LUXEMBOURG
INSTITUTE
OF **HEALTH**
RESEARCH DEDICATED TO LIFE

ANNUAL REPORT
2020

Please note:
all photos (e.g. groups, awards) in which social distancing and other preventive measures (e.g. face masks) are not adhered to were taken prior to the COVID-19 pandemic.

SCAN ME

View our corporate video

Prof Dr Ulf Nehrbass, Chief Executive Officer

FOREWORD
MESSAGE FROM THE CEO

It is now the middle of June 2021. There is light at the end of the long pandemic tunnel. COVID-19 restrictions are being progressively lifted all over Europe. The various vaccine strategies have proven efficacious and vaccination rates are up. Consequently, infections keep going down. And there is realistic hope that the mRNA vaccine approach will be able to swiftly cope with resistant SARS-CoV-2 strains, should these arise. Overall therefore, humanity has done somewhat well in the face of an unprecedented threat. Not all is good, of course, but how much worse it could have been!

On a personal note, 2020 has been an exhausting year, and I know it has been for many of you, too. We will all have our personal stories to tell and lessons to learn. However, in spite of the personal hardships, I think we can be proud of LIH and our performance under challenge. The arrival of a new virus, completely unbeknown to us, with high infectivity and a presumably high case fatality rate, put the spotlight squarely on the Luxembourg Institute of Health. With that name, we would rightly be expected to help decision makers and the population navigate what was becoming a massive pandemic – and a very frightening one too.

LIH quickly lived up to the challenge, first by forming the COVID-19 task force, and then by conceptualising and implementing the large-scale testing (LST) campaign together with partners from the University, the Ministries and from the private sector. LST was designed to test up to 10% of the population per week. After an initial setup phase, the technical and operational processes worked flawlessly. Without the first phase of the LST campaign, case numbers would have been around 43% higher, while intensive care unit peak

occupancy would have been around 50% higher. Over the entire period since its establishment in May 2020, LST helped to suppress epidemic dynamics and stabilise the pandemic. Thereby, it contributed to Luxembourg's shops and schools remaining open during periods where Belgium, France and Germany were under lockdown. Additionally, had COVID-19 case fatality rates been higher, Luxembourg would have been ready with LST coupled to higher participation to guarantee an essential pandemic bulwark.

Beyond LST, LIH rapidly initiated observational studies, CON-VINCE, to understand how the pandemic worked itself through the population, and Predi-COVID to assess the differential disease severity in COVID-19 patients. These studies were a fast forward into LIH's new translational strategy: the CIEC rapidly working to elaborate the observational protocols, nurses collecting samples and IBBL processing such samples during countless extra shifts. Our scientists produced insights that were highly relevant to the specifics of the pandemic in Luxembourg, and were able to shed light on the mechanisms mediating a more severe disease development. And all the while the translational studies were running, the staff were working away at operationally integrating the various translational entities at LIH and IBBL.

In parallel, despite the turmoil caused by the pandemic and the inevitable disruptions to our day-to-day activities, LIH researchers have been pursuing their efforts to advance translational medicine across all key priority research areas. Indeed, the year 2020 saw a string of high-impact scientific publications in prominent international journals. In the field of immunology, the work of LIH researchers highlighting the link between the immune system, metabolism, nutrition and the health-disease balance received widespread international attention, resulting in the publication of their findings in top journals such as Cell Metabolism and Nature Communications. Similarly, major publications were released in the areas of digital health and artificial intelligence, including for instance a paper on machine-learning approaches to advance the diagnosis of neurodegenerative diseases in the Nature Partner Journals Systems Biology and Applications. In oncology, breakthrough research highlighting new therapeutic avenues for personalised treatment, with the immune system acting as a common thread and new patient-based models as enablers, also took the international scientific community by storm, leading to publications in the likes of Science Advances and Nature Communications. The excellence of this research output has also been publicly acknowledged through the award of numerous national and international prizes and accolades to LIH scientists, including the renowned 2019 Galien Prize in Pharmacology and the "Prix du Fonds Léon et Henri Fredericq", alongside many other donations from private and institutional donors.

Are there lessons to learn then?

The pandemic has shown us what we can achieve if we adopt a highly collaborative and integrated approach that transcends institutional boundaries. We do not want to merely "operate" but to "co"-operate, shedding the silo mentality and embracing the collaborative dimension. The establishment of the Research Luxembourg initiative, and of its dedicated COVID-19 Taskforce in this specific crisis context, is a glaring example of this mindset. Instilling this transversal and translational approach among all relevant stakeholders is what has been guiding and will continue to shape all of LIH's activities. The current health context has also further brought forward the value of innovative and disruptive "e-health" digital technologies. From a public health and epidemiology perspective, it suffices to think of the "vocal biomarker" component of the Predi-COVID study to acknowledge that concepts such as "Deep Digital Phenotyping", "digital twin", "digital cohorts" and "vocal biomarkers" are no longer to be relegated to the realm of fiction. They are instead becoming deeply embedded in our daily research activities.

I would like to thank the Ministry of Higher Education and Research, the Ministry of Health and the National Research Fund for their unwavering support throughout this difficult year. My acknowledgements also go to our national and international partners, clinicians and researchers for the enriching cooperation, and of course to our patients for their trust and participation in our clinical studies. Finally, I extend my heartfelt thanks to our dedicated staff, whose commitment is the driving force behind LIH.

Prof Dr Ulf Nehrbass
CEO

SCAN ME

View video /Foreword/

Dr Gregor Baertz
President of the Board of Directors

MESSAGE FROM THE BOARD

Despite the socio-economic and health tumult caused by the COVID-19 pandemic, 2020 was the year LIH could prove its reputation as a truly translational institute and as a leader in clinical research, not just nationally but internationally, thereby contributing to upholding Luxembourg's standing as the hotbed for disease management.

The rapid mobilisation of the Luxembourgish government and of the various research institutes from the very start of the COVID-19 pandemic, as well as the seamless collaboration between all local players, contributed substantially to the protection of public health and the containment of the spread of the disease among the Luxembourg population. Indeed, the prompt establishment of a dedicated taskforce to coordinate all national efforts and the ensuing implementation of several unique research and public health initiatives won the Grand Duchy an unprecedented visibility at the international level as a leading centre of excellence in translational and clinical research. In this context, LIH acted as a central pillar for the fight against COVID-19.

Through its leading position within the national COVID-19 Taskforce and the remarkable work of its staff, LIH set up and coordinated two cohort studies to assess the severity of COVID-19 and its prevalence among the population, focusing particularly on the role of asymptomatic carriers, as well as participating in a European clinical trial aiming to assess the efficacy and safety of novel antiviral treatments. In addition, the institute coordinated a unique and unparalleled nationwide large-scale screening campaign, with the goal of identifying positive cases and breaking infection chains early on. Several LIH scientists also received significant financial support for their innovative COVID-19-related research projects through a novel dedicated funding programme launched by the Luxembourg National Research Fund (FNR).

These achievements relied on the close cooperation between LIH and all relevant local and international partners, as well as on effective and tailored communication support campaigns, making the national response to the pandemic a real illustration of a "Made in Luxembourg" success.

Of course, none of said achievements could have been possible without the passion and dedication of the entire LIH staff, from research to administration, and without the enlightened leadership and mentoring of the management. I therefore take this opportunity to extend my warmest gratitude to the people behind the excellence of LIH. On behalf of the entire Board of Directors, Villmols Merci!

Dr Gregor Baertz
President of the Board of Directors

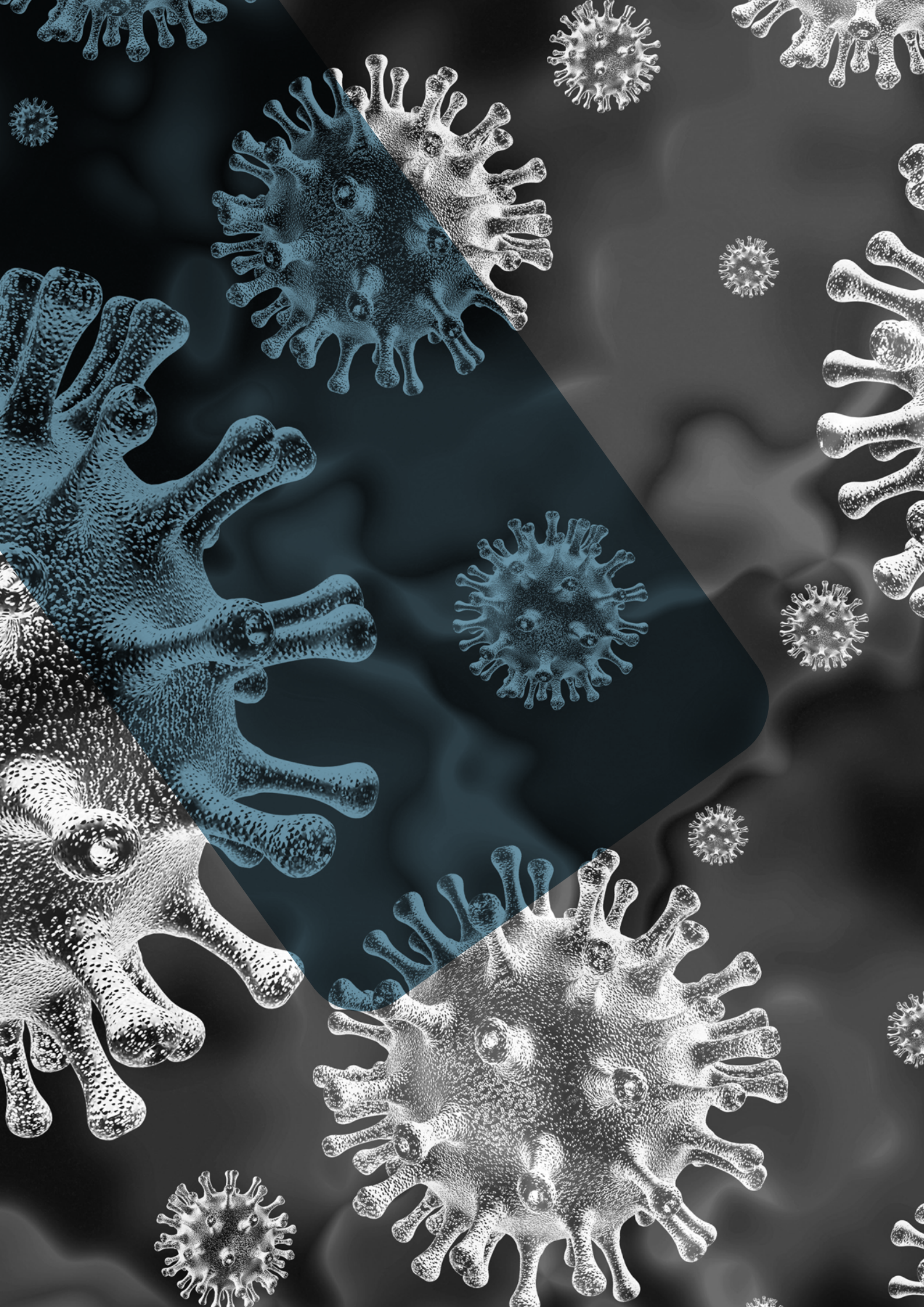
CONTENT


LEITZ
ERMANY

MISSION & VISION

LIH's **mission** is to have a positive impact on patients by performing and translating excellent biomedical research.

LIH's **vision** is to put Luxembourg at the forefront of biomedical research and create a translational hub at the heart of Europe.



