

# RESEARCH FOR HEALTH: *help us make an impact!*

#1 October 2021

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donors /p.07/

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# WHO we are

## The Luxembourg Institute of Health - *Research dedicated to life*

The Luxembourg Institute of Health (LIH) is a public biomedical research organisation that focuses on precision medicine to become a leading reference in Europe, transforming scientific research excellence into meaningful benefits for patients.

At LIH, we put the patient at the heart of everything we do. We strongly believe that we have a collective obligation towards society to use knowledge and technology arising from research on patient-derived data to have a direct and meaningful impact on people's health. That is why our dedicated teams of multidisciplinary researchers strive for excellence and generate relevant knowledge linked to immune-related diseases and cancer.

The institute embraces scientific collaborations, disruptive technology and process innovation as unique opportunities to improve the application of diagnostics and therapeutics with the long-term goal of disease prevention.

# A message from the CEO

Dear reader,

Biomedical research and its perception among the general population are changing rapidly, evolving from the traditional “scientist in the lab” stereotype towards a more “scientist as a caregiver” role. The patient is at the heart of our activities as we aim to develop new innovative therapies to address currently unmet clinical needs.

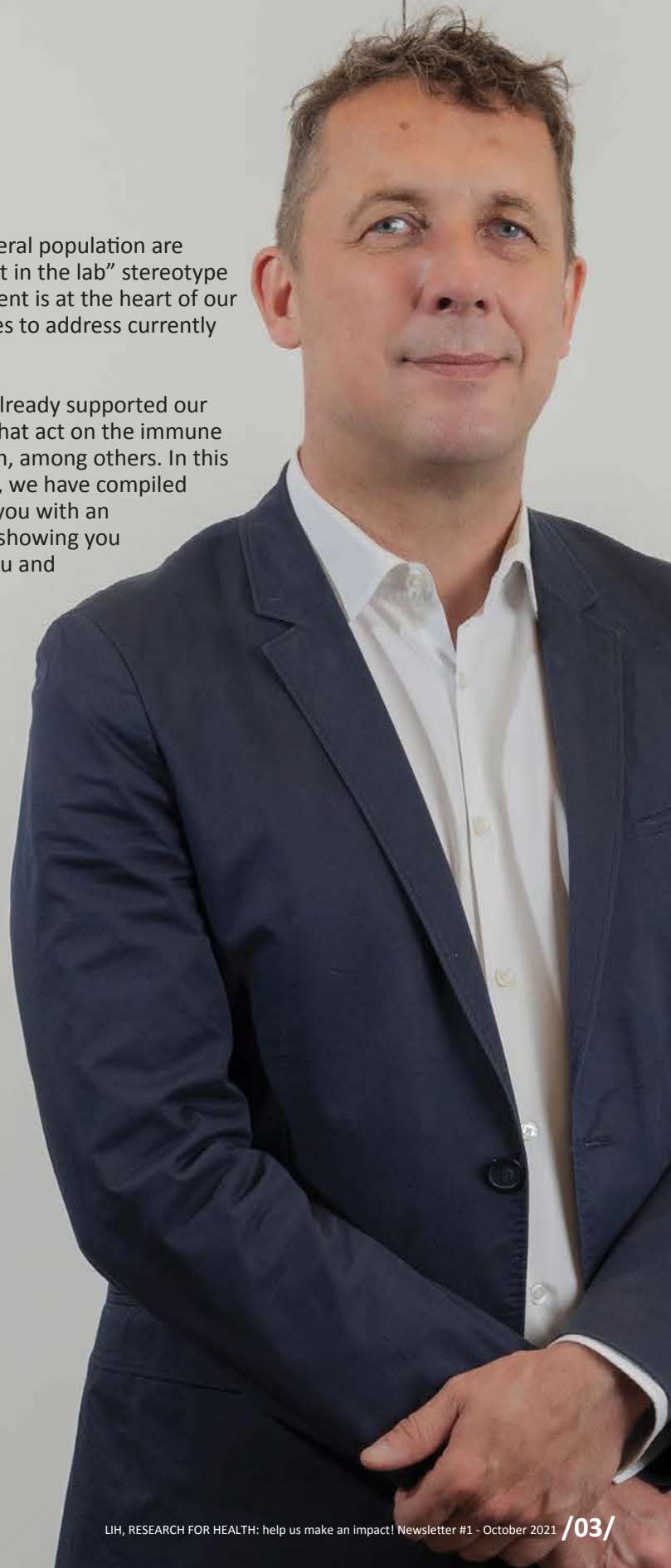
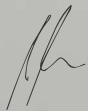
The contributions of our generous donors so far have already supported our scientists in developing and patenting new molecules that act on the immune system to help destroy cancer cells or treat chronic pain, among others. In this first edition of our newly launched biannual newsletter, we have compiled some of these concrete, tangible outcomes. Providing you with an insight into research activities at LIH is the best way of showing you the impact of your donations. It is a way of thanking you and giving you an overview of projects that would need additional support.

