CIC bioGUNE developed SINGULAR, a cell rejuvenation atlas. A first step towards a comprehensive anti-ageing approach.

"Current rejuvenation interventions only improve a few specific cellular processes and the molecular mechanisms underlying these approaches are largely unknown," explains Prof. Antonio Del Sol, head of the research groups in both institutions. "If we want to be able to design rejuvenation strategies that have a more global impact on the organism, we need to better characterise the existing ones and compare their effects at different levels of biological organisation." This is exactly what SINGULAR does: It provides a unified analysis of diverse rejuvenation strategies across multiple organs at single-cell resolution.

The researchers developed an analysis pipeline allowing them to compare nine previously published heterogenous datasets and to explore the effect of six rejuvenation interventions on 73 cell types in eighteen organs. They looked at their impact on the processes controlling which genes are expressed, on the communication between the cells and on how the cells respond to their environment. As a result, the scientists identified master regulators, proteins that mediate rejuvenation effects, as well as molecules that can activate these regulators in different tissues. They then used existing databases to search for drugs that could act on the identified molecules, exemplifying how SINGULAR can be exploited to find relevant compounds that could mimic the effect of complex rejuvenation interventions.



"Among the current strategies, the ones with the largest rejuvenating effects across different organs are difficult to implement. The information provided by SINGULAR opens new alternative avenues," concludes Prof. Del Sol. "In the future, we could directly target some of the identified master regulators to obtain the desired effects more easily and, by acting on a combination of regulators, we could achieve a more holistic improvement of age-dysregulated cellular processes."

SINGULAR offers valuable insights into the mechanisms underlying rejuvenation and provides a comprehensive array of potential target genes. Since the publication of the study in the journal *Aging*, SINGULAR is available as a public interactive database. It will help scientists identify novel rejuvenation agents and will inform further advances in comprehensive anti-ageing strategies. ■

Visit SINGULAR

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Patient association visits the LCSB

On 24 October 2024, twenty members of the Jung und Parkinson patient association from the neighbouring Saar region in Germany visited the LCSB. Prof. Rejko Krüger, head of the Translational Neuroscience group, gave an overview of Parkinson's research in Luxembourg, from fundamental projects to clinical trials, including the many collaborations with other research and healthcare institutions.

The group then visited different laboratories. In the Developmental & Cellular Biology group led by Prof. Jens Schwamborn, they learned how skin samples donated in clinical studies can be reprogrammed into personalised two- or three-dimensional neuronal cell models that can mimic certain aspects of the disease in a dish. With Dr Sophie-Helene Seibel from the Neuroinflammation group, the visitors also discovered the role of zebrafish models in neurodegenerative research and their importance in bridging the gap between cell models and human trials.

"Many of our visitors have actively participated in our clinical studies. We are happy to give back by welcoming them to the LCSB. It is an opportunity to show how their contributions help us progress in our understanding of neurodegenerative diseases and how these advances could in return improve patient's daily lives in the future," explains Dr Sabine Schmitz, team leader of the LCSB communication team. ■

Fasting as a treatment for Long COVID?

Shortly after the pandemic began in 2020, studies indicated that approximately 10% of individuals who contracted COVID-19 developed persistent symptoms lasting months beyond the acute infection. Now widely known as Long COVID syndrome, this condition refers to a range of symptoms that affect multiple organs and include fatigue, shortness of breath and various pains, as well as mental manifestations ranging from depression and anxiety to cognitive impairment. These symptoms can have a severe impact on daily activities, affecting quality of life, work and income.

Despite extensive research efforts, the underlying causes of Long COVID syndrome remain unclear to date. Current hypotheses suggest that the condition may stem from an exaggerated immune response, involving persistent neuroinflammation, vascular damage, metabolic dysregulation, and potential viral persistence in certain tissues. While various pharmacological interventions have been explored, clinical trials have yielded mixed results. Given the complexity of Long COVID and the involvement of multiple organs, existing treatment strategies remain inadequate, underscoring the need for alternative therapeutic solutions.

Fasting has shown promise in alleviating symptoms of various chronic inflammatory conditions, including rheumatoid arthritis, metabolic syndrome and autoimmune diseases. Studies for example indicate that fasting-induced metabolic shifts can promote tissue repair and potentially improve chronic fatigue conditions. Additionally, intermittent fasting might help regulate autonomic nervous system dysfunction, a condition that has been implicated in Long COVID.

"Recent research suggests that caloric restriction may reduce systemic inflammation and modulate immune responses, which makes fasting a potential treatment avenue," explains Prof. Jochen Schneider, head of the Medical Translational Research group at the LCSB and co-principal investigator of the FastCoV study. "However, it is crucial to assess both the benefits and risks before it can be considered a viable intervention for Long COVID patients."

To address all aspects of this complex condition, the FastCoV study brings together an interdisciplinary team


The FastCoV team

of experts from research institutions and hospitals, including the LCSB and the Department of Life Sciences and Medicine of the University of Luxembourg, the Centre Hospitalier Neuro-Psychiatrique (CHNP) and its rehabilitation clinic, the Luxembourg Institute of Health and the Charité University Hospital in Berlin.

The project is comprised of two parts: A pilot phase followed by a larger trial phase. "In the pilot study, a limited number of participants will undergo a 7-day supervised fasting programme before gradually returning to their regular diet," explains Dr Raquel Gómez Bravo, clinician-scientist at the CHNP and co-principal investigator of the study. "The study includes comprehensive health screenings and medical supervision to ensure that participants tolerate prolonged fasting and minimise risks associated with caloric restriction," she continues. Thanks to this structured approach, the pilot phase will allow scientists to optimise the design of the main trial and to generate first high-quality evidence on whether fasting can alleviate chronic Long COVID symptoms.

If fasting proves effective, it could offer a low-cost, accessible strategy to help manage Long COVID symptoms, particularly in cases where pharmacological options remain limited. Further studies will however be needed to tailor the intervention to different patients. As research progresses, a personalised approach incorporating metabolic, inflammatory and nutritional assessments may be key to optimising fasting-based therapies for Long COVID patients. ■

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Nurturing young interdisciplinary talents

At the LCSB, dozens of PhD students work on scientific projects and learn how to become fully fledged researchers. The centre attaches importance to the education of these young talents, striving to train a next generation of scientists that will be well-equipped to address the challenges of cross-disciplinary research, and to contribute to scientific and medical advances. In 2024, three initiatives in doctoral education were launched, giving the LCSB the opportunity to welcome several new doctoral candidates, in collaboration with national and international partners.

Doctoral Training Units (DTUs), supported by the Luxembourg National Research Fund (FNR), are characterised by a comprehensive approach designed to promote interdisciplinary education and to foster collaboration between research institutions. In these frameworks, PhD students receive high-quality training that goes beyond traditional doctoral supervision. In addition, the synergies created by the programmes enhance existing research efforts.

Dr Cedric Laczny and Prof. Emma Schymanski

Among the new DTUs, MICRO-PATH - Pathogenesis in the age of the microbiome - is a collaboration between several research players in Luxembourg. It will explore the links between the human microbiome, consisting of trillions of microorganisms, and chronic diseases. Imbalances in the microbiome have been linked to diseases such as Alzheimer's, food allergies and colorectal cancer, highlighting the importance of interactions between diverse microorganisms and their human host.

"With MICRO-PATH, we want to go beyond observational studies to truly understand the causality and mechanisms at play," explains Prof. Paul Wilmes, coordinator of the DTU and head of the Systems Ecology group at the LCSB. "The interdisciplinary nature of the programme will help us to investigate microbiome-driven impacts of environmental, lifestyle, and socio-economic factors, and to address these complex interplays."

The programme takes advantage of the state-of-the-art research infrastructure in Luxembourg and integrates advanced methodologies, from human cohort studies and animal models to mass spectrometry and *in silico* techniques. Similarly, a second FNR-funded DTU involving the LCSB will rely on local expertise and new technological developments. XPOSE – Exposome and health: Navigating complexity with innovation – aims to explore how the entire spectrum of environmental exposures can interact with human biology to trigger the onset of a disease.

> Let's create an environment in which budding scientists can grow and learn to tackle complex problems.

"We are continuously coming in contact with air pollution, chemicals or processed food. There is an urgent need for a deeper understanding of their influence on our health in order to better inform public health policies," details Prof. Emma Schymanski, head of the Environmental Cheminformatics group at the LCSB and member of the executive committee of XPOSE. "With this DTU, we want to analyse the impact of environmental, chemical, nutritional, social and lifestyle-related exposures on health by leveraging artificial intelligence and machine learning." XPOSE will also take advantage of connections with ongoing international initiatives in the field of exposome research, highlighting how DTUs ensure young scientists are familiar with collaborative work as early as possible.

A doctoral network built at the European level was also launched in 2024, integrating expertise from leading research institutions as well as public and private healthcare service providers across Europe. This initiative, focused on AI-driven healthcare and led by Fraunhofer Institute for Algorithms and Scientific Computing in Germany, is funded by a prestigious Marie Skłodowska-Curie Actions grant from the European Union. The LCSB leads the PhD training programme for the 14 doctoral candidates joining the network. Through their research, these young talents will develop advanced artificial intelligence methods to predict Parkinson's disease progression and offer personalised patient care.

"This translational programme, called AIPD, will prepare PhD students to become AI specialists with a deep understanding of healthcare challenges, including socioeconomic, ethical and legal considerations," says Prof. Jochen Klucken, FNR PEARL Chair in Digital Medicine and principal investigator at the LCSB. "They will not only learn to navigate the complex regulatory landscape of medical data science but also to better meet the patients' needs."