COVID-19: A collaborative priority area for Luxembourg and LIH

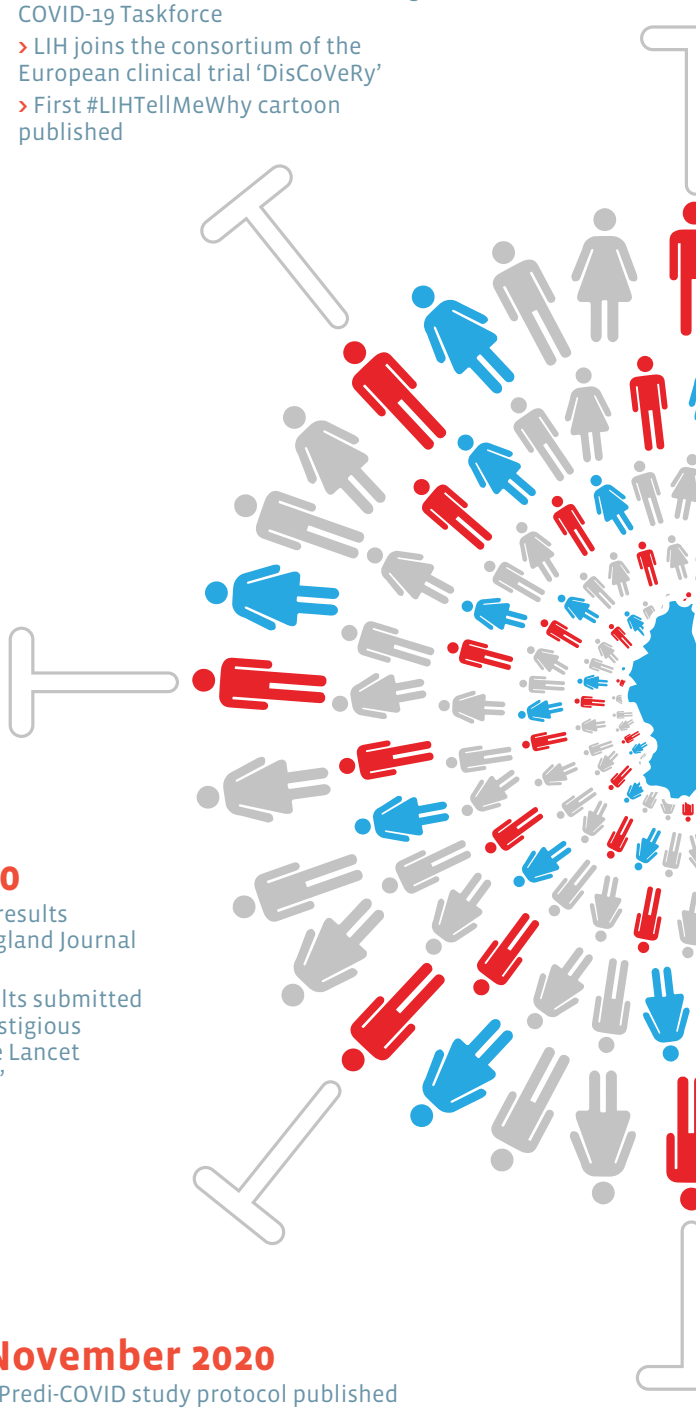
Key 2020 COVID-19 milestones and achievements

March 2020

› Launch of the Research Luxembourg COVID-19 Taskforce

› LIH joins the consortium of the European clinical trial 'DisCoVeRy'

› First #LIHTellMeWhy cartoon published



December 2020

› DisCoVeRy preliminary results published in the 'New England Journal of Medicine'

› Large Scale Testing results submitted for publication in the prestigious international journal 'The Lancet Regional Health – Europe'

November 2020

› Predi-COVID study protocol published in the renowned international journal 'British Medical Journal Open'

April 2020

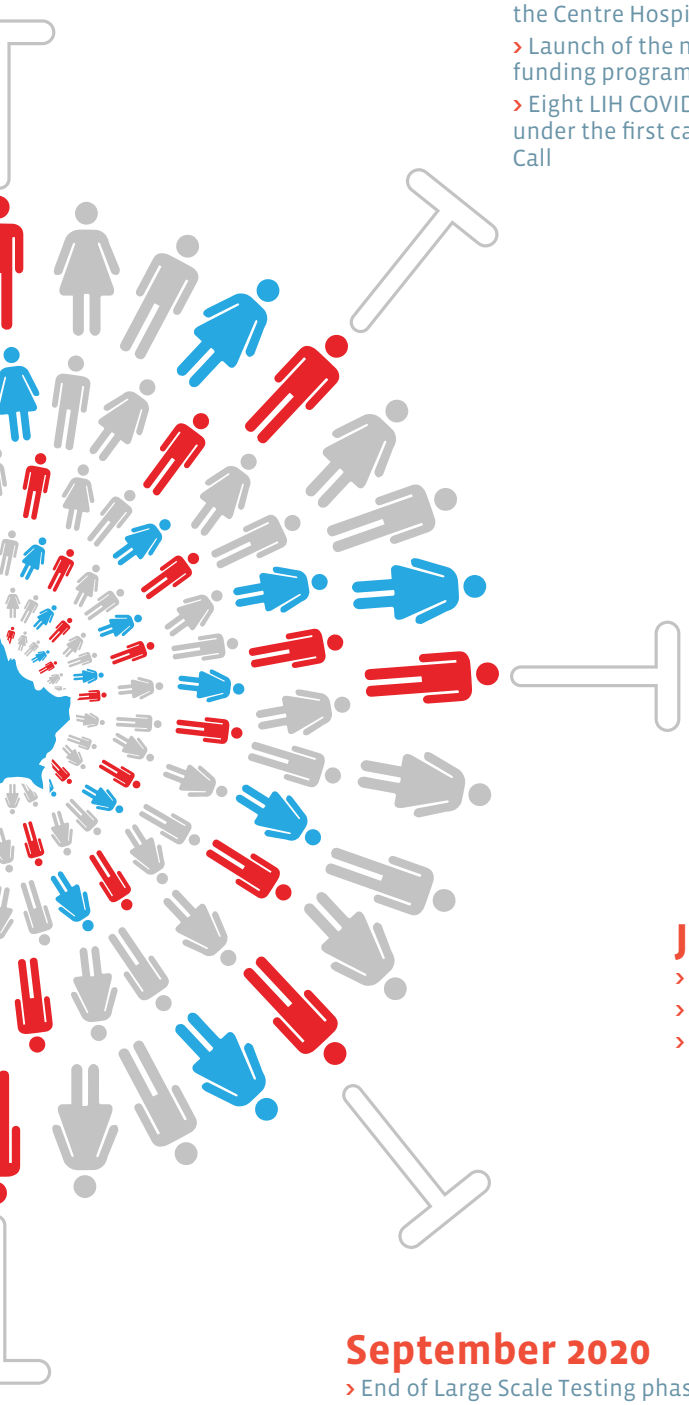
› Launch of the CON-VINCE cohort study with FNR and Fondation André Losch financial support

› Launch of the Predi-COVID cohort study with FNR and Fondation André Losch financial support

› First 'DisCoVeRy' Luxembourg patient recruited at the Centre Hospitalier de Luxembourg (CHL)

› Launch of the novel FNR COVID-19 Fast Track Call funding programme

› Eight LIH COVID-19 projects shortlisted and funded under the first call of the FNR COVID-19 Fast Track Call



May 2020

› Start of Predi-COVID participant recruitment and data/sample collection phase

› Launch of the Large Scale Testing campaign (phase I)

› Four LIH COVID-19 projects shortlisted and funded under the second call of the FNR COVID-19 Fast Track Call

June 2020

› CON-VINCE interim results

› Last #LIHTellMeWhy cartoon published

› Launch of the #AHHH campaign

September 2020

› End of Large Scale Testing phase I and launch of phase II

Research Luxembourg launches the “COVID-19 Taskforce”

As a first response to the COVID-19 pandemic, Research Luxembourg, a joint initiative of all the main players in Luxembourg's public research sector, set up a dedicated COVID-19 Taskforce in March 2020, with LIH’s CEO Prof Ulf Nehrbass as spokesperson and Prof Paul Wilmes (University of Luxembourg, LCSB) as deputy spokesperson. The aim of the Research Luxembourg COVID-19 Taskforce was to help address the emergency by mobilising the knowledge, human and material resources of the Luxembourg public research sector and offering the national healthcare system the combined expertise available within the Research Luxembourg member institutes – namely LIH, the Luxembourg Institute of Socio-Economic Research (LISER), the Luxembourg Institute of Science and Technology (LIST), the Laboratoire National de Santé (LNS), the University of Luxembourg, Luxinnovation and the Luxembourg National Research Fund (FNR) – under the coordination of the Ministry of Higher Education and Research (MESR).

Specifically, the three main missions of the Taskforce were to coordinate the provision of support from the national research community to healthcare providers; help identify and centralise a variety of priority activities, leveraging on the inter-sectoral expertise in molecular biology, epidemiology, clinical trials and fundamental research; and acting as the central point of contact between the national research ecosystem, the clinical community and the authorities. From an operational perspective, the Taskforce focused on three main pillars, namely the implementation of a nationwide prevalence study to assess the extent of the spread of the virus and the number of asymptomatic individuals; a stratification study to identify risk factors that contribute negatively to disease progression; and statistical simulations on the evolution, impact and spread of the COVID-19 pandemic to provide short- and medium-term projections and thus facilitate decision-making on when restrictions could be lifted. These priority pillars resulted in the prompt setup of several national projects and initiatives, which gained international visibility for their seamless and rigorous organisation and for the high quality of the research work carried out.

Research Luxembourg COVID-19 Taskforce spokesperson Prof Ulf Nehrbass (LIH CEO) and deputy spokesperson Prof Paul Wilmes (University of Luxembourg, LCSB) presenting a status update at a press conference

Testing asymptomatic individuals to assess COVID-19 spread in Luxembourg: the CON-VINCE study

The first study launched under the aegis of the Research Luxembourg COVID-19 Taskforce to help contain the pandemic was CON-VINCE (COvid-19 National survey for assessing VIral spread by Non-affected CarriErs), which kicked off in April 2020. Under the leadership of Prof Rejko Krüger, Director of Transversal Translational Medicine (TTM) at LIH, the project aims to evaluate the dynamics of the spread of the COVID-19 disease, with a specific interest in the asymptomatic and oligosymptomatic individuals, within the Luxembourgish population by testing a representative panel of over 1,800 people for the presence of the SARS-CoV-2 virus. The CON-VINCE participants are followed up over a period of 12 months. Asymptomatic individuals – referred to as 'silent carriers' – and mildly symptomatic carriers play a significant role in the spread of the virus, although they often remain undetected, thereby making CON-VINCE a key pillar in the characterisation of the nature, prevalence and transmission modality of COVID-19 in the Grand Duchy.

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/CON-VINCE/

CON-VINCE can be seen as a role model for collaborative translational research in Luxembourg. Indeed, the project is led by a consortium of Luxembourgish research institutions, consisting of LIH, its Integrated Biobank of Luxembourg (IBBL), the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg and the Laboratoire National de Santé (LNS), with the support of the market research company TNS-ILRES for the selection of participants, and of the national diagnostic laboratories Ketterthill, Laboratoires Réunis and BioneXt Lab as associated partners for sample collection. This tight cooperation enabled the smooth running of the technically and logistically complex operations. Within this context, IBBL in particular acted as a key integrator, coordinating the efforts of all partners in terms of biological sample logistics, processing, storage and data entry, with members of the different study institutions and volunteers supporting the activities. Thus, within ten days of the launch of the study, over 1,800 people were recruited, biosampled and tested, and over 2,000 kits for the collection of blood, naso-pharyngeal and stool samples were distributed to the study partner laboratories.

As of June 2020, over 8,900 health questionnaires had been filled out by the 1,870 study participants, and over 8,900 blood samples, 8,900 swab samples and 2,400 stool samples had been collected. Moreover, the prevalence of COVID-19 was shown to have declined significantly between when the project began in April and the end of June, demonstrating that the confinement measures had been efficient and that at least the beginning of the deconfinement was successful in terms of viral spread. The presence of anti-SARS-CoV-2 antibodies in the tested panel also seemed to have increased between April and June, with its prevalence reaching around 3%.

Assembly of sample collection kits at IBBL's Biorepository department

Sample reception at IBBL's Biorepository department

Sample processing at IBBL's Biorefinery department

Data entry at IBBL

In the IBBL labs: Arnaud D'Agostini, Head of LIH Marketing & Communication, Brian De Witt, Microbiome & Sequencing Assistant Scientist, and Prof Ulf Nehrbass, LIH CEO

Mrs Daniela Ragni, Director of the André Losch Foundation, during a visit to LIH (November 2020)

This joint effort was financially supported by the Luxembourg National Research Fund (FNR), which co-funded the study through a EUR 1.4 million allocation, but also by the Fondation André Losch, which committed EUR 800,000 to the study out of a total sum of EUR 1.4 million dedicated to financing two other COVID-19 projects in the framework of the Research Luxembourg Taskforce. These include a study on the severity of COVID-19 (Predi-COVID) and a project that develops statistical projections and modelling of the epidemic.