In research, every penny truly counts!

I wish you an enjoyable read and thank you for your interest in our activities.

Warmest regards,

Prof Ulf Nehrbass, CEO



# Our latest highlights

## Novel approach to improve cancer immunotherapy by turning “cold” tumours “hot”

Scientists from the Tumor Immunotherapy and Microenvironment (TIME) research group led by Dr Bassam Janji at the Luxembourg Institute of Health (LIH) Department of Oncology (DONC), and the Swedish pharma company Sprint Bioscience published the results of an innovative approach that turns “cold” tumours “hot”. “Cold”, immune-desert tumours are classically immunotherapy-resistant. “Hot” or inflamed tumours, by contrast, are infiltrated by the immune system and responsive to immunotherapy. These ground-breaking findings were published on April 29th 2020 in the prestigious journal “Science Advances”.



*Did you know...  
...that not all tumours can be infiltrated  
by immune cells?*

Approaches that drive immune cells into cold poorly infiltrated tumours would significantly enhance the therapeutic benefit of immunotherapy.



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## A lifetime commitment to defeating cancer: Legs Kanning Prize 2019

On Tuesday, January 28th 2020, Dr Anna Golebiewska, Group Leader at the NORLUX Neuro-Oncology laboratory, and Dr Johannes Meiser, Group Leader of the Cancer Metabolism Group at LIH's Department of Oncology, received the “Legs Kanning Prize” from the association “Action Lions Vaincre le Cancer”. The prize rewards the scientific achievement of researchers who devote their career to cancer research in Luxembourg.

*From left to right: M. Frank Beck, Dr Johannes Meiser, Dr Anna Golebiewska and Prof Marc Diederich at the Legs Kanning award ceremony - January 28th, 2020*

## Exposure to pollutants detected in the hair of the Luxembourg population

In a recent study, scientists from the Human Biomonitoring research unit (HBRU) of the Department of Population Health exploited hair analysis to assess the exposure to 67 different organic pesticides in 497 adults representative of the population of the Grand Duchy. The researchers detected an average of 19 pollutants per individual, with some chemicals being present across the entire study cohort. The findings, which were published in April 2021 in the renowned international journal 'Environment International', unequivocally highlight the simultaneous exposure of the population to numerous different pollutants and set the basis for a more holistic understanding of their combined effect on human health.



*Did you know....*

*...that hair can be used to study exposure to pollutants?*

Unlike blood and urine, hair can provide us with information on chronic exposure to chemicals over several months, while fluids only provide an indication of exposure over the few hours preceding their collection.



## Renewed hope for the treatment of pain and depression

Researchers at the LIH Department of Infection and Immunity developed LIH383, a novel molecule that binds to and blocks a previously unknown opioid receptor in the brain, thereby modulating the levels of opioid peptides produced in the central nervous system (CNS) and potentiating their natural painkilling and antidepressant properties. Opioid peptides are small proteins that act as neuromodulators by interacting with four 'classical' opioid receptors on the surface of CNS cells, playing a key role in mediating pain relief but also emotions such as euphoria, anxiety, stress and depression. The molecule was developed by Dr Andy Chevigné, Head of Immuno-Pharmacology and Interactomics at LIH, and his team, based on their previous research that had identified the atypical chemokine receptor ACKR3 as a novel opioid receptor which binds to natural opioids and 'traps' them, thereby dampening their analgesic and antianxiety activity. These findings were published on June 19th 2020 in the prestigious international journal 'Nature Communications', carrying important implications for the development of a novel class of drugs for pain, depression and for brain cancer treatment.



*Did you know...*

*...that the use of opioid painkillers is causing an 'opioid crisis'?*

Despite their effectiveness, the use of the opioid painkillers frequently leads to several side-effects, such as tolerance, dependence and respiratory disorders. There is an urgent need to find new means to modulate the opioid system and reduce complications.