Prof. Jochen Klucken and Prof. Paul Wilmes

Through their well-rounded curriculums, these doctoral training initiatives create a research environment in which doctoral candidates can find innovative ways to tackle complex health issues. The LCSB will nurture these budding scientists, equipping them with good skills when it comes to research practices and self-care, so they can thrive in their subsequent careers. ■

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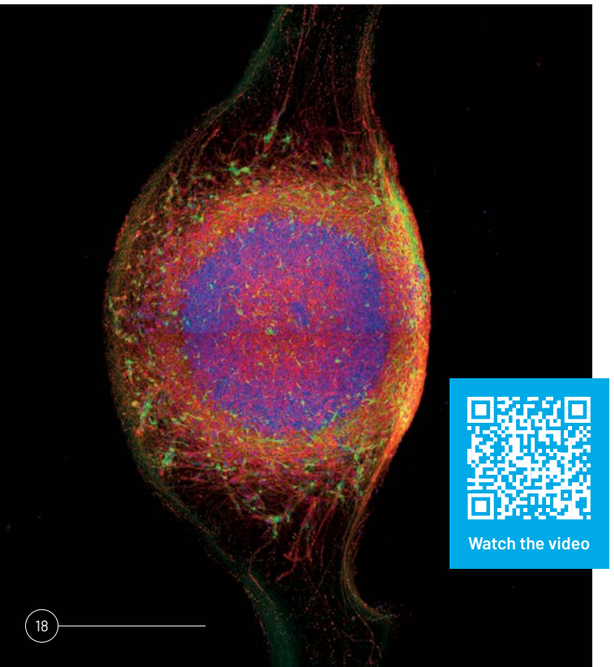
Bringing the Bioimaging Platform into focus

Seven scientific platforms are a cornerstone of research at the LCSB, providing specialised services in bioimaging, genomics, metabolomics and lipidomics, disease modelling and screening, animal model research, and bioinformatics. Through continuous development and new pipelines, these services can be used separately or combined to address complex research questions or preclinical drug discovery. In addition to researchers from the LCSB and the university, the LCSB scientific platforms are open to external users from academia and industry in Luxembourg and abroad.

If microscopes have become a symbol of biomedical research and are ubiquitous in most laboratories, the LCSB Bioimaging Platform exceeds standards. It houses a wide range of equipment, from simple light microscopes to sophisticated multi-photon devices that allow imaging in live animals and high-throughput automated image acquisition platforms. "Our platform goes beyond providing access to microscopes. We offer comprehensive support from project design to data analysis, helping researchers to select the most appropriate imaging systems for their scientific questions," says platform manager Dr Paul Antony. "We have also expanded our expertise to include flow cytometry and state-of-the-art AI-based image analysis."

Like all LCSB platforms, the Bioimaging Platform also supports exploratory research that requires the development of innovative techniques to address complex research questions. In a recent project by the Developmental and Cellular Biology group, the platform's services were key to the characterisation of human midbrain organoids derived from cells donated by patients with a genetic form of Parkinson's disease. "The support of the Bioimaging Platform was essential in this project," explains Prof. Jens Schwamborn, who led the study. "It was through the combination of state-of-the-art microscopes and custom image analysis algorithms that we were able to show that the model organoids exhibit specific characteristics that mirror the disease in humans." High-content microscopy was used to quality control the organoids and to demonstrate the accumulation of α-synuclein in their neurons, a hallmark of Parkinson's disease. Using custom analysis scripts, the team also showed that astrocytes, key support cells in the brain, were entering senescence, a state in which they no longer perform their role, which could open a new avenue for treatment. "The imaging techniques that we developed with the experts from the Bioimaging Platform are now in use across various projects in our group," concludes Prof. Schwamborn.

This example also demonstrates how services from different LCSB scientific platforms can be combined. Once the feasibility of these organoid models has been demonstrated, their metabolomic profile could be studied to analyse the changes resulting from the disease-causing genetic mutation. Later, they could be used for large-scale drug screening in the Disease Modelling and Screening Platform, followed by preclinical testing of selected compounds in fish or mouse models, thus completing the entire preclinical pipeline at the LCSB. ■



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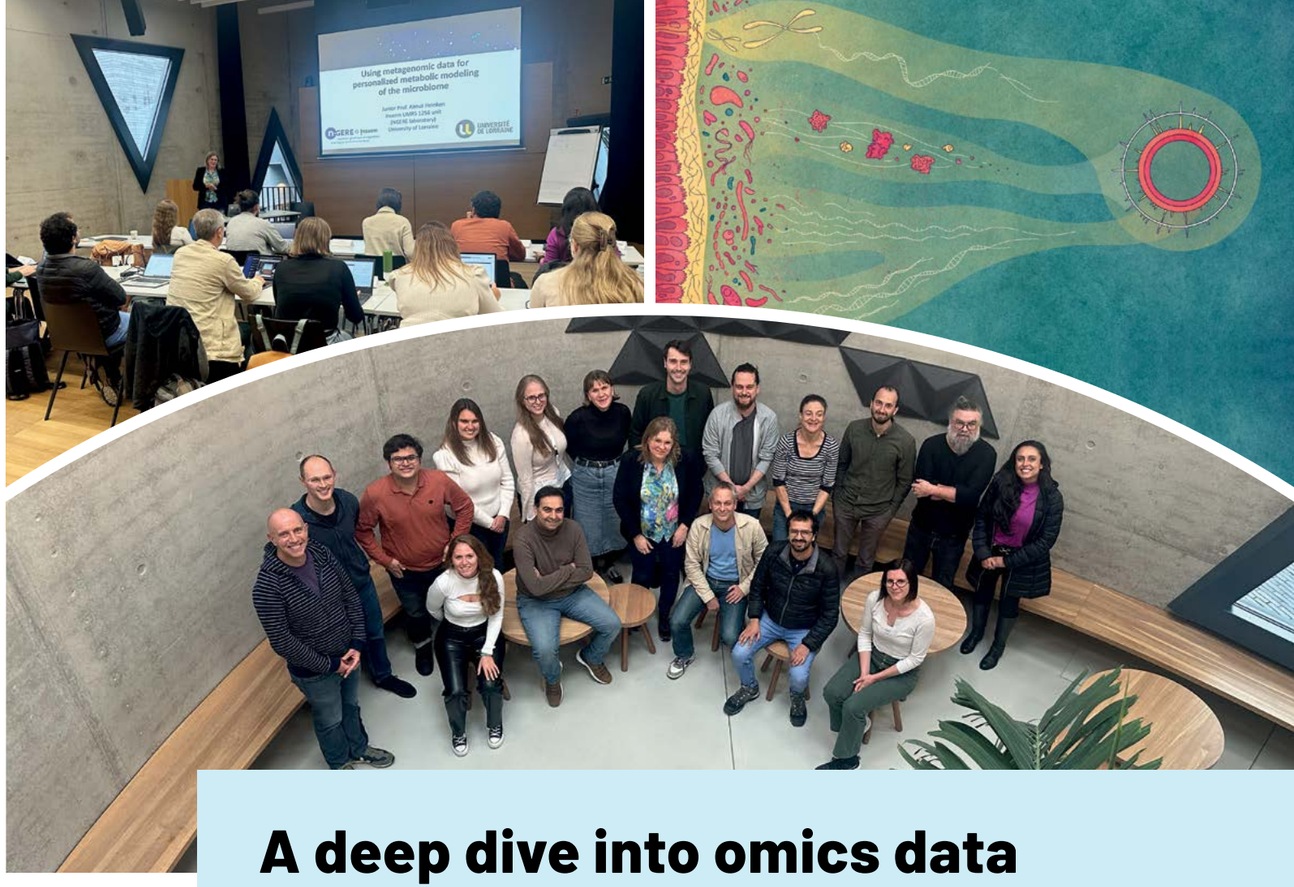

A deep dive into omics data and microbial communities

PROSPECTOMICS is an EU-funded project that uses state-of-the-art "omics" techniques to design a tool for minimally invasive hydrocarbon exploration. In this context, several summer schools were organised by the project's partner institutions to share their expertise and disseminate knowledge in the disciplines brought together by PROSPECTOMICS.

In October 2024, the LCSB welcomed 13 participants from across Europe for a 4-day course dedicated to integrated meta-omics. The Systems Ecology group, together with the Bioinformatics Core as well as LCSB alumni Prof. Almut Heinken and Prof. Anna Heintz-Buschart, developed lectures and hands-on sessions to train these early-career researchers in the analysis and characterisation of mixed microbial communities using high-throughput omics data derived from DNA, RNA and proteins.

"We built upon an EMBO course that we organised previously and covered a wide spectrum: From how to resolve microbial communities using metagenomics, metatranscriptomics and metaproteomics to statistical integration and analysis of multi-omics data," explains Dr Cedric Laczny, researcher in the Systems Ecology group. "The participants also discussed their own experimental plans with our team to get tailored suggestions." The very positive feedback received by the LCSB highlights that courses such as this one represent a major asset in the career development of researchers. ■

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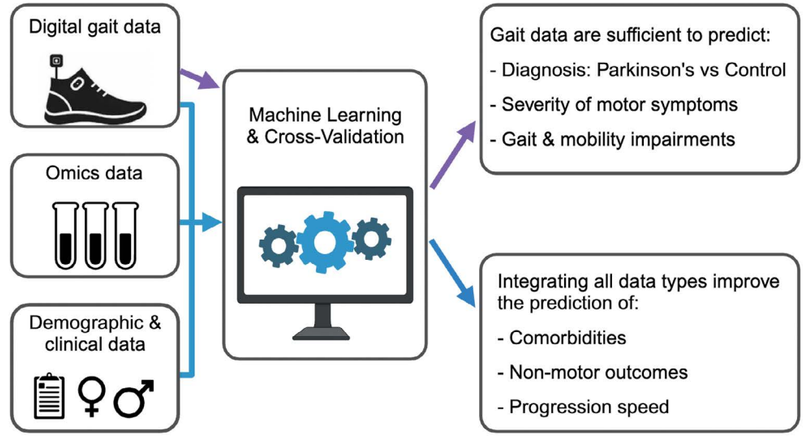
From left to right: Prime Minister Luc Frieden, Minister Stéphanie Obertin, Dr Budinger and Dr Meisch.

Prime minister visits LCSB laboratory

Prime Minister Luc Frieden and Minister for Research and Higher Education Dr Stéphanie Obertin visited the University of Luxembourg on 24 October 2024 for a meeting with the rectorate and representatives of the board of governors. After discussing the university's important role in research and education, the two ministers visited the laboratory of the Neuroinflammation group led by Prof. Michael Heneka, Dr Françoise Meisch and two team members, Dr Arnaud Mary and Dr Dimitri Budinger, presented the group's research on the interactions between immune cells and nerve cells in the brain. They highlighted how these interactions are involved in neurodegenerative disorders, particularly Alzheimer's disease.