Prof Rejko Krüger presenting the interim results of CON-VINCE during a press conference at the Laboratoire National de Santé (LNS) in Dudelange

Predicting the severity of COVID-19 infection: the Predi-COVID study

A second flagship project of the Research Luxembourg COVID-19 Task Force is Predi-COVID, a cohort study launched in April 2020 and coordinated by the LIH Department of Population Health (DoPH). Predi-COVID (Luxembourg cohort of positive patients for COVID-19: a stratification study to predict severe prognosis) aims to define which patient profiles can be associated with a more severe disease prognosis. Specifically, Predi-COVID focuses on the identification of the clinical, epidemiological and socio-demographic characteristics, as well as specific biomarkers from both the SARS CoV-2 virus and the patient, which can help predict the way the disease will evolve in a given individual, according notably to his immune profile. The study will thus contribute to a better understanding of the heterogeneity observed in disease severity and prognosis and of the long-term health consequences of COVID-19, ultimately enabling the accurate evaluation of patients infected with SARS-CoV-2 and more personalised care recommendations.

To this end, the research team has been establishing a cohort of people, over the age of 18, positive for SARS CoV-2. In parallel to Predi-COVID, the ancillary study Predi-COVID-H was launched to specifically include household members of COVID-19 positive participants to study the transmission of the virus in this high-risk population. The recruitment and data/sample collection phase started in May 2020 under the coordination of the Clinical and Epidemiological Investigation Center (CIEC) of the DoPH, and was extended from December 2020 until late June 2021. As part of the study, several biological samples are collected from participants by the CIEC nurses and analysed by the LIH Department of Infection and Immunity (DII) and other project partners to identify human and viral predictive markers. Voice recordings are also collected to identify 'vocal biomarkers' of frequently observed symptoms in COVID-19 patients. An extension of Predi-COVID to children for 2021 was authorised in late 2020.

RESEARCH LUXEMBOURG

/Predi-COVID/

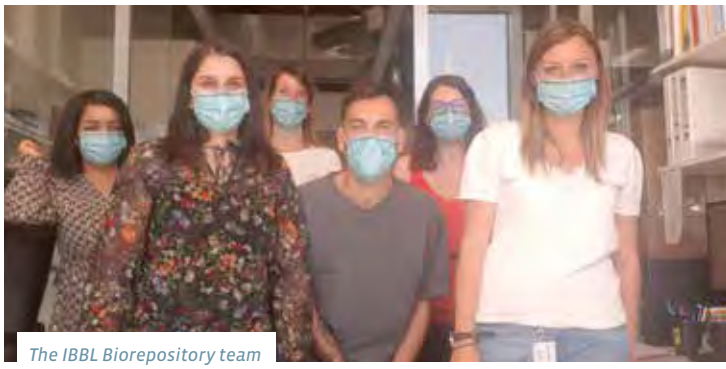
Since the start of patient recruitment in May 2020 and as of December 31st 2020, 1,705 and 73 eligible subjects have been contacted by phone for inclusion in Predi-COVID and in Predi-COVID-H, respectively, 651 of which agreed to be included for data collection in the former and 52 in the latter. The preliminary findings indicate that the majority of the enrolled population experienced few or mild symptoms. The team collected a total of 4,366 voice recordings from 314 different participants, as well as 807 biological specimens (blood, saliva, swabs, stool and hair) from 187 subjects from the Predi-COVID cohort and from 49 Predi-COVID-H participants, to establish a unique biobank to study COVID-19. In this respect, IBBL has been playing a critical role in designing the biobanking and sampling strategy, and is operationally responsible for the centralised management of biological samples, in close cooperation with all other LIH departments involved and with the Luxembourg Centre for Systems Biomedicine (LCSB). Namely, IBBL's Biorepository department oversees the assembly of biospecimen collection kits, sample reception, logistics, storage and distribution, while IBBL's Biorefinery department performs sample processing according to strict standard operating procedures.

In addition to LIH and IBBL, Predi-COVID boasts a highly interdisciplinary consortium of Luxembourgish research institutions, including the Laboratoire National de Santé (LNS), the University of Luxembourg, the Luxembourg Centre for Systems Biomedicine (LCSB), the Centre Hospitalier de Luxembourg (CHL) and the Hôpitaux Robert Schuman (HRS). The study is supported by the Health Inspection Department of the Ministry of Health, which also provided assistance in the identification of potential volunteers, and is co-financed by the FNR and by the André Losch Foundation through a generous donation. The latter also provided funding for four vans, allowing CIEC nurses to collect samples from study participants directly at their residence.

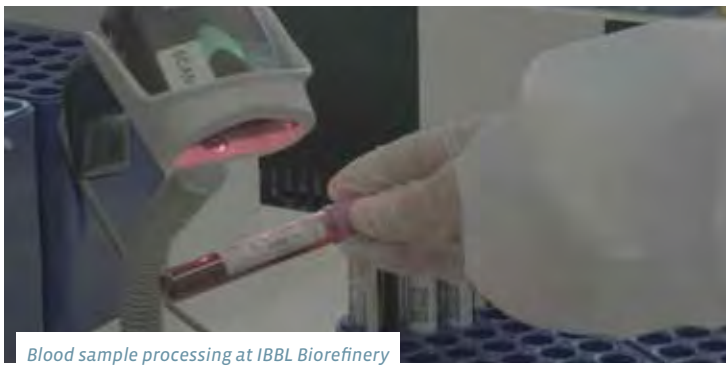
The study protocol, conceived by DoPH and CIEC, was published in November 2020 in the renowned international journal 'British Medical Journal Open', reinforcing the international visibility and success of this highly collaborative "Made in Luxembourg" project. Moreover, three COVID-19 projects involving LIH and leveraging Predi-COVID data and samples were funded by the Horizon 2020 ERAvsCORONA Action Plan and kicked off in late 2020.

The Predi-COVID nurse team of the Clinical and Epidemiological Investigation Center (CIEC) of the LIH Department of Population Health (DoPH)

The CIEC nurses and the vans for patient sample collection provided by the Fondation André Losch



The IBBL Biorepository team



Blood sample processing at IBBL Biorefinery

Assessing the safety and efficacy of potential COVID-19 treatments: the DisCoVeRy clinical trial

In addition to the efforts related to the characterisation of COVID-19, LIH has also been involved in studies seeking to identify treatment options for this novel disease. Thus, in March 2020, the Clinical and Epidemiological Investigation Centre (CIEC) of the LIH Department of Population Health (DoPH), the National Infectious Disease Department (Service National des Maladies Infectieuses – SNMI) and the Intensive Care Unit of the Centre Hospitalier de Luxembourg (CHL) and the Hôpitaux Robert Schuman (HRS) joined the consortium of the European clinical trial 'DisCoVeRy', coordinated by the French National Institute of Health and Medical Research (Inserm) and financially supported by the EU projects COMBACTE, PREPARE and RECOVER. The study, part of the international 'Solidarity' trial led under the auspices of the World Health Organization (WHO), aimed to test the efficacy and safety of four experimental repurposed antiviral therapies — remdesivir, lopinavir/ritonavir, interferon beta and hydroxychloroquine — in hospitalised COVID-19 patients.

The molecules were administered in four different combinations in parallel with standard care, and compared to standard care alone as a reference. These treatment options were randomly allocated to the study participants, although both patients and physicians were aware of the modality administered. Participants were assessed after 15 and 29 days, and clinical data, adverse events, nasopharyngeal swabs, lower respiratory tract specimens and other parameters were collected. The first Luxembourg patient was recruited in April at the Centre Hospitalier de Luxembourg (CHL).

In Luxembourg, the trial was led by Dr Thérèse Staub (CHL), Dr Jean Reuter (CHL), Dr Claude Braun (HRS) and Dr Marc Berna (HRS). The CHL team was responsible for patient recruitment, having included 2 new participants in October 2020, bringing the total number of enrolled Luxembourg patients to 15. CIEC played a key role in setting up the study, ensuring the close cooperation with CHL and Inserm, facilitating the obtainment of all necessary regulatory authorisations and supporting CHL physicians on operational aspects and patient follow-ups. Moreover, CIEC was responsible for biological sample collection and logistics, together with CHL and the Laboratoire National de Santé (LNS), and for recording and closely monitoring the collected patient clinical data prior to their transmission to the study coordinator for analysis. Patient recruitment is currently on hold, as the protocol is being amended to include a new drug to be tested. Indeed, the strength of DisCoVeRy lies in its proactive and adaptive nature, which makes it possible to refine the tested therapies in real time, excluding the ones that prove to be ineffective and replacing them with new and promising drugs being developed under ongoing research projects.

The preliminary results of the DisCoVeRy trial, which were published in December 2020 in the 'New England Journal of Medicine', showed that the investigated drugs failed to both improve the clinical course of COVID-19 in hospitalised patients and to increase their ability to clear the SARS-CoV-2 virus, being instead associated with more severe adverse effects such as acute respiratory failure and renal toxicity. Nevertheless, these findings represent a step forward in the understanding of the disease and in ensuring patient safety. Moreover, they supported the early interruption of ineffective treatment arms, allowing the consortium to focus their research efforts on more promising therapeutic options. DisCoVeRy has now been extended to other European countries with the support of the European Commission, with the goal of becoming a pan-European platform trial for emerging infectious diseases treatment.

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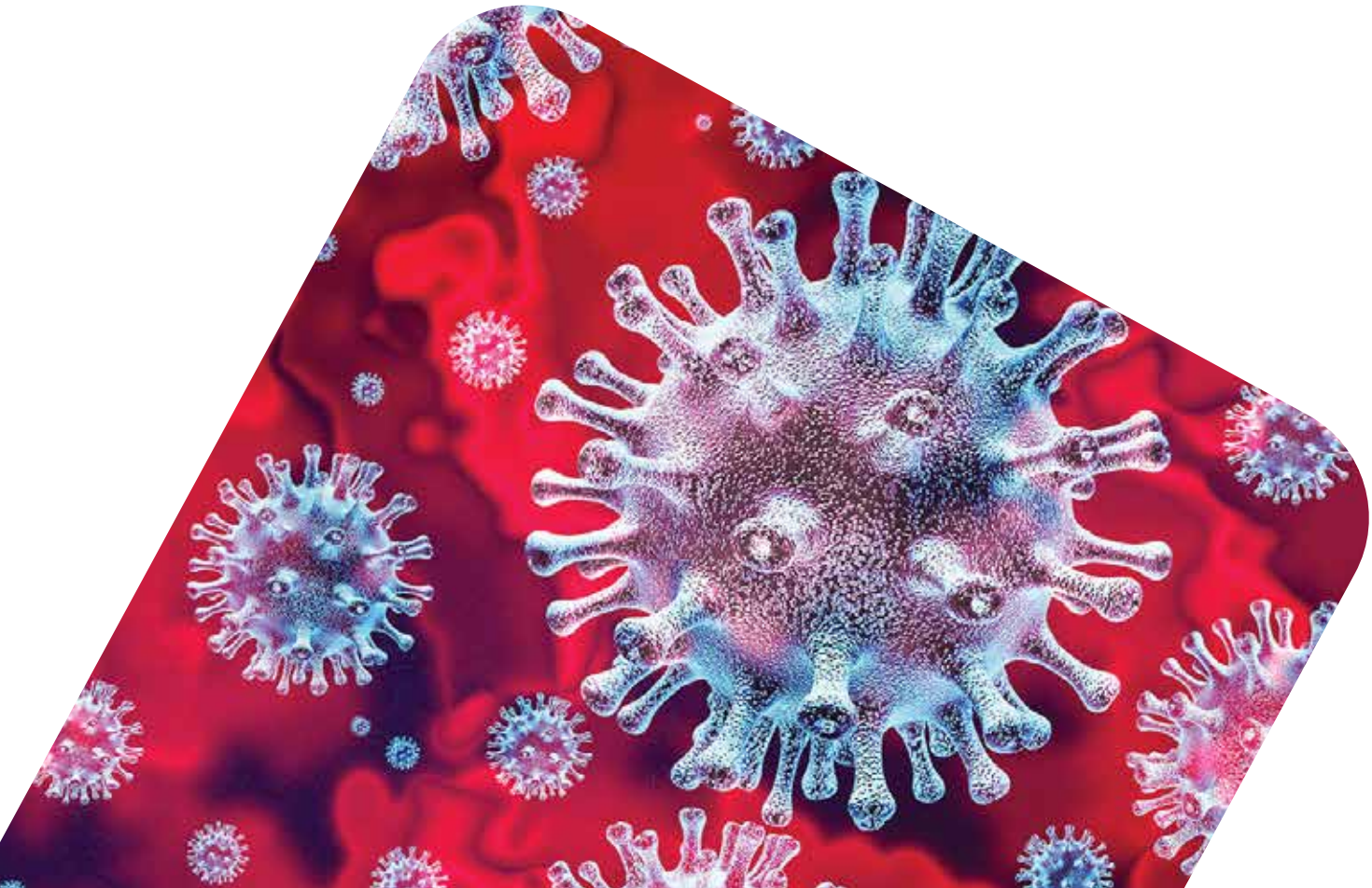
/DISCOVERY/