## Novel approach to cure autoimmunity through specially tailored nutrition and to support cancer therapy

Scientists at the LIH Department of Infection and Immunity revealed a novel mechanism through which the immune system can control autoimmunity and cancer. In the special focus of the researchers were regulatory T cells – a specific type of white blood cells that in general act as a brake on the immune system. The LIH research team led by Prof Dirk Brenner, FNR ATTRACT fellow and Head of Experimental & Molecular Immunology, revealed a mechanism that controls the function of regulatory T cells and determines the balance between autoimmunity and anti-cancer activity. In a preclinical model, the scientists further showed that the elucidation of the metabolic mechanism of a disease can lead to disease reduction by a rationally-designed diet that specifically addresses these metabolic alterations. This sets a new direction for future treatment of metabolic diseases. These findings, which were published in the leading international journal 'Cell Metabolism', hold important implications for the development of personalised treatment options for autoimmune disorders and cancer.



*Did you know...  
...that immune cells could be used to  
treat cancer?*

Regulatory T cells are a small fraction of immune cells which keep the immune system in check. Indeed, if dysfunctional, they can turn the immune system against its own body, causing diseases such as multiple sclerosis. On the other hand, controlling their activation, as scientists at LIH are trying to do, could train the T cells to find and kill cancer cells very, very effectively.

## LIH researchers receive prestigious international award

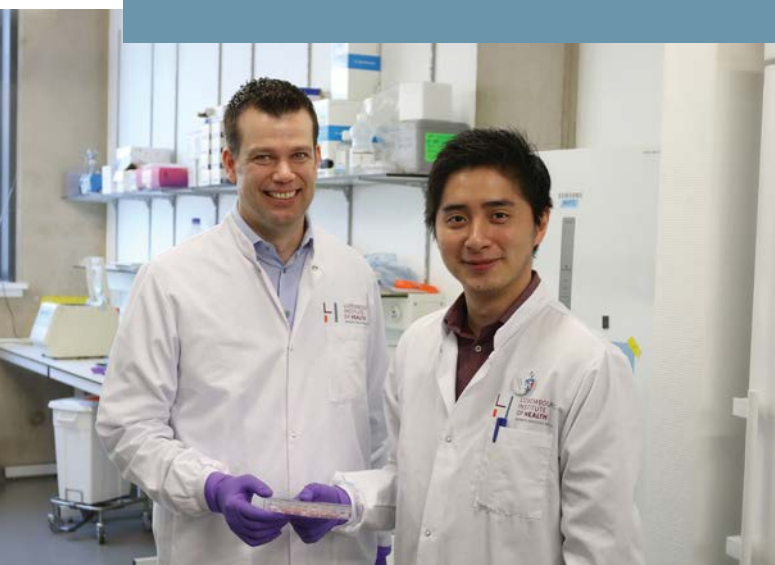
In December 2020, Dr Andy Chevigné and Dr Martyna Szpakowska from the LIH Department of Infection and Immunity (DII) were rewarded with the Galien Prize for their outstanding contribution to molecular pharmacology. The Galien Prize is traditionally organised in Belgium and Luxembourg by Roularta HealthCare on a yearly basis and crowns the most significant discoveries in the fields of pharmacology, drug development and medical devices.



Dr Nicole Kiweler

## LIH post-doctoral fellow wins 2020 Career Launchpad Award to support cancer metabolism research

An initiative that aims to support brilliant young researchers in finalising or initiating promising innovative research projects selected Dr Nicole Kiweler, a post-doctoral fellow within the Cancer Metabolism Group of the LIH Department of Oncology, based on her remarkable profile and the quality of the project. Dr Kiweler is working on elucidating the metabolic alterations that arise in cancer cells in response to chemotherapy, conferring them the ability to adapt to a changing microenvironment, escape from the primary niche and survive, a process that underpins the formation of metastases. In addition to covering the cost of additional experiments to strengthen her findings, the grant will allow her to attend a Lab Leadership course in Heidelberg, organised by the European Molecular Biology Organisation (EMBO), so that she can develop the critical soft skills necessary to one day manage a team as a Principle Investigator.