While this was Dr Obertin's second visit to the LCSB since taking office in 2023, it was Minister Frieden's first tour of the centre. In a social media post following his visit, he mentioned how inspired he was by the work conducted at the LCSB and how it tackles one of the greatest challenges facing our society. ■

Integrated biomarkers to monitor Parkinson's disease



Parkinson's disease presents a wide range of motor and non-motor symptoms, complicating its diagnosis and treatment. In a study, conducted in the framework of the European project ERA PerMed - DIGIPD, with the support of the Luxembourg National Research Fund (FNR), researchers from the LCSB and collaborators from Germany examined if digital gait sensors could be used to better monitor motor symptoms and their severity. They also explored if combining these devices with metabolomics and clinical data could help to assess the risk of developing other symptoms or comorbidities associated with the disease.

Thanks to shoe-attached sensors that captured motor function and gait variability, the Luxembourg Parkinson's Study collected detailed gait measurements for some of its participants. By using the raw time-series data obtained, LCSB scientists developed machine learning models capable of making a distinction between patients and healthy controls with high accuracy. "Our findings demonstrate that digital gait biomarkers could serve as a non-invasive tool for diagnosing motor impairments," explains Dr Cyril Brzenczek, postdoctoral researcher in the Biomedical Data Science group.

Next, the team explored if these machine learning models based on gait sensor data could also assess the severity of motor symptoms. By comparing their results to scores based on the MDS-Unified Parkinson's Disease Rating Scale, a tool widely used to evaluate Parkinson's symptoms, the researchers showed that the models could classify the severity of patients' motor symptoms with success rates up to 75% and identify key predictors of motor severity. "At-home gait assessments based on the same principle could be developed to track the progression of motor impairment," says Dr Brzenczek. "It could allow remote and continuous monitoring of motor symptoms, facilitating timely adjustments in treatment, informed by current, real-time data rather than periodic clinical observations."

Non-motor symptoms and comorbidities, such as hallucinations, dopamine dysregulation syndrome and depression, often make Parkinson's disease harder to manage and reduce patients' quality of life. When integrating gait data with metabolomics and clinical data, the team found that it significantly improved the detection of hallucinations, dyskinesia and freezing of gait. "Our research shows that integrating complementary data types, from digital gait measurements to molecular markers, could help develop more comprehensive approaches for tracking and detecting specific symptoms and comorbidities in people with Parkinson's disease," concludes Prof. Enrico Glaab, head of the Biomedical Data Science group. "This combined approach may help us to better understand individual differences in how this complex disease manifests and progresses. It could also enable the seamless monitoring of patients' conditions through less invasive methods, allowing for earlier detection of changes." ■

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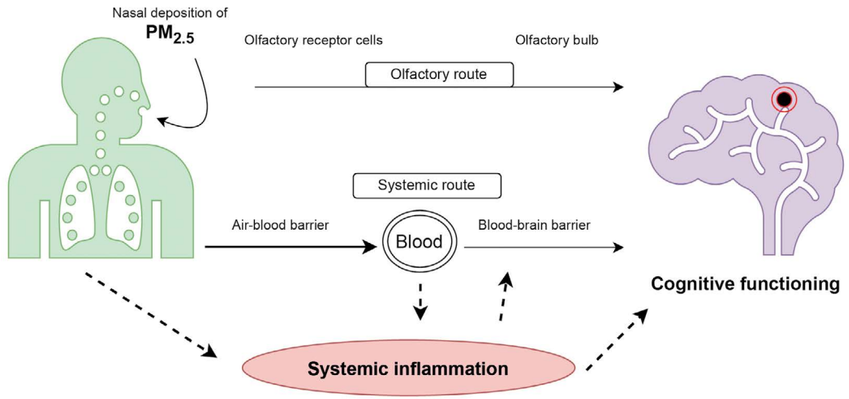
Environmental exposure: An ever-present risk for brain health

Environmental exposure to various pollutants is increasingly recognised as a major risk factor for declining cognitive health and the development of neurodegenerative diseases such as Parkinson's and Alzheimer's. Understanding the role of environmental factors in these diseases has become a key focus for several research groups at the LCSB, studying various aspects ranging from the role of air pollution in cognitive decline, to understanding how chemicals found in household dust could influence the development of Parkinson's disease.

The pollutants present in various environments are as diverse as their sources. One kind of pollutant is fine particulate matter, less than 2.5 microns in size and suspended in the ambient air. In a recent population-based study, LCSB director Prof. Michael Heneka collaborated with German colleagues to discover a link between this fine particle pollution, also called $PM_{2.5}$, and cognitive decline. "By combining population-based data of over 66,000 participants in the Dutch Lifelines cohort with satellite data that captures the level of air pollution, we were able to show that people exposed to higher levels of $PM_{2.5}$ pollution performed more poorly in a cognitive test that analyses how quickly the brain responds to new stimuli," Prof. Heneka explains.

Many of the microscopic particles that make up $PM_{2.5}$ pollution originate from vehicle emissions or industrial processes. Due to their small size, they can be inhaled deep into the lungs where they enter the bloodstream and can even traverse the blood-brain barrier. While

> Environmental exposure is emerging as one of the key risk factors for cognitive decline and the development of neurodegenerative diseases.



this would allow them to directly affect the brain, the study suggests that the mechanism by which exposure affects the brain may be more systemic. "Participants exposed to higher levels of pollution had an increase in the number of monocytes, a particular type of white blood cell involved in immune reactions," Prof. Heneka continues. This suggests that prolonged exposure could trigger systemic inflammation, which is known to also disrupt immune function in the brain, thereby impairing cognitive health and contributing to the development of neurodegenerative diseases. "This study suggests that pollution can contribute to the inflammatory processes that we know can influence our brain health. Now, we need to identify which chemicals drive this inflammation and through which mechanisms," he concludes.

The identification and classification of chemicals present in different types of samples, from blood and faeces to air and water, lies at the heart of the Environmental Cheminformatics group led by Prof. Emma Schymanski, FNR ATTRACT fellow. In a separate study, carried out in collaboration with colleagues from the Molecular and Functional Neurobiology group and the Systems Ecology group, the researchers pioneered new approaches to detect different chemicals and microorganisms in household dust and investigate their influence on the development of neurodegenerative diseases. In particular, they focused on people carrying pathogenic variants in the *LRRK2* gene, the most common genetic cause of Parkinson's disease. However, in a phenomenon known as reduced penetrance, many people who carry such a mutation never develop the disease. "The aim of this pilot study was to see if we could link the presence of different chemicals or microbes in household dust to the development of Parkinson's disease in individuals carrying this high-risk gene variant," explains Prof. Schymanski.

By analysing dust samples collected from the homes of participants, including patients with Parkinson's disease and healthy people who carry the *LRRK2* mutation, the researchers were able to identify numerous chemicals that were present at higher levels in the dust from homes of people who had developed the disease. Among the 90 chemicals of interest they found, bisphenol S (BPS), perfluorobutanesulfonic acid (PFBuS) and 2-benzothiazolesulfonic acid ($BThSO_3$), a benzothiazole derivative, are particularly intriguing. "Although we know that all these chemicals can have negative effects on brain health, we were particularly interested in BPS, since it is supposed to be a safe replacement for BPA," explains Dr Begoña Talavera Andújar, first author of the study. "Using cell cultures, we were able to show that BPS significantly disturbs mitochondrial function, a hallmark of Parkinson's disease," she continues.

While limited in sample numbers, pilot studies like this one are essential to establish protocols that pave the way for larger studies and to identify individual chemicals that warrant further investigation. $BThSO_3$, which was elevated in the dust from homes of participants with Parkinson's disease, could come from vehicle tire rubber – which could in turn be part of $PM_{2.5}$ pollution. The connection between this targeted study and the population-based study on air pollution opens yet another avenue for interdisciplinary collaboration within the LCSB. ■

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Luxembourg's Parkinson's disease research goes global

In July 2024, the National Centre of Excellence in Research on Parkinson's disease (NCER-PD) officially became one of the 51 clinical sites participating in the Parkinson's Progression Markers Initiative (PPMI), a landmark observational clinical study sponsored by the Michael J. Fox Foundation for Parkinson's Research.

Launched in 2010, PPMI is highly renowned as the most ambitious and impactful initiative in the history of research on Parkinson's disease. It aims to identify biological markers of Parkinson's disease risk, onset and progression by establishing a large collection of clinical, imaging and biological samples in multiple cohorts. In a recent breakthrough, PPMI made possible the development of a novel biological test, which demonstrates high diagnostic accuracy, detects the disease before movement symptoms arise and differentiates between several molecular subtypes. In the next phase, PPMI is expanding its study population to include individuals who have not yet developed Parkinson's but are at increased risk of developing the disease.

In this context, NCER-PD qualified as one of the recruitment sites for PPMI worldwide and will contribute to the initiative with Luxembourg's expertise in establishing diverse and deeply-characterised cohorts of participants. Indeed, since its launch in 2015 with the support of the Luxembourg National Research Fund (FNR), thousands of study participants in Luxembourg and the Greater Region have supported NCER-PD. Over 2000 Parkinson's patients and control volunteers joined the initial cohort and additional "at-risk" cohorts, including people with risk factors such as REM sleep behaviour disorder and individuals carrying mutations in the *GBA1* gene.

"Although progress has been made in terms of improving the diagnosis of Parkinson's disease, we still need to further explore the role of different factors in its onset and progression. To this end, following longitudinal cohorts of individuals displaying known risk factors is key for early treatment and prevention," explains Prof. Rejko Krüger, coordinator of NCER-PD. "We are therefore delighted to contribute to such a prestigious international clinical study."

The NCER-PD consortium, led by the Luxembourg Institute of Health in collaboration with the LCSB, the Centre Hospitalier de Luxembourg and the Laboratoire National de Santé, is responsible for the recruitment of local participants, including both individuals living with the disease and people at risk of developing it. Participant enrolment at the Luxembourg PPMI site successfully started in April 2024 and will continue to invite patients and people at risk of developing neurodegeneration.