The Clinical and Epidemiological Investigation Centre (CIEC) team of the LIH Department of Population Health (DoPH)

Supporting Luxembourg's diagnostic capacity and large-scale testing strategies

As part of the many initiatives of the Research Luxembourg COVID-19 Taskforce, Prof Markus Ollert, Director of the LIH Department of Infection and Immunity (DII), has been leading a work package dedicated to creating additional diagnostic capacity at LIH, with the goal of supporting studies such as CON-VINCE and Predi-COVID, but also Luxembourg's healthcare providers and diagnostic laboratories in testing and diagnosing the growing number of potentially infected patients. The first activity in the work package, under the coordination of Dr Chantal Snoeck of the DII Clinical and Applied Virology group, entailed the setup of a diagnostic research lab at LIH where virologists and volunteers have been working in collaboration with other Luxembourgish partners on developing a novel and extremely sensitive PCR assay to screen patient samples for SARS-CoV-2. A second activity entailed the validation and testing of a serological immunoassay to detect and measure the presence of antibodies against the virus in the blood, as well as the recombinant expression and production of antigens from SARS-CoV-2. This aspect relied on the interdisciplinary expertise of several DII team members, including Dr Christiane Hilger and Dr Annette Kühn from the Molecular and Translational Allergology research group, Dr Andy Chevigné from the Immuno-Pharmacology and Interactomics group and Dr Judith Hübschen from the Clinical and Applied Virology group. A third activity of the work package, directed by Dr Danielle Perez–Bercoff, consisted in verifying whether serum containing anti-SARS-CoV-2 antibodies can effectively neutralise the virus, in order to develop a virus neutralisation test. Finally, the DII team aimed to test a selection of drugs commonly used for other diseases on the specific SARS-CoV-2 virus present in a given patient, so as to observe which therapeutic molecule the virus responds to and therefore provide doctors with a personalised treatment plan for each individual patient. This personalised antiviral profiling task is coordinated by Dr Carole Devaux, leader of the HIV Clinical and Translational Research group. This entire work package also benefited from the support of DII scientists Dr Cathy Leonard, from the Allergy and Clinical Immunology Group, and Erica Grant, PhD candidate in the Eco-Immunology and Microbiome Group.



Enabling evidence-based decision making in Luxembourg

LIH has been contributing to another key work package of the Research Luxembourg COVID-19 Taskforce, namely the provision of evidence-based advice on the novel coronavirus to the Luxembourg government and other relevant stakeholders. This work package was led by Prof Dirk Brenner, Deputy Head of Research & Strategy and Head of the Experimental and Molecular Immunology research group at the LIH Department of Infection and Immunity (DII). Specifically, the team responded to COVID-19-related requests from the government and from other implicated stakeholders. They provided advice, suggested concrete solutions and prepared strategic decisions. For instance, in the context of the work package, the LIH team supported the Research Luxembourg COVID-19 Taskforce in defining an appropriate exit strategy following the lifting of the restrictions in May 2020. In addition, the team performed an ongoing literature review for the Ministry of Health and set up a selected scientific literature feed in order to keep the scientific and healthcare community up to date on the latest developments in the field. The activities performed in the framework of this work package relied on a multidisciplinary and holistic core team of dedicated collaborators, namely LIH PhD candidates Anouk Ewen, Luana Guerra, Leticia Soriano Baguet and postdoctoral fellow Takumi Kobayashi, who have been involved in the evidence review. By sharing knowledge and expertise and collaborating closely with each other, the team contributed to ensuring that this challenging situation is tackled in a holistic and cross-sectoral manner.

A unique “Large Scale Testing” campaign as the pillar of the deconfinement strategy

As part of the national exit strategy, the Research Luxembourg COVID-19 Taskforce, in close cooperation with the Ministry of Higher Education and Research and the Ministry of Health, implemented a unique nationwide “Large Scale Testing” (LST) campaign, encouraging residents and cross-border workers to voluntarily get tested for COVID-19 through a PCR test on a throat swab. With a testing capacity of up to 20,000 PCR tests per day, this unprecedented public health initiative aimed to break infection chains as early as possible – detecting for the first time asymptomatic individuals which were estimated to account for up to 80% of cases – thereby containing the spread of the virus and enabling a safer and speedier lifting of the lockdown restrictions.

The first phase of the campaign, which ran from May 27th until July 27th 2020 under the coordination of LIH, relied on 16 ‘drive-through’ and 1 ‘walk-through’ test stations, as well as on a total of 400 employees. The population was divided into three main categories and received invitations by post to get tested voluntarily. The first category included people with a high risk of exposure and infection due to their professional activity (such as healthcare professionals), whereas the second category consisted of those having resumed their professional activity or being about to get back to work. The third category encompassed representative samples of the general population. The tests were carried out by Laboratoires Réunis, with the logistic support of Ecolog. Individuals testing positive for the SARS-CoV-2 virus were contacted personally by the Health Directorate and asked to spend two weeks at home in self-isolation.

LIH contributed significantly also to the contact tracing efforts, supporting the Inspection Sanitaire in following-up each newly diagnosed individual and tracing back personal contacts, through the provision of manpower and IT expertise. Specifically, Dr Michaël Schnell and his team at the IT expertise in Health Data (ITX HD) group of the LIH Department of Population Health (DoPH) put in about 1,900 hours in 2020 to develop Care+, an application enabling the follow-up of positive cases and their contacts, as well as the collection of information obtained during calls and follow-up rounds. Care+ was used by around 670 contact tracing users to monitor 52,548 positive cases and their 265,891 contacts, allowing the generation of over 264,000 documents, including quarantine orders, test prescriptions and other information.

From April 21st to May 29th 2020, Dr Sophie Couffignal at the Public Health Expertise Unit of DoPH coordinated the testing of residents and staff of nursing homes on behalf of the Inspection Sanitaire. Volunteers from LIH reinforced the mobile teams and over 10,000 people were screened across 49 institutions.

An extension period of Phase I was set up until September 15th 2020, with the second phase of the LST beginning immediately after under the coordination of the Health Directorate of the Ministry of Health, being foreseen to last until March 2021 with a capacity of 53,000 tests per week.
In total, during Phase I, over 1.4 million invitations to participate in the LST were sent and over 566,000 tests were conducted, covering 49% of Luxembourg residents. Among the cross-border workers, over 87,000 of the invited individuals got tested, giving a participation rate of 22%. The LST detected 26% of all positive cases related to the epidemic wave. Out of the identified positive cases, 33% were asymptomatic. These findings bring forward the significant role of the LST initiative in containing the pandemic. Indeed, the total number of cases would have been 43% higher without the LST. Moreover, the results show that asymptomatic carriers infect on average the same number of people as symptomatic individuals, implying that asymptomatic and pre-symptomatic individuals are an important factor in the transmission of the virus. The full results of the LST, including contact tracing data, were submitted to the prestigious international journal "The Lancet Regional Health – Europe" in December 2020 and were published in March 2021.

Luxembourg's Prime Minister Xavier Bettel participates in the LST campaign. From left to right: Gauthier Destenay, Dr Jasmin Schulz (LST project manager at LIH), Xavier Bettel (Prime Minister) and Arnaud D'Agostini (Head of Marketing and Communication at LIH)

The LST Handover conference, September 14th. From left to right: Dr Gregor Baertz (Chairman of the Board, LIH), Prof Dr Ulf Nehrbass (LIH CEO), Paulette Lenert (Minister of Health), Claude Meisch (Minister for Higher Education and Research) and Prof Paul Wilmes (LCSB)

Developing the LST strategy at LIH

All in all, this unparalleled initiative has been widely recognised at the international level, further strengthening the institute's and the country's reputation as a leader in public health and biomedical research. Furthermore, the LST confirmed Luxembourg's high level of resilience, adaptability and reactiveness to an unprecedented crisis of global dimensions, contributing to reinforcing national preparedness to future epidemics.

FNR COVID-19 Fast Track Call: 12 LIH projects shortlisted and funded

In April 2020, the Luxembourg National Research Fund (FNR) launched the novel COVID-19 Fast Track Call funding programme in the framework of the Research Luxembourg Task Force work packages. The COVID-19 Fast Track Call aims to (co-)support short-term research projects on COVID-19, to accelerate the understanding and treatment of the disease, as well as addressing the legal, socio-economic and infrastructural aspects associated with the pandemic. Following the first deadline of the call on April 14th, eight LIH projects from the Quantitative Biology Unit (QBU), the Department of Population Health (DoPH) and the Department of Infection and Immunity (DII) were shortlisted and funded, for total financial support amounting to almost EUR 416,000. These aim to investigate multiple aspects of the COVID-19 infection, from tissue damage, microbiome alterations and disease severity, to immunity, virus neutralisation and epidemiology.

They include:

1

› 'CovSerum' (Early Detection Of Covid19-induced Tissue Damage And (Hyper)Inflammation From Serum Samples), led by Prof Gunnar Dittmar of the LIH QBU;

2

› 'miRCOVID' (Microrna Biomarkers Of Covid-19 Severity), led by Dr Yvan Devaux of the Cardiovascular Research Unit of the LIH DoPH as part of the Predi-COVID study;

3

› 'Funbiome' (Functional Characterisation Of Covid-19 Patient Gut Microbiome), led by Prof Mahesh Desai of DII;

Dr Chantal Snoeck and her team at DII. From left to right: (first line) Sophie Mériaux, Emilie Charpentier, Aurélie Sausy, (second line) Gilles Iserentant, Chantal Snoeck, Manuel Counson

4 › ‘NEUTRACOV’ (A Novel High Throughput Assay To Measure Plasma Neutralizing Activity Against Sars-cov-2), led by Dr Danielle Perez Bercoff at DII. The project also received financial support from Luxembourg’s Rotary Clubs;

5 › ‘Colide’ (Role Of Companion And Livestock Animals In The Epidemiology Of Sars-cov-2), led by Dr Chantal Snoeck;

6 › ‘HorCoVIS’ study (Hormonal Status As Predictor Of Covid-19 Infection Severity), led by Dr Brice Appenzeller at DoPH

7 › ‘RAS CoV-2’ (Peptide/Protein/Single-cell Map Of The Renin-angiotensin System In Covid-19), led by Dr Antonio Cosma of LIH QBU;

8 › ‘COV-Immun’ (Development Of A High Performance Covid-19 Immunoassay, An Essential Tool To Establish Immunity Passports In The Luxembourgish Population), led by Dr Christiane Hilger of DII.

An additional 4 projects from the Department of Oncology (DONC), DII and QBU were selected for funding under the second call of the programme in May 2020, for total support amounting to over EUR 197,000. These will investigate multiple aspects of the COVID-19 infection, from serological profiling and PCR testing, to novel antiviral therapies and vaccines.