Prof Dirk Brenner (left) and Henry Kurniawan (right)

# Thank you to our donors



♥ Villmools Merci:  
to The Luxembourgish non-profit association  
Plooschter Projet

## Understanding how chronic lymphocytic leukaemia evades the immune system //

The research group, led by Dr Etienne Moussay and Dr Jérôme Paggetti of the LIH Department of Oncology, is investigating the cellular microenvironment of the lymph nodes of patients with chronic lymphocytic leukaemia (CLL), the most common form of leukaemia. CLL cells make the surrounding cellular environment immunosuppressive to ensure their survival and proliferation. A better understanding of the way the immune cells are subverted by tumour immune escape mechanisms will provide hints as to potential targets for new innovative immunotherapies. //

♥ Villmools Merci:  
to Fondation Cancer and the Luxembourg  
National Research Fund (FNR)

## Paving the road towards personalised treatment of recurrent brain tumours //

GLASS-LUX (Glioma Longitudinal AnalySiS in Luxembourg: ex vivo and in vivo Functional Profiling of Recurrent Gliomas), which was launched in the spring 2021 for a duration of 36 months, aims to characterise the molecular and genetic differences between primary and recurrent brain tumours, and test their differential responses to a broad selection of both novel and existing drugs. This will enable the prediction of personalised treatment options for recurrent glioma patients after the standard of care has been unsuccessful. //

♥ Villmools Merci:  
to the Luxembourg National Research  
Fund (FNR) and the Quebec Research Fund (FRQ)

## Luxembourg and Canada researchers join forces //

Following a first call for proposals in December 2020, a bilateral project involving the Human Biomonitoring Research Unit of the LIH Department of Population Health and the University of Québec in Montréal (UQAM) was selected for funding on March 29th 2021 under the Québec-Luxembourg programme AUDACE, a joint initiative of the Luxembourg National Research Fund (FNR) and of the Quebec Research Fund (FRQ). The scheme aims to support innovative and high-impact interdisciplinary and intersectoral collaborations between Quebec and Luxembourg scientists. //



From left to right: Christiane Lieners (Plooschter Projet asbl), Yannick Lieners (Plooschter Projet asbl), Dr Jérôme Paggetti (LIH), Dr Etienne Moussay (LIH) and Dr Anne Largeot (LIH)



**Villmoools Merci:**  
 to the Luxembourg National Research Fund (FNR)  
 and the André Losch Fondation

## United against COVID-19 //

Originally launched in April 2020 under the aegis of the Research Luxembourg COVID-19 Taskforce, the CON-VINCE study aims to evaluate the prevalence and dynamics of the spread of COVID-19 within the Luxembourgish population, with a specific focus on asymptomatic and mildly symptomatic individuals. The last round of testing of the CON-VINCE participants started in April 2021, and will provide a comprehensive insight into the evolution and transmission of the disease over an extended timeframe, particularly from an immunity perspective. In parallel, the Predi-COVID (Luxembourg cohort of positive patients for COVID-19: a stratification study to predict severe prognosis) study, the final follow-up of which started in May 2021, will shed light on the features of “Long COVID”, contributing to a better understanding of why some patients infected by SARS-CoV-2 develop severe symptoms while others present only mild forms. //

The Predi-COVID nurse team



From left to right: Dr Etienne Moussay (LIH), Dr Jerome Paggetti (LIH), Prof Simone Niclou (LIH), Dr Carole Bauer (president, Fondation Cancer), Prof Ulf Nehrbass (CEO LIH) and Dr Marc Schiltz (CEO FNR)

**Villmoools Merci:**  
 to Fondation Cancer and the Luxembourg  
 National Research Fund (FNR)

## Reactivating the patient’s immune system to mount an anti-cancer response //

The three-year project, led by Dr Jérôme Paggetti, co-Group Leader of the Tumor Stroma Interactions research group at the LIH Department of Oncology, will specifically investigate the exact mechanisms through which small ‘vessels’ involved in intercellular communication can induce tumour development and progression in chronic lymphocytic leukaemia. //

“ Our project will allow the identification of new druggable targets by improving our understanding of these promising extracellular particles. Ultimately, we aim to foster progress towards a more effective personalised treatment which could either directly target the tumour or reactivate a patient’s immune system to mount an anti-cancer response that permanently reverses the disease”, explains Dr Paggetti.

Thank you  
 to our donors





**Villmools Merci:  
to Rotary Club Luxembourg**

## A blood donation with a difference //

**“** *The aim of our project is to provide an accurate and useful tool to maximise the efficacy of plasma transfusions as a viable therapeutic option for COVID-19, thereby tangibly improving patient outcomes. Moreover, the test will be a valuable tool for the development of a vaccine. We are therefore extremely grateful to the Luxembourg Rotary Clubs for their generous donation”,* says Dr Danielle Perez Bercoff at the LIH Department of Infection and Immunity.