"We are extremely grateful to the Michael J. Fox Foundation for this unique opportunity and we look forward to contributing further to advances in the diagnosis, treatment and most importantly prevention of Parkinson's," concludes Prof Krüger. "I would also like to renew our gratitude to all our current and prospective study participants for tangibly helping us in the ongoing fight against this neurodegenerative disease." ■

Researchers' Days: Rare diseases in the spotlight

At the end of November, during the 2024 edition of the Researchers' Days, organised by the Luxembourg National Research Fund (FNR), the Rockhal in Belval transformed into a hub for science outreach. Over three days, the event welcomed more than 5500 visitors, including 2660 high school students and teachers, eager to explore the fascinating world of science. As usual, the LCSB was among the exhibitors, offering hands-on experiments and a closer look at groundbreaking research.

This year, the LCSB booth, imagined by the Enzymology & Metabolism group led by Prof. Carole Linster, was dedicated to research on rare diseases. Visitors were invited to observe samples under a microscope, investigate the effect of genetic mutations, experiment with enzymes and a diagnostic test, and discover how scientists search for new treatments. Young and old alike had the opportunity to learn more about these diseases that affect millions of people around the world. A huge thank you to the incredible researchers who made the LCSB booth come to life. Together, let's continue to inspire, educate and care for rare! ■

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Elevating science: Making complex research visible and understandable


The communication team

The LCSB communication team plays an important role in bridging the gap between scientific research and society, strengthening the centre's position as a key research institution in the field of neurodegenerative diseases in Luxembourg and beyond. LCSB researchers can rely on their support to disseminate findings to the public, encourage public participation in research and boost exchanges between groups within the LCSB and with its partner institutions.

"As neurodegenerative diseases are a major challenge for our ageing societies, it is crucial to communicate about our research effectively and understandably," explains team leader Dr Sabine Schmitz. "This not only builds trust and support for science among the public but also contributes to LCSB's reputation as a leading institution in brain research." To achieve this, the team's mission goes beyond traditional communication tasks: It is about fostering curiosity, understanding and collaboration among LCSB's various stakeholder groups. From translating complex scientific results into engaging yet factual stories and organising scientific conferences or outreach events to recruiting participants for clinical studies, the team connects the lab to society.

Ensuring the centre's visibility is also crucial for attracting new talents, collaborators and funding, directly contributing to scientific research. Another key element at the LCSB is fostering interdisciplinarity, which requires continuous exchanges between various disciplines. "It is essential for research groups from different domains to stay informed about each other's work, to identify synergies and opportunities for collaboration," Dr Schmitz explains. To this end, the team organises the traditional LCSB team meetings and retreats, while also keeping all staff up to date on recent developments through the intranet and a bi-weekly newsletter. "These activities aim beyond mere information exchange. We want to build and maintain a culture where people like working at the LCSB and in which interdisciplinarity can thrive."

To cover these wide-ranging responsibilities, the communication team brings together people from diverse backgrounds, from former researchers and dedicated science communicators, to experts in web development and event management. "This blend of expertise allows us to cover the diversity of projects at hand. In all we do, we aim to combine our love for science with creativity and proximity to our stakeholders to help the LCSB reach its goals," concludes Dr Schmitz, who herself holds a PhD in neuroscience. This is how the LCSB communication team supports research and makes sure that the centre's achievements are widely shared, understood and appreciated. ■

Supporting research through targeted fundraising

Raising funds to back innovative endeavours has always been a key part of the LCSB strategy. Besides competitive third-party funding, support by foundations and private donors is crucial to push scientific boundaries and conduct cutting-edge research. It allows the LCSB to pursue ambitious pilot projects and to develop its research infrastructure further. To fine-tune its operations and better adapt to all types of donations, the LCSB recently created three research funds dedicated to specific diseases. These new fundraising tools will ensure that all donors' contributions make a difference where it matters.

"We were looking for a way to further improve the impact of donations and this is what this initiative is all about," explains Dr Lisa Smits, fundraiser at the LCSB. "Through these three funds, we are also able to collect smaller amounts which, when added together, can have a bigger effect." On top of pulling resources together, the funds bring some flexibility: With this set-up, the projects' needs can be assessed at different points in time and the resources distributed where they will be the most useful.

"It could for example mean some financial support towards the last phase of a project to help carry out additional experiments that will increase the project's significance and the chances of publication in a high-impact scientific journal," details Dr Smits. "Or money to kick-start a project and generate initial data that will then help secure competitive public funding. In short, through our three research funds, we will be able to put all the contributions to good use, in a very targeted and carefully thought through manner."

Two of the research funds contribute to the fight against neurodegenerative disorders, more precisely Parkinson's and Alzheimer's, while the third one focuses on rare childhood diseases. Taken together, these diseases affect millions of people worldwide, presenting significant challenges for healthcare systems across the globe. For patients, diagnosis can be a long journey and effective treatments are still limited. By giving to one of these funds, donors can support scientific progress, which will in turn facilitate the development of diagnostic tools and innovative therapies.

"This is a collective effort to address some of the most pressing health issues of our time," concludes Dr Lisa Smits. "Together, we can improve the lives of patients and their families in Luxembourg and beyond. Together, we can make a meaningful difference." ■

More information

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Digital transformation in healthcare: Getting it right

Digital medical devices range from medical-grade apps on your smartphone to wearable sensors on your shoes and, through evidence-based medicine, they will play a pivotal role in shaping the future of healthcare. Many of these innovative tools already enable health data collection and contribute to medical research. However, the real aim is to develop and validate devices that support clinical decision, empower patients and improve their quality of life. To this end, the Digital Medicine group at the LCSB studies the existing challenges – from ensuring clinical utility and digital adoption to building a regulatory framework – to contribute to the implementation of digital healthcare in Europe.

Many digital medical devices (DMDs) start as research tools designed to collect data for scientific studies. In that regard, recent publications by LCSB scientists showcase their relevance. In Parkinson's research for example, digital sensors provide continuous and precise measures for gait that, combined with standard clinical metrics, help to predict disease progression or symptoms' severity. "Associated with computational modelling, these sensors provide objective digital biomarkers that can be used to run cost-efficient clinical studies and to monitor patients," explains Prof. Jochen Klucken, head of the Digital Medicine group. "When it comes to research, digital devices are clearly an asset, but we need to go further and ensure they have value for healthcare professionals and patients alike."

This is where his multidisciplinary team takes on its full meaning, combining the expertise of computer scientists, medical engineers, clinicians and socio-economic specialists to define the next steps in improving the design and implementation of DMDs. The group recently reviewed wearable sensors used for home monitoring in Parkinson's disease and their analysis shows that clinical utility, meaning how helpful these devices are as decision-support tools for doctors, is often not assessed properly in existing studies. "We should better quantify the benefits associated with these wearables. Evidence of their added value for medical practice will facilitate the transition from using digital technologies for research to integrating DMDs in disease management," details Dr Stefano Sapienza, researcher in the Digital Medicine group.

The team also investigates the patients' perspective as the successful implementation of DMDs relies on patients' willingness to adopt digital tools. Dr Ivana Paccoud, post-doctoral researcher in the group, conducted surveys on the topic. While her findings reveal an eagerness to use DMDs and share personal health data, they also highlight that opinions and preferences vary depending on age, level of education and disease severity. "For example, older participants and patients with a more advanced disease voiced concerns regarding their ability to handle digital technologies," details Dr Paccoud. "They are often the ones who stand to benefit the most from innovative devices but only if their specific needs are considered from the very beginning of DMD development. Our study underscores the critical importance of systematically incorporating patients' perspectives to ensure effective design and deployment of DMDs for personalised care."

Offering opportunities to increase digital literacy in populations at the highest risk of being digitally excluded and guaranteeing equal access to technology will be crucial in ensuring that the use of DMDs in healthcare mitigates rather than exacerbates health inequities. Similarly, future users should be at the heart of the design process, to better understand the hurdles they face when using these devices and to find adequate solutions. The Digital Medicine group is active on that front as well with a project, called MyPD, aiming to co-design an electronic diary application for Parkinson's patients with the help of people living with the disease and of their caregivers. Projects such as this one, where users work in partnership with researchers constitute an important step towards the sustainable implementation of digital medical devices.

The Digital Medicine team

> Let's leverage digital technology for personalised medicine in an inclusive manner, with patients and healthcare professionals.

Ensuring inclusive and user-centred design of DMDs is only the beginning. A regulatory framework is also needed to integrate these new technologies into the existing healthcare systems. Many questions must be raised: What criteria should be chosen to evaluate digital devices? What types of data policies are needed to ensure the transparent use of the data collected?

What can be done to harmonise procedures across Europe? "When a company wants to bring a new medication to the market, there are guidelines and a clear process to follow, with development studies and clinical validation trials," explains Prof. Jochen Klucken, FNR PEARL Chair of Digital Medicine. "This concept of evidence-based medicine and the related "health technology assessment – HTA" procedures are just starting for DMDs in Europe and abroad. We should strive to build this global framework, to make sure we develop and reimburse devices that are validated for being both safe and effective."