They include:

9 › ‘COMPARE’ (Comparing The Technical Performances Of Three Real-time Pcrs To Counteract The Covid-19 Outbreak In Luxembourg), led by Dr Carole Devaux of DII;

10 › ‘RD-Vac’ (Rapid Development and Initial Preclinical Evaluation of an Effective Candidate Vaccine against SARS-CoV-2), led by DII Director Prof Markus Ollert;

11 › ‘CIAO-COVID-19’ (Comparative Antiviral Efficacy Of Different Autophagy Inhibitors Against Covid-19), led by Dr Muhammad Zaeem Noman of the Tumour Microenvironment (TIME) group of the DONC;

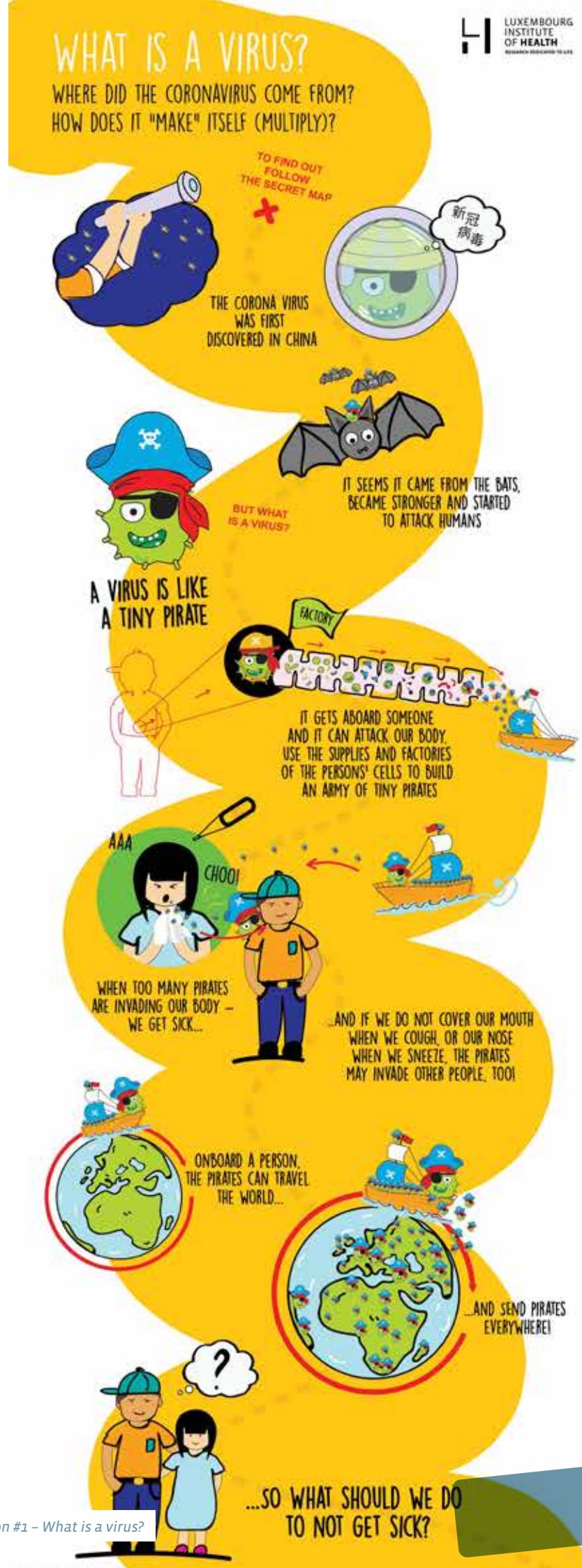
12 › “Coronavirus Antigen Array For Parallelized Serological Profiling”, led by Dr Joseph Longworth from QBU.

#LIHTellMeWhy: explaining COVID-19 to children!

In addition to supporting the communication efforts of the COVID-19 Taskforce tailored to scientific and adult audiences, the LIH Communication team implemented a communication campaign dedicated specifically to children. Launched in March 2020, #LIHTellMeWhy is an original collection of ten catchy digital cartoons providing simplified details on ongoing COVID-19 research and developments to kids between the ages of four and eight. This LIH initiative aims to support parents in explaining a very delicate situation to their little ones, ensuring they receive a level of information that is adjusted to their age and vision of the world. Indeed, aside from carrying out complex research in high-security labs, the LIH staff also seeks to inspire the younger generations and arouse their interest in biomedical sciences. This is in line with one of the missions of the Institute, namely finding approachable and understandable ways of communicating its activities to lay audiences, making complex topics more easily comprehensible and therefore raising awareness on Luxembourg's research efforts among the general public..

Each of the ten cartoons, published on a weekly basis between March and June 2020, addresses a specific question submitted by children or their parents in a fun, entertaining and accurate way. The questions covered by the ten cartoons include the definition of a virus, what steps can be taken to avoid getting sick and what the virus 'eats', among many others.

The cartoons are available on the dedicated section of the LIH website in four languages (English, French, German and Luxembourgish).


LUXEMBOURG INSTITUTE OF HEALTH
WHAT IS A VIRUS?
WHERE DID THE CORONAVIRUS COME FROM?
HOW DOES IT "MAKE" ITSELF (MULTIPLY)?
TO FIND OUT FOLLOW THE SECRET MAP
新冠病毒
THE CORONA VIRUS WAS FIRST DISCOVERED IN CHINA
IT SEEMS IT CAME FROM THE BATS, BECAME STRONGER AND STARTED TO ATTACK HUMANS
BUT WHAT IS A VIRUS?
A VIRUS IS LIKE A TINY PIRATE
FACTORY
IT GETS ABOARD SOMEONE AND IT CAN ATTACK OUR BODY. USE THE SUPPLIES AND FACTORIES OF THE PERSONS' CELLS TO BUILD AN ARMY OF TINY PIRATES
AAA
CHOO!
WHEN TOO MANY PIRATES ARE INVADING OUR BODY – WE GET SICK...
...AND IF WE DO NOT COVER OUR MOUTH WHEN WE COUGH, OR OUR NOSE WHEN WE SNEEZE, THE PIRATES MAY INVADE OTHER PEOPLE, TOO!
ONBOARD A PERSON, THE PIRATES CAN TRAVEL THE WORLD...
...AND SEND PIRATES EVERYWHERE!
?
...SO WHAT SHOULD WE DO TO NOT GET SICK?

‘Large Scale Communication’ for the Large Scale Testing: the #AAAH campaign

A nationwide initiative such as the Large Scale Testing (LST) – the success of which depends largely on the adhesion and buy-in of the population – requires a highly effective nationwide communication support, encouraging as many people as possible to get tested and overcoming any reticence and unwillingness to participate. To this end, as part of the first phase of the LST, LIH set up a comprehensive communication campaign, supported by external providers and the COVID-19 Taskforce, covering all key national and international media. The first stage of this communication campaign, implemented in parallel to the launch of the LST, consisted in the production and dissemination of flyers, animations on social networks and radio spots broadcast on all major national stations (L'Essentiel, RTL Radio and Eldoradio), to provide information and practical details on the LST.

#AAAH campaign shooting session

The second stage of the communication plan consisted in the so-called '#AAAH campaign', which ran between June 2020 and September 2020. The idea behind this original concept was to give additional visibility to the LST and raise awareness of its benefits, both for each individual as well as for society as a whole, in a friendly, relaxed, straight-to-the-point and visual way, particularly as the summer holidays approached. The #AAAH campaign, developed by LIH with the support of an external agency, entailed the shooting of a funny video consisting of a series of open mouths saying "AAAH", alternating with larger frames showing local celebrities all saying "AAAH". The celebrities then get tested to show how easy and quick the procedure is and how getting tested could contribute to a safer lockdown exit and a more relaxed summer. This multilingual campaign (in Luxembourgish, German, French, English and Portuguese) was disseminated locally and internationally to cross-border workers. It was also transmitted as a radio and TV spot on national and Greater Region radio stations and shared on multiple channels via an extensive media plan, including on social media, online (e.g. through bannering and Search Engine Marketing) and in print formats in the media and in public places (e.g. buses and bus stops).

View video /say #AAAH/

This second phase was then followed by the third and final stage of the communication campaign, which consisted in a more educational and informative animation aiming to act as a transition between the end of the first phase of the LST and the beginning of the second.

The #AAAH campaign was very well received by the public and reached its objective of raising awareness of the LST nationally and internationally. Indeed, between June 2020 and September 2020, the 121 posts, tweets, videos and ads published on social media to advertise the LST received 6.5 million impressions (views) and generated over 200,000 engagements (reactions, clicks, shares, comments). All in all, after the start of the campaign, over 10,000 test bookings per day were recorded in July 2020, helping keep the pandemic under control during the summer. As a result, Luxembourg was considered to be the global leader in mass screening in August 2020.

"On social media, the LST received 6.5 million impressions and generated over 200,000 engagements!"

International excellence

Advancing translational research beyond borders

The excellence and reputation of LIH and IBBL (Integrated Biobank of Luxembourg) as valuable partners for European-funded projects was further confirmed in 2020. Indeed, the two institutes joined the consortia of six highly competitive European studies, which kicked off in 2020. Moreover, several LIH scientists obtained financial support from a prestigious funding scheme of the European Commission for their innovative and high-potential research projects. These contracts and grants span a variety of priority areas for LIH and IBBL, including the use of digital technologies and Artificial Intelligence to improve cancer therapies, the advancement of translational research and, importantly, the improvement of COVID-19 diagnosis, treatment and pandemic preparedness. Participation in these projects consolidates LIH and IBBL collaborations with leading international partners and further contributes to strengthening the visibility of the institutes, and of Luxembourg's biomedical research ecosystem in general, as an international centre of excellence in translational and transversal medicine.

// REVERT: artificial intelligence to fight colorectal cancer

Through its biobank IBBL, LIH joined the consortium of REVERT (TaRgeted thErapy for adVanced colorEctal canceR paTients). This four-year project, coordinated by the San Raffaele Scientific Institute for Research and Healthcare, is a collaboration between 14 partners from six European countries and is funded under the European Commission's Horizon 2020 programme. REVERT, which kicked off in January 2020, aims to leverage artificial intelligence (AI) to identify a predictive algorithm to be used in the treatment of patients with advanced colorectal cancer (CRC). Over 400,000 people are diagnosed annually with CRC in Europe, and almost half end up developing distant metastases. Despite the ability of drugs such as bevacizumab, cetuximab and panitumumab to significantly improve median survival in patients with unresectable metastatic CRC, their efficacy depends on a patient's clinical characteristics and disease biology. Moreover, side effects and considerable costs constitute additional downsides. In this context, REVERT aims to understand the specific pathophysiology of metastatic CRC (mCRC) in patients responding well or poorly to therapies, in order to design an optimal strategy for the treatment of mCRC on a case by case basis, with therapeutic interventions tailored to patient's particular features. Specifically, the consortium seeks to create an innovative decision support algorithm based on AI techniques and real-world data generated by several European hospitals, which will ultimately be able to identify the most appropriate and cost-effective therapeutic intervention for patients with unresectable mCRC. As part of this collaborative translational study, IBBL will contribute to developing new Standard Operating Procedures for pre-analytical and analytical validation protocols to measure classic and novel biomarkers, leveraging the long-standing expertise in biomarker validation of Dr Monica Marchese, Translational Biomarker Group Leader at IBBL, and her team.

Dr Monica Marchese, Translational Biomarker Group Leader at IBBL and coordinator of REVERT

// EATRIS-Plus: supporting translational medicine through capacity building

Personalised medicine relies on the identification of reliable biomarkers to evaluate the likelihood of developing a disease, diagnose a disorder, assess its severity and progression, and determine the most accurate treatment strategies. However, the road to biomarker validation before their effective application in the clinical context is complex. To assist scientists in the challenging phase of translating research results into tangible medical applications, the European Infrastructure for Translational Medicine (EATRIS) was set up in 2014. As a research infrastructure, EATRIS provides access to laboratory, clinical, industrial, legal and regulatory expertise, technology and services to academia, industry and patient associations, in order to help researchers decrease the risk associated to the early stages of drug or biomarker development. Building on the success of the EATRIS initiative, the EATRIS-Plus project, which kicked off in January 2020, aims to further expand the infrastructure's service offering, expertise, technologies and capacity so as to keep addressing research needs in personalised and translational medicine. Specifically, over its 4-year duration, EATRIS-Plus seeks to consolidate EATRIS capacities to better serve academia and industry; further strengthen the long-term sustainability of the EATRIS financial model; drive patient empowerment through active involvement in the infrastructure's operations; and expand strategic partnerships with RIs and other relevant stakeholders. As part of the project's consortium and under the coordination of IBBL project manager Sabrina Saracino, IBBL will be leading a specific task focused on the implementation of an inter-laboratory performance assessment for biospecimen processing, owing to its renowned expertise in the development of proficiency testing (PT) schemes. This aims to ensure that samples are fit for the purpose of downstream "omics" analyses and will allow the comparison of processing performance between laboratories. EATRIS-Plus boasts a highly interdisciplinary consortium of 19 partners from academia, industry and patient organisations from 16 European countries. It is funded through the Horizon 2020 programme of the European Commission.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 871096

// “Marie Sklodowska-Curie Individual Fellowships” for LIH researchers

Drs Amela Jusic, from the LIH Department of Population Health (DoPH), Marie Boudaud and Tomasz Uchanski, from the LIH Department of Infection and Immunity (DII), were awarded financial support in the framework of the European Commission’s “Marie Sklodowska-Curie Individual Fellowships” (MSCA IF) funding scheme in February 2020. The programme will back the scientists’ work on hypertension, receptor-chemokine interactions and Inflammatory Bowel Diseases (IBD). Specifically, Amela Jusic, postdoctoral fellow in the DoPH Cardiovascular Research Unit led by Dr Yvan Devaux, will investigate the function and biomarker potential of mitochondrial microRNAs in hypertension under the “MITO” project, with the goal of discovering novel methods to improve health outcomes in hypertension patients. The MSCA IF will also support Tomasz Uchanski, postdoctoral fellow in the DII Immuno-Pharmacology and Interactomics Research Group under the supervision of Dr Andy Chevigne, in advancing the structural and functional analysis of chemokines through his project “Novel tools for structural insight into receptor-chemokine complexes”. Finally, Marie Boudaud, postdoctoral fellow working in the DII Eco-Immunology and Microbiome Research Group under the supervision of Dr Mahesh Desai, was awarded the MSCA IF for her project “Mucobiome-mediated immune pathways in Inflammatory Bowel Diseases” (MUCO-IMMUN). Under this study, she will investigate the mechanisms by which the mucobiome – i.e. the microbial communities living in the human gastrointestinal tract that can digest the intestinal mucus layer – activates specific disease-promoting immune pathways under low dietary fibre conditions, a factor which is believed to play an important role in IBD pathogenesis.