## We thank our partners for their generous support:

**Action Lions Vaincre le Cancer asbl**

**Association luxembourgeoise des Oeuvres du Rotary asbl**

**André Losch Fondation**

**Fondation Cœur-Daniel Wagner, Fondation Marie Jeanne et Edmond Schumacher,  
COVID-19 Foundation, Fondation CINVEN  
(Foundations under the aegis of Fondation de Luxembourg)**

**Fondatioun Kriibskrank Kanner**

**Fondation Cancer**

**Fondation Recherche Cancer et Sang**

**Plooschter Projet asbl**

**Think Pink Lux asbl**

**... and many private donors**

# Thank you

# A glance at the *future*

interview with Dr Guy Fagherazzi

## CoLive Voice - 'Vocal biomarkers' to monitor health

The LIH Deep Digital Phenotyping (DDP) research unit recently launched CoLive Voice ([www.colivevoice.org](http://www.colivevoice.org)), an international study that aims to collect and analyse voice recordings in several languages from both the general population and people living with chronic or infectious diseases, to identify so-called 'vocal biomarkers'. In this exclusive interview, Dr Guy Fagherazzi, Director of the LIH Department of Population Health (DoPH) and Principal Investigator of CoLive Voice, provides more insight into the project.

### Can you tell us a little bit about your new study – CoLive Voice?

G.F.: CoLive Voice is a first-of-its kind digital health study that aims to advance the diagnosis, risk prediction and remote monitoring of various chronic conditions and symptoms by evaluating voice features by leveraging breakthrough artificial intelligence approaches.

### Why use the voice?

G.F.: Human voice is a powerful communication medium that conveys feelings and emotions, but that can also immediately reflect the changes in an individual's health. A vocal biomarker is a feature or a combination of features from the voice that can be associated with a specific clinical outcome and that can therefore be a valuable tool to monitor patients, diagnose a condition, assess the severity of a disease and even to develop new drugs.

### Could you give us an example?

G.F.: Acoustic features extracted from recordings of a sustained vowel such as 'aaaa' can help us detect Parkinson's disease, whereas linguistic features extracted from spontaneous or semi-spontaneous speech could be more suitable for mental health disorders.



## How will you collect the voice samples?

G.F.: Through an anonymous online survey on the dedicated CoLive Voice web-application, study participants will first answer a questionnaire on their health status. They will then be asked to complete voice recordings by reading short predefined texts, coughing, breathing deeply and counting, among others.

## What will you do with the voice samples?

G.F.: LIH scientists will process the collected data and extract the most significant audio features, depending on the disease or type of voice recording. The audio characteristics will then be used to “train” machine- and deep-learning models to predict the symptom or disease of interest.

## Who can participate in the study?

G.F.: Adults and adolescents above the age of 15, from any country and regardless of their health status, are eligible to participate in CoLive Voice. In addition to people with no particular health issues, we are interested in including patients living with cancer, diabetes, multiple sclerosis, inflammatory bowel disease or COVID-19.

## What difference do donations make?

G.F.: Though a Luxembourgish initiative, the strength of the study lies in its international dimension. Indeed, we expect the participation of over 50,000 individuals worldwide, contributing to making CoLive Voice a unique international multilingual audio databank to identify vocal biomarkers. We hope that vocal biomarkers will soon be used in various contexts such as telemedicine purposes, telemonitoring of patients between clinical visits or to assess the effectiveness of a drug in a clinical trial. To this end, audio, clinical, epidemiological data and patient-reported outcomes need to be collected simultaneously and systematically via well-structured methodologies. Donations, volunteers and patients are all key to this end. It is an ambitious project and every private contribution, big or small, brings us one step closer to achieving the breakthrough we are working towards. We cannot do this alone.



Dr Guy Fagherazzi

  
**ColiveVoice**  
BY LUXEMBOURG INSTITUTE OF HEALTH

To participate in the study, simply access the CoLive Voice application in English, French, German and Spanish here: [www.colivevoice.org](http://www.colivevoice.org)



## *Make a donation and support biomedical research*

A donation can help our scientists to create innovative approaches that will enhance prevention, early diagnostics and effective treatments of many diseases.

### **SUPPORT US:**

**Account name:** Luxembourg Institute of Health

**IBAN:** LU30 0019 1106 2926 0000

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### **CONTACT**

Please address any questions you might have by e-mail to [donations@lih.lu](mailto:donations@lih.lu) or by phone to **+352 26 970-1**.

We will get back to you with great pleasure.

For any questions on the processing of your personal data in connection with a donation, you can visit our website <https://www.lih.lu/page/makeadonation> or contact us at the above address.

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