The Digital Medicine group is currently working with e-Delphi, a method widely used to develop guidelines for health services, to gather expert opinions and reach a consensus around the use of DMDs for Parkinson's disease. This exercise will generate recommendations that could ultimately help decision-makers to develop a regulatory framework and bring Europe one step closer to digital healthcare. ■

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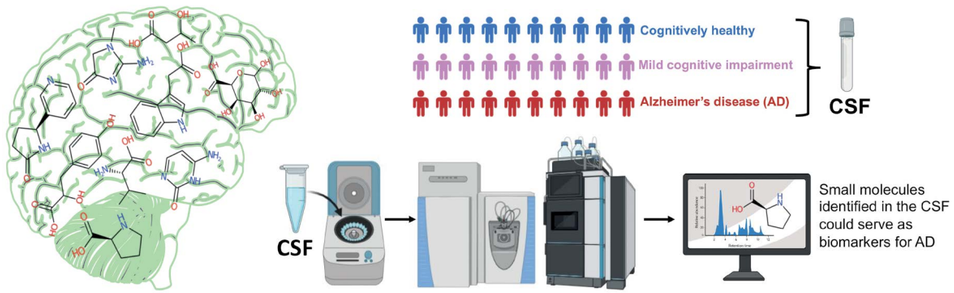
Uncovering new biomarkers in the cerebrospinal fluid

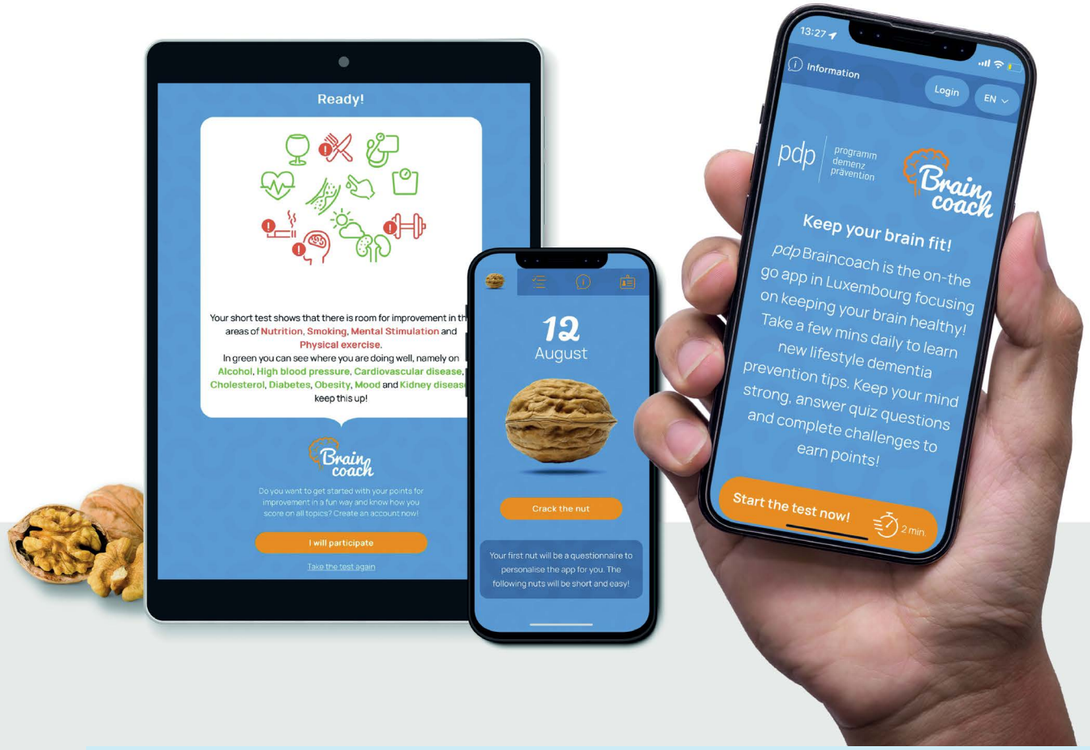


Until the early 2000s, definitive diagnosis of Alzheimer's disease was difficult and clinicians had to rely on clinical assessments, including cognitive decline and memory loss over time, while ruling out other causes for the observed symptoms. A definitive diagnosis could only be made *post-mortem*. Since then, steady progress in our understanding of the disease, coupled with technical advances in imaging and analysis techniques, has dramatically improved the specificity and precision of diagnosis. While still not fully established in everyday practice, protein biomarkers first discovered in the cerebrospinal fluid (CSF) can now be detected by simple blood tests. "These first protein biomarkers in the blood not only allow us to make an initial diagnosis but can also provide a first estimate of disease progression," explains Prof. Michael Heneka, director of the LCSB and head of the Neuroinflammation group. "However, we could still deepen our understanding of the disease and potentially obtain complementary diagnostic information by looking at more subtle changes in the metabolite composition of blood or CSF."

To further explore this avenue, researchers from the Environmental Cheminformatics group, in collaboration with the Neuroinflammation group, used liquid chromatography-mass spectrometry to analyse the global chemical composition of CSF samples. "To our knowledge, this is the first time that such an approach has been applied to cerebrospinal fluid in the context of Alzheimer's disease," underlines Prof. Emma Schymanski, principal investigator of the Environmental Cheminformatics group. The study included samples from three groups of participants: cognitively healthy individuals, patients with mild cognitive impairment indicative of early-stage Alzheimer's disease, and individuals with confirmed Alzheimer's dementia. "By developing a tailored experimental and analytical pipeline adapted to the specificities of CSF samples, we were able to detect subtle variations associated with different stages of the disease," Prof. Schymanski continues.

One of the most intriguing findings was the altered composition of bile acids in the cerebrospinal fluid of Alzheimer's patients compared to the other two groups. While a more in-depth analysis is ongoing, the researchers have already identified a significant accumulation of 3-keto-LCA, a bile acid metabolite which is known to originate in the gut microbiome. Prof. Schymanski explains: "While the role of the microbiome has become quite clear in Parkinson's disease, this is yet another hint that it might also play an important role in Alzheimer's."

While this result opens up new avenues for future research, it could also serve as the basis for a whole new set of biomarkers that would complement the proteins found in the blood and potentially better reflect the progression of the disease. "While these compounds in the CSF could be used as new biomarkers directly, we first want to better understand the mechanism through which they accumulate, what complementary information they can give us about disease progression and see if we could find them in blood or urine, which are more easily accessible," Prof. Schymanski concludes. ■



An app to keep your brain fit!

The Programme for Dementia Prevention (*pdp*), supported by the Ministry of Health and Social Security, launched the Braincoach app in October 2024. Its aim: Encouraging people to maintain their brain's health through lifestyle changes, thereby helping to reduce the risk of developing dementia.

pdp is a collaboration between the LCSB, the Luxembourg Institute of Health and the Centre Hospitalier de Luxembourg that has so far helped more than 600 people with mild cognitive impairment. "While we already offer support to those who are experiencing their first cognitive problems, the new app - available in French, German and English - focuses on early prevention, specifically targeting people in their forties and fifties," explains Prof. Rejko Krüger, coordinator of *pdp*.

The Braincoach app addresses twelve modifiable risk factors for dementia. Users complete a detailed questionnaire and receive personalised daily tips, quizzes and challenges. The app provides guidance on diet, exercise, cardiovascular health and social activities: Lifestyle changes that could reduce the risk of developing dementia by up to 45%.

Scan the QR code to download the *pdp* Braincoach app and keep your brain healthy. ■

The *pdp* Braincoach app is not a substitute for medical advice, please consult your doctor or a specialist about your personal medical situation.

Braincoach app
www.pdp-app.lu

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From COVID-19 to Long COVID and pandemic preparedness

Launched in 2021, CoVaLux is a comprehensive research framework that aims to address key unanswered questions related to the COVID-19 pandemic, with a particular focus on vaccination, long-term health and societal consequences, and pandemic preparedness. At a consortium meeting held on 14-15 November 2024 on Campus Belval, representatives from the various research and healthcare institutions involved met with international colleagues to discuss recent results and future perspectives.

"Since the end of the immediate phases of the pandemic, we have moved towards trying to understand its longer-term impact on health and society," states Prof. Paul Wilmes, co-spokesperson for CoVaLux and head of the Systems Ecology group at the LCSB. "One of the major challenges that we are still facing today is the prevalence of Long COVID, where people continue to suffer from symptoms long after the initial infection with the virus."

In this regard, the large amount of patient data and samples that were gathered over the years have allowed researchers to clearly delineate different subgroups of patients. "We have observed that fatigue, the most frequent symptom of Long COVID, manifests differently across patients," explains Dr Guy Fagherazzi, director of the Department of Precision Health at the Luxembourg Institute of Health (LIH). "Some experience gradual improvement, while for others the fatigue increases with time and persists over the long-term, causing severe challenges in daily life." Which factors underlie these differences is now an area of continued investigation.

Two avenues of increased interest are dysregulations of the immune system and the gut microbiome, both of which, alongside many other mechanisms, appear to be severely compromised during severe initial COVID-19 infection and Long COVID. "Thanks to all the samples collected since the pandemic, we have been able to join the 1 Million Microbiomes from Human Project, a global initiative that aims to build a global microbiome dataset," explains Prof. Wilmes. "Through this initiative, we will be able to sequence and analyse over 1000 microbiome samples in much more detail, which will help us understand what might be causing the dysregulation in the gut."

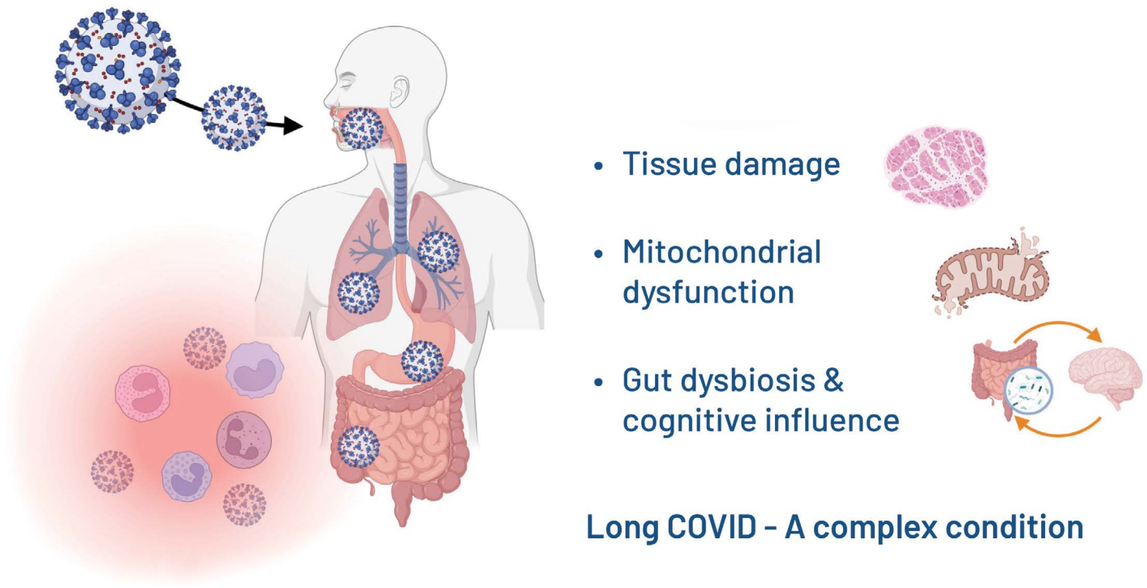
Based on the results of such studies, researchers hope to identify effective treatments targeting the cause of Long COVID, as opposed to the current strategies aiming mainly at reducing symptoms. A first hypothesis is already being tested: Rebalancing the microbiome and reducing inflammation through a period of fasting, an approach which has shown promising results in preliminary studies.