Dr Amela Jusic, Postdoctoral Fellow,
Cardiovascular Research Unit,
Department of Population Health (DoPH)

Dr Tomasz Uchanski, Postdoctoral Fellow,
Immuno-Pharmacology and Interactomics Research Group,
Department of Infection and Immunity (DII)

Dr Marie Boudaud, Postdoctoral Fellow,
Eco-Immunology and Microbiome Research Group ,
Department of Infection and Immunity (DII)

Dr Kristin Kornerup,
MIRABANK Project Manager at IBBL

// MIRABANK: a bank of multi-resistant bacterial strains in Luxembourg

In July 2020, the Laboratoire national de santé (LNS) and IBBL launched MIRABANK, a joint project on behalf of the European Centre for Disease Prevention and Control (ECDC) based on the creation of a bank of multi-resistant bacterial strains in Luxembourg. Under the coordination and responsibility of IBBL Project Manager Dr Kristin Kornerup, the biobank will collect bacterial strains – which are a new type of sample for the institute – resistant to carbapenems and/or colistin antibiotics, as well as temporarily storing them prior to analysis. The LNS, for its part, will be responsible for confirming the identification of the strains. Specifically, IBBL will receive some 4,000 strains from 37 European countries, which will be forwarded to the Bacteriology, Mycology, Antibiotic Resistance and Hospital Hygiene Unit of the LNS Microbiology Department, before returning to IBBL for freezing, storage and shipment to a genomic analysis laboratory. The first strains integrated into MIRABANK in July 2020 were the strains from Luxembourg, collected owing to the participation of the country's four hospitals. The project will significantly contribute to the fight against resistance to antibiotics of last resort, a phenomenon that has particularly increased in Europe in recent years.

// 'ERAvsCORONA Action Plan': three LIH COVID-19 projects funded

The European Commission confirmed its support to three new research projects involving LIH, submitted within the framework of the Horizon 2020 call "Innovative and rapid health-related approaches to respond to COVID-19 and to deliver quick results for society for a higher level of preparedness of health systems" as part of the Horizon 2020 ERAvsCORONA Action Plan. The total funding for the three studies amounts to EUR 26.2 million.

Specifically, LIH, through the Cardiovascular Research Unit (CVRU) of its Department of Population Health (DoPH), will be coordinating "COVIRNA" (A diagnostic test to improve surveillance and care of COVID-19 patients). Led by Dr Yvan Devaux, CVRU Group Leader, COVIRNA is a 24-month patient-centred Innovation Action (IA) aiming to generate a diagnostic tool to identify COVID-19 patients at risk of developing fatal cardiovascular complications, ultimately leading to their improved surveillance and care. The project, which boasts a complementary consortium of 15 partners from healthcare, academia and industry from 12 European countries, officially started in November 2020.

Dr Yvan Devaux, Cardiovascular Research Unit (CVRU) Group Leader and coordinator of "COVIRNA"

In addition, the LIH Competence Centre for Methodology and Statistics (CCMS), led by Dr Michel Vaillant, together with the Digital Epidemiology and E-health unit, led by Dr Guy Fagherazzi, will contribute with the Predi-COVID study data to "unCoVer" (Unravelling Data for Rapid Evidence-Based Response to COVID-19), a functional network of research institutions collecting data derived from the care provided to COVID-19 patients by European and international healthcare services. These real-world data will enable the study of patient characteristics, risk factors, safety and effectiveness of treatments and potential strategies against COVID-19 in real clinical settings. The 24-month project, which counts 29 partners from 18 nations, officially started in November 2020.

Dr Guy Fagherazzi, Group Leader of the Deep Digital Phenotyping Research Unit and "unCoVer" contributor

Finally, the LIH Transversal Translational Medicine team, led by Prof Rejko Krüger, and CCMS will contribute to "ORCHESTRA" (Connecting European Cohorts to Increase Common and Effective Response to SARS-CoV-2 Pandemic). This 36-month project – which integrates ongoing efforts of the CON-VINCE study and of the National Centre of Excellence in Research on Parkinson's disease (NCER-PD) – aims to provide an innovative approach to learning from the COVID-19 health crisis and deriving recommendations for increasing preparedness for future outbreaks. The main outcome of the project is the creation of a new pan-European cohort built on existing and new large-scale population and susceptible people cohorts in European and non-European countries. ORCHESTRA, which started in December 2020, involves 26 partners from 15 countries.

Dr Michel Vaillant, Head of the LIH Competence Centre for Methodology and Statistics (CCMS) and "unCoVer" contributor

Prof Rejko Krüger, Director of Transversal Translational Medicine (TTM) at LIH and "ORCHESTRA" contributor

Translational research excellence

Taking LIH findings “from the bench to the bed”

LIH aims to perform research that transcends the classical boundaries of individual diseases and that can be tangibly applied in the clinical practice to improve health outcomes for patients and society as a whole. In the context of this translational and transversal research strategy, LIH researchers published their high-impact findings in a variety of prestigious international journals throughout 2020, spanning the institute’s key priority areas. These publications will contribute to advancing the understanding and treatment of cancer, autoimmune diseases and neurodegenerative disorders, as well as offering new perspectives on public health and preventive medicine, thereby being concrete instances of translational “bed-to-bench-to-bed” research.

Fighting Autoimmunity and Cancer: The Nutritional Key

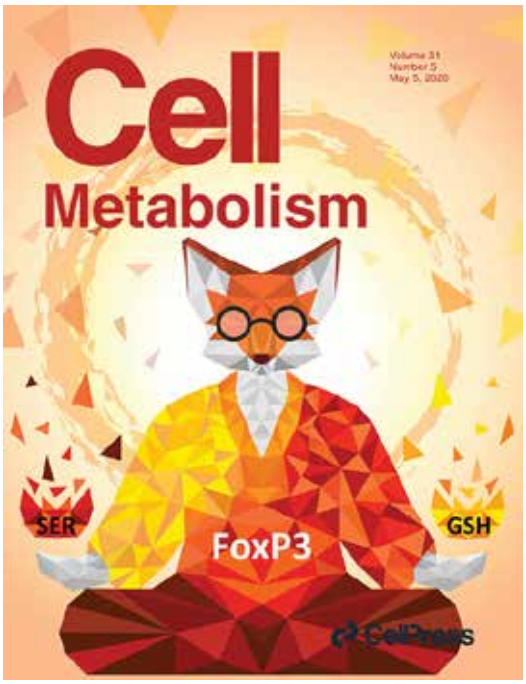
Prof Dirk Brenner (left) and Henry Kurniawan (right)

Prof Dirk Brenner, Head of the Experimental & Molecular Immunology research group of the Department of Infection and Immunity (DII), and postdoctoral fellow Henry Kurniawan revealed a novel mechanism through which the immune system can control autoimmunity and cancer.

The immune system ensures a healthy body function, providing protection from a variety of diseases. Regulatory T cells are particularly important in this context. These are a specific type of white blood cells that can "slow down" the human immune response, thus keeping it in check. When regulatory T cells are impaired, the immune system turns against its own body. This can lead to harmful autoimmune diseases such as multiple sclerosis, type I diabetes or arthritis. The LIH group has identified a key metabolite named glutathione that controls the function of regulatory T cells. Regulatory T cells lacking glutathione lose their ability to act as a brake on the immune system, leading to massive immune activation and a fatal autoimmune reaction. These dysfunctional regulatory T cells showed a significantly altered metabolism and the scientists uncovered a novel mechanism that controls the balance between an extreme or subdued immune response. Specifically, these regulatory T cells consumed and synthesised more of the amino acid serine, a building block of proteins. On the basis of these findings, a tailored diet was established, lacking serine and the closely related glycine. Astonishingly, this treatment worked against the lethal autoimmune reaction and restored the function of these regulatory T cells as a 'brake of the immune system'. However, a strong immune system can kill cancer cells very efficiently. Consequently, the researchers used the same mechanism to increase anti-tumor immunity, thereby limiting the spread of cancer. This means that if the cause of a disease is known, one can respond to it accordingly, for example through a diet tailored to the disease mechanism.

The Brenner lab's groundbreaking results show that minimal interference – in this case the absence of two amino acids in a complex diet – can suppress a severe autoimmune disease. Therefore, the group laid the groundwork for a mechanism-driven personalised treatment strategy for metabolic disorders, autoimmunity and cancer.

These findings were published in May 2020 in the leading international journal 'Cell Metabolism'. Due to its significance, the publication was also selected by Cell Metabolism to be featured as the cover story of its May 2020 issue and included in the 'Landmark Reviews & Articles: Immunometabolism' collection of the journal.



The publication was featured on the 'Cell Metabolism' May 2020 cover

SCAN ME

View animation /The Nutritional Key/

Renewed hope for treatment of pain and depression

From left to right: Dr Andy Chevigné, Dr Martyna Szpakowska and Max Meyrath

Dr Andy Chevigné, Dr Martyna Szpakowska and Max Meyrath from the Immuno-Pharmacology and Interactomics research group of the LIH Department of Infection and Immunity developed 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. Opioid-related disorders such as severe pain are currently predominantly treated through opioid prescription drugs that act on the opioid system by targeting and activating opioid receptors. Despite their effectiveness, these painkillers are associated with several side-effects, such as tolerance, dependence and respiratory disorders. New means to modulate the opioid system through novel drugs are therefore needed to tackle the growing abuse of and addiction to synthetic opioids.

The novel molecule LIH383 binds and blocks the atypical chemokine receptor ACKR3, which the LIH researchers had previously shown to be a new opioid receptor with negative regulatory properties. Specifically, the scientists demonstrated that ACKR3 possesses a high affinity for a variety of naturally secreted opioids. However, the interaction between ACKR3 and these opioids does not generate the typical painkilling 'messages' that arise when opioids bind to the so-called 'classical' opioid receptors. On the contrary, ACKR3 acts as an opioid scavenger, 'trapping' them and reducing the levels that can bind to traditional receptors, thereby dampening their analgesic and antianxiety activity. By targeting and blocking ACKR3, LIH383 has the overall effect of increasing the availability of opioid peptides that bind to classical opioid receptors in the brain, thereby potentiating their natural beneficial effects on pain and negative emotions. Following a successful proof of concept of the efficacy of LIH383 in modulating ACKR3 activity, the team filed a patent application in April 2020.

These results open up alternative options for the treatment of chronic pain, stress, anxiety and depression, but also for cancer therapy. Indeed, ACKR3 also binds to chemokines — small proteins secreted by immune cells which mediate immune responses but which have also been shown to be involved in tumour initiation and metastasis. Specifically, ACKR3 is expressed abundantly in tumours such as glioblastoma and breast cancer, and its presence correlates with increased tumour growth, metastasis, resistance to chemotherapy and poor prognosis. As an ACKR3 modulator, LIH383 therefore also holds promise for the treatment of metastatic cancers, leveraging on the team's remarkable discovery of the dual chemokine-opioid 'scavenging' activity of this receptor.

The study, which was published in June 2020 in the prestigious international journal 'Nature Communications', was supported by the Luxembourg National Research Fund, the Ministry of Higher Education and Research, as well as the charitable initiative 'Télévie'. Due to its significance, the publication was selected by Nature Communications to be featured in the 'Structural biology, biochemistry and biophysics' section of the journal's Editors' Highlights webpage.