With limited treatment options available, prevention of persistent COVID symptoms is even more important, especially as the virus has begun to circulate seasonally in our society. The data from the pandemic very clearly shows that the main predictor of Long COVID is a severe initial infection. "Here vaccination remains a key strategy to minimise the impact of COVID-19. Since it protects against severe symptoms during initial infection, it also offer considerable protection against Long COVID," Prof. Wilmes highlights.

During the meeting, the consortium also discussed strategies to prepare for future pandemics, be it from coronaviruses or other infectious agents. Various tools developed within CoVaLux can here be of crucial importance. One example is the algorithm modelling the interaction between the SARS-CoV-2 spike protein and its human ACE2 receptor. "Based on the genetic code of a new virus variant, we can predict its epidemic potential. This approach can now be used for new SARS-CoV-2 variants, but also for other viruses," explains Prof. Alexander Skupin who leads the Integrative Cell Signalling group at the LCSB that developed the algorithm.

Finally, the consortium underscored the importance of continued waste water surveillance, which can help identify new outbreaks early, gaining important time in case of a new health emergency. Prof. Markus Ollert, director of the Department of Infection and Immunity at the LIH stressed the importance to stay prepared for the future: "Based on the collaborations and partnerships built during the pandemic, we need scalable clinical research networks and testing strategies that can be quickly reactivated to deal with the next pandemic." ■

> Within CoVaLux, we are building the scientific foundation for a healthier, more prepared future.



CoVaLux is a coordinated effort at the national level relying on an interdisciplinary approach. The consortium is composed of the following Luxembourgish institutions:

- Research Luxembourg
- Luxembourg Centre for Systems Biomedicine
- Luxembourg Institute of Health
- Integrated Biobank of Luxembourg
- Laboratoire national de santé
- Luxembourg Institute of Socio-Economic Research
- Luxembourg Institute of Science and Technology
- Centre Hospitalier de Luxembourg
- Centre Hospitalier Neuro-Psychiatrique

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LCSB on Tour: Research at your doorstep

In 2024, the LCSB launched the "LCSB on Tour" initiative, a series of free public lectures across Luxembourg to share developments in biomedical research with local communities. These conferences focused on neurodegenerative diseases, with topics such as Parkinson's disease, dementia research and prevention, and the role of the microbiome in brain health. To reach different audiences, the lectures were organised in collaboration with several municipalities across the Grand Duchy.

The first one took place in April in Diekirch, where Prof. Rejko Krüger presented the latest advances in Parkinson's research to over 80 people. Three more lectures were held in 2024, including a talk by Prof. Michael Heneka in Ettelbrück, a talk by Prof. Paul Wilmes in Echternach, and a second talk by Prof. Krüger in Steinfort. Each presentation was followed by a Q&A session and a small reception, offering the participants the opportunity to interact with the speakers and learn more about LCSB's research.

The audiences, who appreciated the researchers coming to their communities, showed a strong interest in learning about ongoing research in Luxembourg. More "LCSB on Tour" events with an even wider range of topics are already planned for 2025. ■

Industry collaborations take off

The LCSB Industry Partnering Day is a yearly event designed to position the centre as a key player in the biomedical research and innovation landscape. It aims to attract industry collaborators and to explore additional funding opportunities through public-private partnerships. One such partnership was successfully launched in 2024 with Transcend-PD, demonstrating that the Industry Partnering Day is bearing fruit.

Transcend-PD is a collaborative project between the Translational Neuroscience group, led by Prof. Rejko Krüger, and Accure Therapeutics, a translational R&D pharmaceutical company in neuroscience based in the biotech hub of Barcelona. It aims to assess the efficacy of ACT-02, a drug candidate from Accure Therapeutics' portfolio, in lab-derived neurons from selected Parkinson's patients and in the corresponding genetic mouse models.

During his visit to the LCSB for the first Industry Partnering Day, the CEO of Accure Therapeutics learned about the different cellular models used in translational studies on Parkinson's disease. Having identified the potential of these models and confirmed a common research interest between the company and the LCSB, a proof-of-concept pilot study was conducted successfully. The entire process was supported by the Innovation and Partnering team of the LCSB.

Throughout the pilot study, Dr Giuseppe Arena, senior research scientist in the Translational Neuroscience group at the time, and the industry partners established the scientific and collaborative basis to expand the project. "It helped us build a solid application for a BRIDGES grant, leading to the successful funding of Transcend-PD," explains Dr Léa Delacour, the Technology Transfer Officer dealing with Transcend-PD. "It is great to see that our efforts to attract industrial collaborators through the Industry Partnering Day are already leading to the launch of promising projects." The BRIDGES programme from the Luxembourg National Research Fund (FNR) supports partnerships between public research institutions and private companies to promote innovation and sustainable value creation.

"This collaboration will allow us to get further insights into Parkinson's disease by understanding the mechanisms of action of the new compound, which seems to target a protein involved in mitochondrial dysfunction and the accumulation of alpha-synuclein, two cardinal features of this complex disease," details Dr Arena, who has now taken on a scientific advisor role in Transcend-PD. "The cellular models will also allow us to narrow down the subset of patients most likely to respond positively to the treatment in future clinical trials." A hurdle that many previous treatments have failed to overcome due to the heterogeneity of the disease.

"We are delighted to have successfully launched Transcend-PD," concludes Dr Clemens Ostrowicz, Innovation and Partnering team leader. "What is even more exciting is that this project gave us the inspiration to create the InnSta-Fund to kick-start projects at the LCSB that have the potential to later apply for further, larger innovation grants." This internal funding scheme is based on an FNR KITS project awarded to the LCSB Innovation and Partnering team. It provides a valuable tool for LCSB researchers to initiate collaborative proof-of-principle projects with industry, contributing to the centre's standing as a desirable collaboration partner beyond the academic world. ■

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Art meets science

In 2024, several artists stayed at the LCSB. Initiated by Espace cultures, a team coordinating cultural events on campus, these two artist residencies, the first ones at the university, contributed to the conception of original creations through exchanges between scientists and the artists.

In March, Giovanni Zazerra, dancer and choreographer, Fabio Godinho, writer and stage director, and Marco Godinho, plastic artist and scenographer, spent a week at the LCSB. Through lab visits and discussions with researchers from the Neuroinflammation and Developmental & Cellular Biology groups, they learned about Alzheimer's disease and the complex processes that govern brain functions. "This residency is a first step to collect information and meet people who have a different outlook," explains Giovanni Zazerra. This immersion in the world of neuroscience fed the creative process for LABYRINTH, a choreographic project around the human brain, its capacity to remember and forget, that will be on stage in theatres in Luxembourg in 2026.

This very first residency was followed by the two-week stay of Berlin-based artist Max Kreis in autumn. Well-versed in science and technology, he worked on an artistic project dedicated to the plasticity of memory, relying heavily on artificial intelligence. A symposium at Casino Display at the end of the residency showcased part of his work and gathered artists and scientists. The intense exchanges highlighted how artistic and scientific processes can be similar, from the curiosity being a driving force to the need for experimentation, trials and errors. "If you think about it, during the Renaissance artists and scientists were often one and the same, Leonardo Da Vinci being the most obvious example," underlines Max Kreis. "Today, I feel we still question the world in similar ways and we share the same passion for understanding." ■

From memory circuits to biocomputers, philanthropy kicks off novel projects

The Fondation du Pélican de Mie et Pierre Hippert-Faber was created under the aegis of Fondation de Luxembourg to encourage scientific and cultural initiatives in the country, more specifically biomedical research at the University of Luxembourg. It is a long-term supporter of the LCSB. In 2024, through its Hippert Research Programme, the foundation awarded a total of 1,672,000€ to three innovative research projects.

Fondation du Pélican
sous l'égide de la Fondation de Luxembourg

A first project, called NomAD, will focus on the locus coeruleus, a dense group of cells located in the brainstem and one of the first regions to deteriorate in Alzheimer's disease. It is vital for the production of noradrenaline, a neurotransmitter modulating various brain functions, including memory formation. "We want to understand how the deterioration of the noradrenergic system influences Alzheimer's progression, particularly memory decline," explains Dr David Bouvier, researcher in the Neuroinflammation group and co-lead of the project. "In collaboration with the Laboratoire national de santé and the Paris Brain Institute, we will combine *in vitro* and mouse models with cross-validation in human brain tissue to explore the relationship between the degeneration of the locus coeruleus and molecular changes in memory-associated regions of the brain." NomAD will rely on cutting-edge technologies, such as super-resolution microscopy, spatial profiling and single-nuclei RNA sequencing, for in-depth analyses, aiming amongst other things to identify new biomarkers.

If, with its focus on neurodegeneration, NomAD is characteristic of the LCSB's work, COMPUTE on the other hand ventures into a brand-new field: Organoid intelligence. The goal of this second project is to develop a novel generation of biocomputers combining the advantages of electronics, artificial intelligence and the exceptional computing capacities of the human brain. Researchers will make use of the LCSB expertise in 3D cell cultures to produce a biological processer unit based on stem cell-derived brain organoids. "According to a recent scientific publication, a single human brain is a million times more energy efficient than a traditional computer," underlines David Smeele, doctoral researcher in the Developmental & Cellular Biology group. "Considering the enormous energy demands of today's computers, brain organoid-based computers could be a major game changer when it comes to more climate friendly technologies, with similar or higher performances."

While the COMPUTE team will work hard to harness the computing power of brain tissue, the Immunology & Genetics group will concentrate on emerging treatment strategies for multiple sclerosis and cancer. "By studying the metabolism of regulatory T cells that play a key role in regulating our immune system, we want to identify mechanisms which could be used to mitigate these diseases," states Dr Melanie Gusdat-Pozdeev who is working on this third project. Thanks to a novel high-throughput screening method that they will develop to specifically examine cell metabolism, the researchers plan to screen 240 compounds known to modulate key metabolic regulators. Their goal is to unveil pathways that either enhance or inhibit the function of regulatory T cells, offering new dual therapeutic avenues for both autoimmunity and cancer.

Thanks to philanthropic programmes like this one, research at the LCSB is teeming with new projects, projects that elicit out-of-the-box thinking, bring about technological developments and aim for societal impact. ■

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LCSB short stories

LCSB spin-offs in The Elevator

The Elevator, Silicon Luxembourg's short video format, dedicated two of its 2024 episodes to ITTM and OrganoTherapeutics. ITTM specialises in preclinical, clinical and real-world data management. Its goal is to enhance data quality and accessibility, enabling federated data analysis. OrganoTherapeutics develops 3D cell culture models for *in vitro* disease modelling. Have a look at the videos. →

Successful Open Day

On 16 March 2024, the LCSB participated in the Open Day of the university which drew over 5,000 visitors. People interested in our research could participate in interactive activities on brain function and digital medicine at the LCSB booth, listen to a talk on the human microbiome & health, or join one of our six guided lab tours. Over fifty people had the chance to explore the LCSB labs, learning more about neuroinflammation, drug discovery and neurodegenerative diseases.

The Scienteens Lab at the Researchers' Days

In November 2024, the Researchers' Days welcomed over 3,000 high school students and teachers at the Rockhal to explore together the fascinating world of science. The Scienteens Lab joined this festive event with a booth called "The eye in AI". The team invited visitors to discover the art of giving eyesight to machines thanks to artificial intelligence. Participants could observe an electronic brain at work, learn how a computer detects a line in an image and be part of a human neural network!

Team building in all its forms

Throughout the year, the LCSB members had the opportunity to participate in retreats to foster engagement and team spirit. At the end of June, the whole LCSB gathered for a day of fruitful discussions and fun activities – constructing fantastic racing cars made of cardboard – while earlier in the month group leaders, platform managers and the management team embarked on a kayaking excursion and biking tour that turned quite adventurous! Individual teams also went on to learn new skills from brewing to spray-painting, bringing back LCSB-themed beer and artwork to the centre. These occasional escapades capture the spirit of collaboration, dedication and creativity that defines the LCSB.

Scientific awards aplenty

Several prizes were awarded to LCSB researchers in 2024. Dr Begoña Talavera won the Best Poster Award at the Benelux Metabolism Days. Dr Mara Lucchetti was awarded a best oral presentation prize at the European Organ-on-Chip Society meeting. HuMIX TEER, a collaborative patent application involving Prof. Paul Wilmes, was identified as an Attractive Innovation Project by the University of Uppsala, rewarding its progress on the path from idea to innovation. LCSB alumni were in the spotlight as well with Dr Carlos Vega getting the 3rd prize of the local Science Writing Competition and Dr Laura de Nies winning the prestigious Wellcome Trust Early-Career Award.

Bold new projects

The Institute of Advanced Studies aims to leverage bold and interdisciplinary research at the very forefront of science. In 2024, it funded three Audacity projects involving LCSB researchers. Prof. Alexander Skupin works with the Department of Physics on molecular dynamics simulations to guide pharmacological treatments of neurological disorders. Prof. Anne Grünewald collaborates with engineers to study mitochondrial metabolism and uncover novel treatment strategies for Parkinson's. Dr Patrick May and social scientists explore dementia prevention hand in hand, to unravel the complex interactions between lifestyle, genetics and dementia risk.

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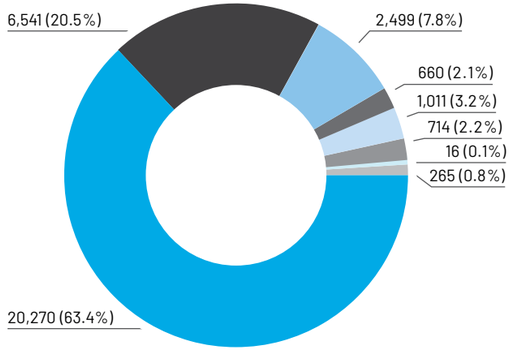
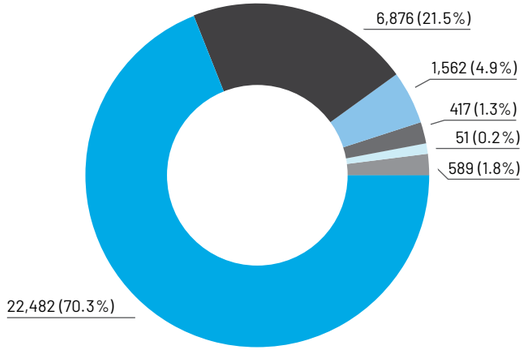
Facts & Figures

2024 LCSB income (in kEUR)



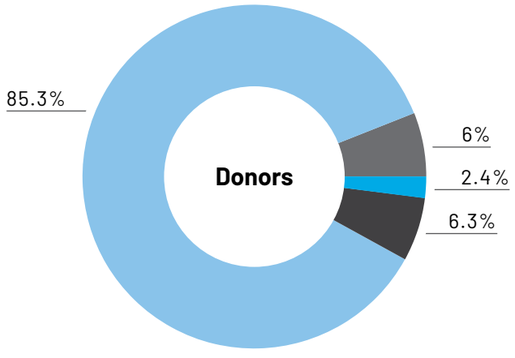
- University of Luxembourg
- Luxembourg National Research Fund (FNR)
- EU programmes
- Fundraising
- Further grants
- Ministries
- Funds for knowledge transfer
- Industry cooperation

2024 LCSB expenses (in kEUR)

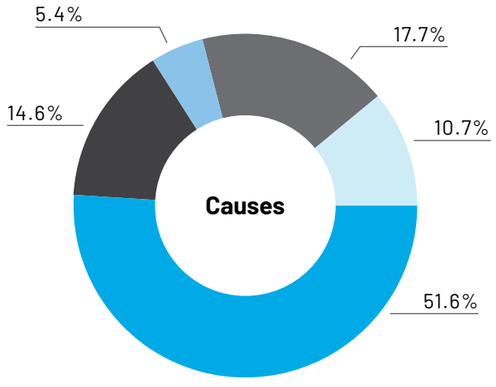


- Wages
- Operating expenses
- Investments
- Representation and registration
- Sub-contracting
- Travel

Fundraising



- Associations
- Corporate
- Foundations
- Private individuals



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

LCSB organisation chart

LCSB Director (M. Heneka)

Director's office
- Research Strategy
- Personal assistant

Research groups

AI Modelling & Prediction (J. Gonçalves)	**Bioinformatics Core** (R. Schneider)	**Biomedical Data Science** (E. Glaab)
Chemical & Molecular Neurobiology (I. Nikić-Spiegel[6])	**Clinical & Translational Informatics** (V. Satagopam[4])	**Computational Biology** (A. Del Sol)
Developmental & Cellular Biology (J. Schwamborn)	**Digital Medicine** (J. Klucken[1])	**Environmental Cheminformatics** (E. Schymanski)
Enzymology & Metabolism (C. Linster)	**Gene Expression & Metabolism** (E. Williams)	**Gene Expression Dynamics** (R. Schieweck[5])
Immunology & Genetics (D. Brenner[2])	**Integrative Cell Signalling** (A. Skupin)	**Medical Translational Research** (J. Schneider)
Molecular & Functional Neurobiology (A. Grünewald)	**Neuroinflammation** (M. Heneka)	**Systems Ecology** (P. Wilmes)
	Translational Neuroscience (R. Krüger[3])	

Scientific central services (J. Rozman)

Aquatic (M. L. Cordero Maldonado)	**Bioinformatics**
Bioimaging (P. Antony)	**Disease modelling & screening**[2]
Genomics (R. Halder)	**Metabolomics & Lipidomics** (C. Jäger)
Rodent (D. Coowar)	

[1] in cooperation with CHL
[2] in cooperation with LIH
[3] in cooperation with LIH & CHL
[4] start January 2025
[5] start February 2025
[6] start June 2025

Infrastructure (N. Bonjean)

Safety, Quality & Sustainability
- Safety & Biosafety# (safety culture, emergency response plans & trainings)
- Quality assurance & SOPs (electronic laboratory notebook, R3 support & PPC§)
- Green lab initiatives

Equipment
- Instrument purchase & care
- Technology platforms

Procurement & Logistics
- Laboratory procurement
- Laboratory supplies
- Sample shipment
- Technical support

Infrastructure
- Facility management & development
- Access management
- Infrastructure business continuity plans
- Lab space coordination

Operations (A. Vogler)

Communication
- External comms & outreach
- Internal communication
- Event management
- Onboarding & alumni

Fundraising
- Donor acquisitions & mgmt.
- Charity events

Scienteens Lab
- Curriculum development
- Outreach to schools

Management & Strategy*
- Strategic planning
- Process management

Innovation & Partnering
- Business development & legal
- Technology transfer

Finance & Grants
- Budget planning, reporting & control
- Grant funding opportunities, submission, project support, contracts & reporting

Secretariat
- Business trip arrangements
- Purchase orders & invoices
- Newcomer & guest mgmt.
- PI-level event organisation
- Office supplies

Shared UL Functions
HR, IP, DPO, etc.