Innovative machine-learning approach for future diagnostic advances in Parkinson's disease

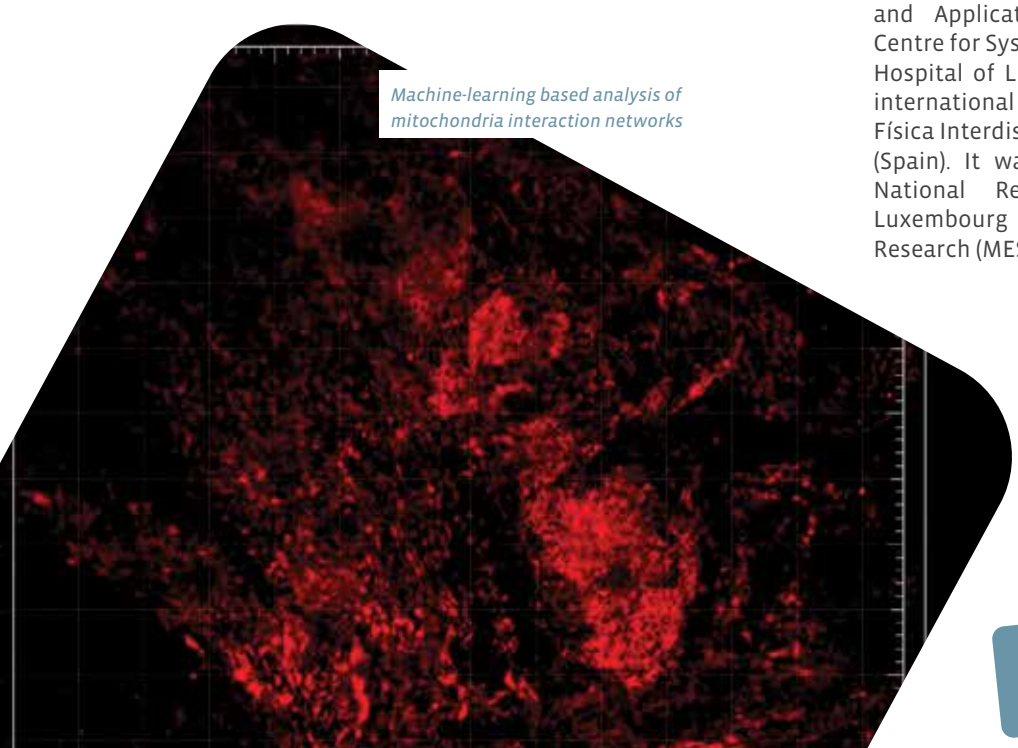
Parkinson's disease (PD) is the second most common neurodegenerative disease, although the detailed molecular and cellular mechanisms underlying its pathogenesis remains unclear. Recent evidence has pointed towards the role of mitochondrial dysfunction in the onset of the disease. Mitochondria — small cellular 'subunits' involved in cell metabolism and energy generation — constantly and dynamically interact with each other, forming perpetually changing networks known as mitochondria interaction networks (MINs). Since conventional research focusing on individual mitochondria has not provided satisfying insights into PD pathogenesis, Dr Feng He, Group Leader of the Immune Systems Biology research group of the LIH Department of Infection and Immunity, Prof Rejko Krüger, Director of Transversal Translational Medicine at LIH, and their teams investigated the interaction networks between these organelles, in order to understand the correlation between the mitochondrial impairments observed in PD and any specific network topological changes in MINs, ultimately aiming to advance the early diagnosis and classification of PD patients.

Leveraging their strong expertise in network analysis and machine learning, the scientists analysed a large 700 Gigabyte dataset of three-dimensional (3D) mitochondrial images of colonic neurons, collected from PD patients and healthy controls, and dopaminergic neurons derived from stem cells. They found that particular network structure features within MINs were altered in PD patients compared to controls, possibly meaning that energy and information are produced, shared and distributed less competently in the neuronal mitochondria of PD patients relative to healthy controls, suggesting their connection to mitochondrial damage, deficiencies and fragmentation typical of neurodegenerative disorders.

Moreover, the research teams found these different MIN patterns to be highly correlated with the commonly-used PD clinical scores of individual patients. Indeed, through an advanced machine learning approach, the researchers observed that the use of a combination of those network features alone allowed them to accurately distinguish between PD patients and healthy controls.

The findings therefore bring forward the potential of using neuronal mitochondrial networks and their features as novel biomarkers for the early diagnosis and classification of PD patients, thereby providing new insights into the pathogenesis, diagnosis and treatment of this neurodegenerative disorder. The results may also offer new perspectives for the understanding of various other neurodegenerative diseases characterised by mitochondrial dysregulation, such as Huntington disease and Alzheimer's, making this work a true instance of translational and transversal research.

The interdisciplinary study, which was published in November 2020 in the prestigious international journal Nature Partner Journals Systems Biology and Applications, involved the Luxembourg Centre for Systems Biology (LCSB) and the Central Hospital of Luxembourg (CHL), as well as other international partners such as the Instituto de Física Interdisciplinar y Sistemas Complejos IFISC (Spain). It was supported by the Luxembourg National Research Fund (FNR) and the Luxembourg Ministry of Higher Education and Research (MESR), among others.



Machine-learning based analysis of mitochondria interaction networks

Improving cancer immunotherapy by turning “cold” tumours “hot”

Dr Bassam Janji, Group Leader, Tumor Immunotherapy and Microenvironment

Immune checkpoint inhibitors (ICI), exemplified by anti-PD-1, are immunotherapeutic drugs that act by removing the “brakes” on the immune system and unleashing an immune attack on cancer cells. Though very promising for the treatment of many cancers, only relatively few cancer patients show significant therapeutic benefits when treated with ICI alone. One of the major causes of tumour unresponsiveness to ICI is the poor infiltration of cytotoxic immune cells into the tumour bed.

In this context, Dr Bassam Janji, leader of the Tumor Immunotherapy and Microenvironment (TIME) research group of the LIH Department of Oncology (DONC), and his team, together with the Swedish pharma company Sprint Bioscience, devised an innovative strategy that turns “cold”, immune-desert immunotherapy-resistant tumours into “hot” inflamed tumours, infiltrated by the immune system and responsive to immunotherapy. At the epicentre of this strategy lies a novel molecule developed by Sprint Bioscience, SB02024, which was shown to successfully inhibit autophagy, a process of “self-digestion” that allows cancer cells to acquire nutrients to sustain their growth.

Specifically, SB02024 acts against Vps34, a key protein for autophagy. The researchers used preclinical mouse models to evaluate the effects of genetically and pharmacologically targeting Vps34 on tumour growth and mice survival. Interestingly, they found that inhibition of autophagy led to an increase in the release of CCL5 and CXCL10, two pro-inflammatory cytokines involved in the recruitment of cytotoxic immune cells such as Natural Killers (NK), macrophages and T-cells into the tumour microenvironment. Such infiltration resulted in reduced tumour growth and prolonged survival in both melanoma and colorectal tumour-bearing mice. These findings highlighted Vps34 inhibitors as valuable drugs making tumours eligible or responsive to immunotherapy based on ICI. Furthermore, Dr Janji’s team showed that combining the Vps34 inhibitor SB02024 with anti-PD-1 significantly improves the efficacy of this ICI in resistant melanoma and colorectal cancer.

Based on their preclinical results, the scientists also established a “Vps34 response signature” to stratify 470 melanoma patients into three groups, exhibiting a high, intermediate, and low expression level of Vps34. These three groups correspond to patients displaying “hot”, “intermediate” and “cold tumours”, respectively. The team showed that the overall and disease-free survival of patients displaying a high “Vps34 response signature” (“hot tumour”) is significantly better compared to those bearing a low “Vps34 response signature” (“cold tumour”).

The study, co-authored by Dr Janji and Dr Guy Berchem, was published in April 2020 in the prestigious journal Science Advances. It was carried out in collaboration with Sprint Bioscience (Sweden), the Centre Hospitalier de Luxembourg (CHL), the Karolinska Institute (Sweden) and the University of Pennsylvania (USA), and supported by grants from the Luxembourg National Research Fund, FNRS Televie, Fondation Cancer, Foundatioun Kriibskrank Kanner, Janssen Cilag Pharma, Action LIONS Vaincre le Cancer Luxembourg and the Swedish Foundation for Strategic Research.

New insights into Glioblastoma invasiveness

One of the hallmarks of Glioblastoma (GBM), the most aggressive type of brain cancer, is its high invasive capacity, which leads to its expansion into the normal brain tissue and migration to more distant locations, giving rise to metastases. 'Stray' cancer cells can therefore escape surgical resection, radio- and chemotherapy, thereby accounting for the limited success of current treatment approaches and for the poor patient prognosis observed. Novel molecular targets that regulate invasion and that can be leveraged during drug development are therefore a priority in modern-day oncology.

In this context, Prof Simone Niclou, Director of the LIH Department of Oncology, together with Dr Anne Schuster and Eliane Klein from the NORLUX Neuro-Oncology Laboratory, sought to elucidate the genes responsible for GBM invasiveness and the specific molecules that 'switch' them on. The team progressively silenced and deactivated the entire set of genes of highly invasive patient-derived GBM cells and observed the consequences on the cell's ability to invade healthy tissues. They found a set of 17 invasion-essential candidate genes, including Colony stimulating factor 1 (CSF1), a small protein known to be involved in invasion and metastasis. This selection was further narrowed down by analysing their expression in non-invasive (NI), low-invasive (LI) and highly invasive (HI) GBM cells, both in vitro and when implanted into mouse brains in vivo. The gene coding for the AN1-Type Zinc Finger protein 3 (ZFAND3) showed a significantly higher expression in HI cells compared to NI and LI, both in vitro and in vivo, with the amounts of ZFAND3 protein produced being consequently greater in HI cells located in the periphery of the tumours. Indeed, deactivating the ZFAND3 gene in highly invasive GBM cells impaired the colonisation of healthy tissue, while overexpressing it in non-invasive GBM cells in mice resulted in the loss of the tumour's circumscribed growth pattern and increased invasiveness.

The team also noted that ZFAND3 was predominantly localised in the nucleus of invasive cells and that this feature was necessary to maintain their invasiveness, suggesting that ZFAND3 may act directly in the nucleus to regulate the activation of specific genes invasion-related genes associated with cell adhesion and migration. Moreover, the researchers saw that the ZFAND3 protein binds to the promoter of these genes and interacts with several nuclear proteins, including PUF60, Pontin and Treacle. The authors therefore propose that ZFAND3 forms a protein complex that activates gene transcription, giving rise to the penetrative behaviour that characterises highly invasive GBM cells.

The findings bring forward ZFAND3 as a novel key regulator involved in the malignancy of GBM and provide a new molecular mechanism against which future drugs may be directed. The study, published in December 2020 in the renowned journal Nature Communications, was supported by grants from the Fondation Cancer Luxembourg, Télévie-FNRS and the Luxembourg National Research Fund.

The NORLUX Neuro-Oncology Laboratory team at the LIH Department of Oncology

Advancing personalised cancer treatment through tumour organoids and patient “avatars”

From left to right: Dr Anna Golebiewska, Anaïs Oudin, Dr Ann-Christin Hau and Prof Simone Niclou from the NORLUX Neuro-Oncology Laboratory at the LIH Department of Oncology

The success of clinical trials is significantly dependent on the quality of the results obtained during preclinical drug testing studies on experimental models of a patient’s tumour, prior to the clinical phase. The availability of accurate and comprehensive models in the preclinical setting that reflect the full range of genetic variations observed in brain cancers and that are able to reliably predict the sensitivity of specific types of tumours to new personalised treatments is therefore of utmost importance for translational oncology.

To address this currently unmet need, Prof Simone Niclou, Dr Anna Golebiewska, Dr Ann-Christin Hau and Anaïs Oudin from the NORLUX Neuro-Oncology Laboratory at the LIH Department of Oncology (DONC) have been working in close cooperation with the Centre Hospitalier de Luxembourg (CHL), the Laboratoire National de Santé (LNS), the Luxembourg Centre for Systems Biomedicine (LCSB) and other international partners to establish a collection of brain tumours from over 1,000 patients. Through the samples provided by the Neurosurgery department of the CHL, NORLUX has been generating a biobank of brain tumour organoids – three-dimensional tissue cultures derived from viable cells from patient tumours. Organoids offer innovative possibilities for cancer modeling, being amenable to a large variety of pre-clinical applications including proliferation and invasion assays, drug screening and the generation of so-called patient-derived orthotopic xenografts (PDOX) for validation of biological responses in vivo. Indeed, tumor organoids can be implanted in immunodeficient mice to give rise to PDOX models, which act as clinically relevant patient “avatars”, faithfully reproducing the main biological, histological and genomic features of the original patient tumors. NORLUX currently established a comprehensive cohort of over 130 organoids and 40 PDOXs from primary and recurrent malignant gliomas including glioblastoma, one of the deadliest forms of brain cancer, at different stages, from different subtypes and carrying different genetic mutations. Unique PDOXs derived from tumour samples of the same patient prior to and after treatment are also available, improving the understanding of how specific cancers respond to various treatments, according to their genetic characteristics. The findings were published in October 2020 in the international journal Acta Neuropathologica.