*in cooperation with LCSB Research Strategy §in cooperation with LCSB Bioinformatics Core #in cooperation with responsible UL department

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National grants in 2024

Project acronym	Programme	LCSB responsible(s)	Project coordinator (if applicable)
ADAM17inAD	FNR AFR Individual	Lena Schaack, Jochen Schneider	
GLYMPH-PD	FNR AFR Individual	Marco Bartolini, Jens Schwamborn	
TRANSCEND-PD	FNR BRIDGES	Rejko Krüger	
AsynIntact	FNR CORE	Enrico Glaab, Jens Schwamborn, Manuel Buttini	
MitoDefinePD	FNR CORE International	Anne Grünewald, Emma Schymanski, Enrico Glaab	
AIDOA - IF	FNR Industrial Fellowships	Shekoufeh Gorgi Zadeh	
PAROMIN	FNR INTER MOBILITY	Paul Wilmes, Robert Friedland	
HuMiX-HT	FNR JUMP	Paul Wilmes	
InnSta-Fund	FNR KITS	Clemens Werner Ostrowicz	
MICRO-PATH	FNR PRIDE	Paul Wilmes, Michael Heneka, Patrick May, Emma Schymanski, Evan Williams, Jochen Schneider	Paul Wilmes, LCSB
Xpose	FNR PRIDE	Emma Schymanski, Paul Wilmes	Brice Appenzeller, LIH
CausalBio	FNR RESCOM Lecture Series	Enrico Glaab	
ECDO Conference 2024	FNR RESCOM Conference (co-funded by the MECO)	Michael Heneka, Dirk Brenner	
NeuroLS	FNR RESCOM Lecture Series	Michael Heneka	
8th Venusberg Meeting 2025	FNR RESCOM Conference	Michael Heneka	
Let's care for rare	Researchers' Days	Carole Linster	
The Eye in AI	Researchers' Days	Elisabeth John	
IonMolDyn	IAS Audacity	Alexander Skupin	
MITO-MANIAK	IAS Audacity	Anne Grünewald	
PRECIDEM	IAS Audacity	Patrick May	Anja Leist, FHSE
AMiPD	IAS Young Academics	Ilaria Goglia	
PFAS-QUEST	IAS Young Academics	Federica Piras	

European grants in 2024

Project acronym	Programme	LCSB responsible	Project coordinator (if applicable)
BE READY Plus	Horizon Europe	Paul Wilmes	INSERM, France
AIPD	MSCA Doctoral Networks	Jochen Klucken, Rejko Krüger	Fraunhofer SCAI, Germany
immuno-ALZ	MSCA Postdoctoral Fellowship	Michael Heneka	
DMD-MA	EIT Health	Jochen Klucken	IESE Business School, Spain
LABEL-APP	EIT Health	Jochen Klucken	IESE Business School, Spain
ELA2023	ELA International	Carole Linster	
COVID-PATH	FNR INTER ANR	Paul Wilmes	CEA, France
mitoERsgnl	FNR INTER DFG	Anne Grünewald	Rostock University, Germany
TRIUMPH	FNR INTER DFG	Evan Williams	EMBL
WISER	FNR INTER EUROSTARS	Jens Schwamborn	Elastin Biosciences
EPI_T-ALL	FNR INTER TRANSCAN	Enrico Glaab	IRCCS Casa Sollievo della Sofferenza, Italy
STEP 4 NAMs	INTERREG North-West Europe	Jens Schwamborn	BioRegio STERN Management GmbH

International grants in 2024

Project acronym	Programme	LCSB responsible	Project coordinator (if applicable)
BLENDS	FNR INTER NRF Korea	Jorge Gonçalves	Chung-Ang University, South Korea
SIREN	FNR INTER NRF Korea	Michael Heneka	Seoul National University, South Korea
FUN-MITO	Michael J Fox Foundation	Anne Grünewald, Patrick May	
GPNMB	Michael J Fox Foundation	Michael Heneka	Alector
Stratify-NDD	Michael J Fox Foundation	Rejko Krüger	Amsterdam University Medical Centers, The Netherlands
Mito NAXD	Mito Foundation	Carole Linster	Murdoch Children's Research Institute, Australia

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Key performance indicators

Personnel	
Research groups:	18
PEARL (active):	2
ATTRACT (active):	1
ERC (active):	1
Total staff:	259
Externally funded staff:	116
PhD students:	45
Nationalities:	55

External competitive funding 2024	
Total:	>8.42 M EUR

Fundraising 2024	
Total:	1.85 M EUR

Collaborations	
Research agreements signed in 2024:	60
Industrial partners active in projects in 2024:	9

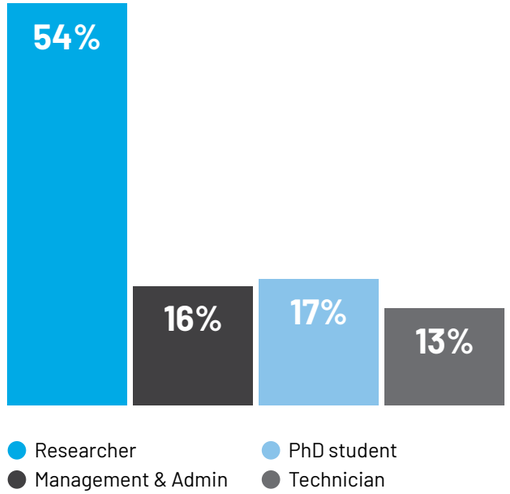
Publications	
Total publications:	155
Publications IF>10:	41
Publications in 25% best of field*:	79%
Open Access (OA) publications:	82%
Publications in OA journals:	48%
Cumulative number of publications°:	1,719

Innovation	
Patents°:	37
Proof of concept°: (total 4.3 M EUR)	10
Spin-offs active:	3

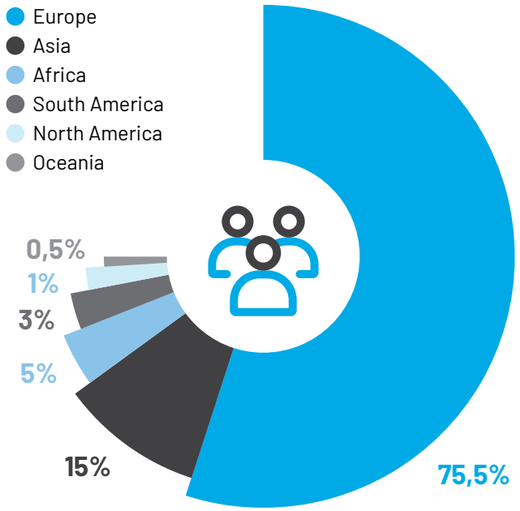
* based on WoS

° cumulative (2009-2024)

Staff categories 2024



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
Andreas Beyer	Professor for Systems Biology, University Cologne

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Publications 2024

Book

1. Daniele Proverbio et al., Early warning of SARS-CoV-2 infection. Features, Transmission, Detection, and Case Studies in COVID-19, 13-24, 10.1016/B978-0-323-95646-8.00021-4

Book Series

1. Jesús Fuentes et al., Conceptual Problems in Quantum Squeezing. *Trends in Mathematics*, Part F3359 - 413-426, 10.1007/978-3-031-62407-0_28

Comparative Study

1. Anne-Marie Hanff et al., Mixed effects models but not t-tests or linear regression detect progression of apathy in Parkinson's disease over seven years in a cohort: a comparative analysis. *Bmc Medical Research Methodology*, 24 - (1) - 183, 10.1186/s12874-024-02301-7

Conference Proceeding

1. Marianna Rizzo et al., CSF ATN and alpha-synuclein co-pathology in AD, PD, and DLB. *Alzheimers & Dementia*, 20 - (Suppl 2) - 10.1002/alz.086864

2. Roisin M McManus et al., NLRP3 regulates immunometabolism, impacting microglial function in Alzheimer's disease. *Alzheimers & Dementia*, 20 - (Suppl 8) - 10.1002/alz.095562

English Abstract

1. A Naegele et al., [Chat messenger use in the care of patients with Parkinson's disease]. *Der Nervenarzt*, 95 - (8) - 714-720, 10.1007/s00115-024-01686-6

Journal

1. Mohamed Soudy et al., Sex-dependent molecular landscape of Alzheimer's disease revealed by large-scale single-cell transcriptomics. *Alzheimers & Dementia*, 10.1002/alz.14476

2. Rola Shaaban et al., Personalized modeling of gut microbiome metabolism throughout the first year of life. *Communications Medicine*, 4 - (1) - 281, 10.1038/s43856-024-00715-4

3. Janika Harm et al., Navigating the metabolic landscape of regulatory T cells: from autoimmune diseases to tumor microenvironments. *Current Opinion In Immunology*, 92 - 102511, 10.1016/j.coi.2024.102511

4. Lara Blomeke et al., Blood-based quantification of Abeta oligomers indicates impaired clearance from brain in ApoE epsilon4 positive subjects. *Communications Medicine*, 4 - (1) - 262, 10.1038/s43856-024-00690-w

5. Michael T Heneka et al., Neuroinflammation in Alzheimer disease. *Nature Reviews Immunology*, 10.1038/s41577-024-01104-7

6. Frida Lind-Holm Mogensen et al., Protocol for immunofluorescence staining and large-scale analysis to quantify microglial cell morphology at single-cell resolution in mice. *Star Protocols*, 5 - (4) - 103467, 10.1016/j.xpro.2024.103467

7. Sarah Schrempel et al., Identification of isoAsp7-Abeta as a major Abeta variant in Alzheimer's disease, dementia with Lewy bodies and vascular dementia. *Acta Neuropathologica*, 148 - (1) - 78, 10.1007/s00401-024-02824-9

8. Peter Haglund et al., Comprehensive characterization of European house dust contaminants: Concentrations and profiles, geographical variability, and implications for chemical regulation and health risk. *Science Of The Total Environment*, 957 - 177639, 10.1016/j.scitotenv.2024.177639

9. Adam Šmelko et al., Maboss for HPC environments: implementations of the continuous time Boolean model simulator for large CPU clusters and GPU accelerators. *Bmc Bioinformatics*, 25 - (1) - 199, 10.1186/s12859-024-05815-5

10. Parviel Chirsir et al., Grouping strategies for assessing and managing persistent and mobile substances. *Environmental Sciences Europe*, 36 - (1) - 102, 10.1186/s12302-024-00919-4

11. Valeria Dulio et al., Beyond target chemicals: updating the NORMAN prioritisation scheme to support the EU chemicals strategy with semi-quantitative suspect/non-target screening data. *Environmental Sciences Europe*, 36 - (1) - 10.1186/s12302-024-00936-3

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