Brain cancer organoids and the resulting mouse avatars have a unique value as a drug screening platform in both preclinical and co-clinical studies. They can be leveraged in the context of precision oncology, such as in the ongoing clinical trial for Personalised Functional Profiling (PFP), led by LIH in collaboration with CHL, Hopitaux Robert Schuman (HRS), IBBL and LNS, as well as in research studies in partnership with pharmaceutical companies. Indeed, the LIH researchers tested the efficacy of VAL-083, a compound from DelMar Pharmaceuticals, in their organoids and PDOXs, showing its potential as a promising candidate for glioblastoma.

The collection of 40 PDOX glioma models and associated data are available to the international scientific community on PDXfinder, an open global catalogue co-developed by the European Molecular Biology Laboratory - European Bioinformatics Institute (EMBL - EBI) and the Jackson Laboratory.

Parkinson's disease and the gut microbiome

Parkinson's disease (PD) is a complex disease, shaped by both genetic and environmental factors. While the role of the former in the pathogenesis of the disease has been widely accepted, the contribution of various environmental and lifestyle factors remains largely unclear. For instance, constipation is one of the earliest symptoms of the disease, with recent studies reporting an altered gut microbiome composition in PD patients compared to age-matched controls.

Prof Rejko Krüger, Director of Transversal Translational Medicine at LIH, and the Integrated Biobank of Luxembourg (IBBL) collaborated with a team of researchers from the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg within the National Centre for Excellence in Research on Parkinson's disease (NCER-PD) to study the changes in microbial composition associated with PD, as well as the potential influencing factors, in order to better understand the functional metabolic consequences of gut microbiome variations. Specifically, the team aimed to characterise the faecal microbial composition and abundance in stool samples collected from PD patients and healthy controls from the Parkinson's study funded by the Luxembourg National Research Fund (FNR). These data were subsequently used to develop personalised computational models simulating the metabolism of each individual's microbial community, allowing the scientists to predict the potential secretion of numerous bacterial metabolites. The resulting information was then statistically analysed to identify microbial and metabolic differences between PD patients and controls.

The researchers found that seven microbial species and eight genera changed significantly in their relative abundances between PD patients and healthy controls. Specifically, Akkermansia muciniphila was the most significantly altered species, being more abundant in PD patients than in controls. At the genus level, Prevotellaceae were shown to decrease significantly compared to healthy controls, a phenomenon that was also observed in other PD populations worldwide. Moreover, the team found that microbiome changes in PD patients are dependent on gender, age, body-mass index (BMI) and constipation, reflecting the systemic and complex nature of PD. From a metabolic perspective, the scientists observed that the predicted production of nine metabolites was different in PD cases compared to controls, with the predicted production of some metabolites being also dependent on additional factors, such as constipation. The study therefore suggests that the altered microbial composition observed in PD individuals could result in significant functional changes in microbial metabolism, particularly when looking at non-motor symptoms such as constipation, thereby providing a novel hypothesis to explain PD pathogenesis.

The study, published in June 2020 in the international journal BMC Biology, is an international collaboration between the LCSB, LIH, IBBL, the National University of Ireland, Galway, the University Medicine Greifswald (Germany), the Parkinson Research Clinic at the Centre Hospitalier de Luxembourg (CHL) and APC Microbiome (Ireland). It was funded by grants from the European Research Council (ERC) under the European Union's Horizon 2020 programme and by the Luxembourg National Research Fund (FNR).

Cholesterol levels dropping in Western nations but rising in Asia

Dr Ala'a Alkerwi, LIH Department of Population Health

High blood cholesterol has typically been regarded as a feature of wealthy western countries. However, dietary and behavioural determinants of blood cholesterol, as well as the adoption of medications such as statins, have been evolving throughout the world in the last decades. These changes have significantly altered the levels of HDL and non-HDL cholesterol worldwide, possibly with diverging geographical patterns. However, no global study had previously reported or quantified the trends in HDL and non-HDL cholesterol levels over time.

In this context, a global public health study led by Imperial College London in the framework of the international Non-Communicable Diseases Risk Factor Collaboration (NCD-RisC) was conducted to address this gap. Dr Ala'a Alkerwi from the LIH Department of Population Health (DoPH) contributed to this international effort with data generated from the national population-based study "ORISCAV-LUX", which had been carried out in 2007-2008 on more than 1,400 residents to assess cardiovascular health and risk factors in Luxembourg.

The researchers analysed 1,127 population-based studies that measured blood lipids in 102.6 million adults, in order to estimate trends in total, non-HDL and HDL cholesterol levels for 200 countries from 1980 to 2018. The study found that, at the regional level, total cholesterol decreased significantly in high-income western countries and in Central and Eastern Europe, where it had been the highest in 1980, largely due to a decline in non-HDL cholesterol. This can be explained by changes in dietary habits, such as the reduction in saturated and trans fats, coupled with the growing use of statins. Conversely, total cholesterol rose considerably in East and Southeast Asia due to an increase in non-HDL cholesterol, linked to the growing consumption of animal fats and processed foods. In parallel, the number of deaths attributable to high non-HDL cholesterol more than tripled in East Asia and more than doubled in Southeast Asia. As a result, these regions accounted for half of all deaths attributable to high non-HDL cholesterol by 2017, compared with a quarter in 1990.

These diverging patterns mean that European countries that had the highest levels of non-HDL cholesterol in 1980, such as Belgium, Finland, Greenland, Iceland, Norway, Sweden, Switzerland and Malta, have been replaced by nations in Asia and the Pacific, such as Tokelau, Malaysia, the Philippines and Thailand, where non-HDL cholesterol increased by as much as 0.23 mmol l−1 per decade. These findings reverse the view that high cholesterol is a feature of higher-income countries, indicating instead that low- and middle-income countries have emerged as the new global epicentre of non-optimal cholesterol.

The study was published in June 2020 in the prestigious journal Nature and was funded by the Wellcome Trust and by the British Heart Foundation.

Fruit and vegetable intake prevents risk of type 2 diabetes

Type 2 diabetes (T2D) has become a major public health crisis over the last decades, with its prevention being a key priority globally. Diet, and particularly high fruit and vegetable intake, has been suggested to play an important role in the prevention of this metabolic disorder. Nevertheless, the lack of reliable evidence on their association remains a challenge. Previous studies suggested vitamin C and carotenoids circulating in the bloodstream as reliable biomarkers of fruit and vegetable intake. Investigating the association between these biomarkers and type 2 diabetes could therefore provide a clearer picture of the link between fruit and vegetable intake and T2D.

To address this question, Dr Guy Fagherazzi, Director of the LIH Department of Population Health (DoPH), contributed to an international cohort study led by the University of Cambridge School of Clinical Medicine, aiming to investigate the link between plasma vitamin C and carotenoids with the risk of developing T2D. Specifically, the team observed the baseline levels of circulating vitamin C and six different carotenoids from 9,754 patients with incident T2D and from a subset of 13,662 individuals from the European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct cohort study. The researchers found that the average concentration of plasma vitamin C and total carotenoids was significantly lower in individuals who went on to develop T2D compared to healthy controls. Moreover, dietary intake of different types and forms of fruits and vegetables was all positively associated with both plasma vitamin C and total carotenoid concentration, confirming the value of these elements as biomarkers of fruit and vegetable consumption.

When looking at the risk of developing T2D, the team found that higher levels of plasma vitamin C and carotenoids were associated with a lower hazard of the disease. Specifically, the group observed a 25% reduction in T2D risk for every 66 g/day increase in total fruit and vegetable consumption. The study therefore suggests that even a minor increase in fruit and vegetable intake in the diet could contribute to decreasing the risk of T2D, regardless of whether the increase is among people with initially low or high intake. The seven biomarkers can also help study more precisely the impact of the distinct concentrations of specific fruit and vegetable types on T2D onset.

The study was published in July 2020 in the British Medical Journal.

Dr Guy Fagherazzi, Director of the LIH Department of Population Health (DoPH), Group Leader of the Deep Digital Phenotyping Research Unit and "unCoVer" contributor

Special recognition

LIH scientists rewarded for their outstanding research

The year 2020 brought several LIH scientists under the national and international spotlight through the award of a number of prestigious accolades and prizes. These are a recognition of the excellent patient-centric research carried out by the institute in the field of pharmacology, immunity, population health and oncology.

Dr Martyna Szpakowska and Dr Andy Chevigné

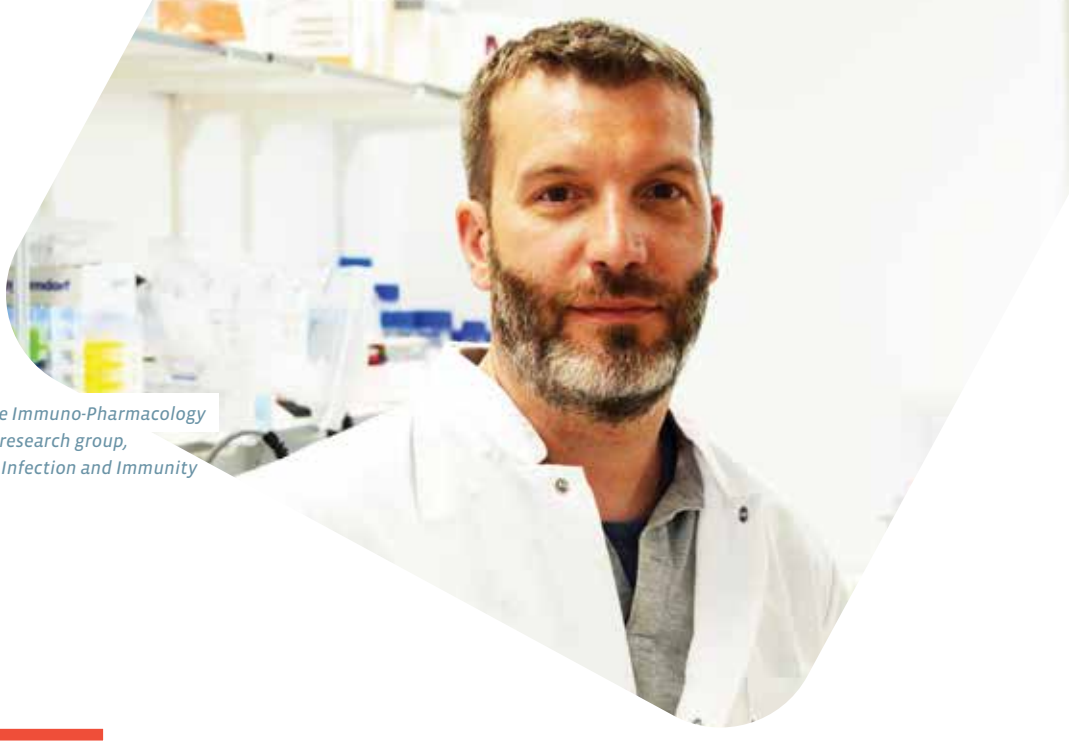
2019 Galien Prize in Pharmacology for DII researchers

Dr Andy Chevigné and Dr Martyna Szpakowska of the Immuno-Pharmacology and Interactomics group of the LIH Department of Infection and Immunity (DII) were awarded the prestigious international prize during a virtual ceremony in December 2020, in the presence of Frank Vandenbroucke, Belgian Minister of Public Health and Social Affairs, and of representatives of pharmaceutical companies and healthcare hubs. The Galien Prize, traditionally organised in Belgium and Luxembourg by Roularta HealthCare on a yearly basis, crowns the most significant discoveries in the fields of pharmacology, drug development and medical devices. The 2019 Galien Prize in Pharmacology rewards the two LIH researchers' outstanding achievements in advancing the understanding of the relevance, role, function and pharmacology of atypical chemokine receptors (ACKRs) and their ligands. Specifically, the award is a recognition of Dr Chevigné's and Dr Szpakowska's efforts over the last eight years to establish the first molecular pharmacology academic laboratory in Luxembourg – the 'Immuno-Pharmacology and Interactomics' – research lab, located at the LIH Department of Infection and Immunity and co-supervised by the two laureates. The main objectives of their research group are to investigate the roles of chemokines and their receptors in immune disorders, cancer, viral infections and neuro-inflammatory diseases, ultimately leading to the development of drugs targeting these molecular components.

2019 Galien Prize award ceremony, December 2020

SCAN ME

View video
/Andy&Martyna/



Dr Andy Chevigné,
Group Leader of the Immuno-Pharmacology and Interactomics research group,
LIH Department of Infection and Immunity

“Prix du Fonds Léon et Henri Fredericq" for Dr Andy Chevigné

In addition to receiving the 2019 Galien Prize in Pharmacology, Dr Chevigné was awarded the ‘Prix du Fonds Léon et Henri Fredericq’ in December 2020 by the Royal Academy of Science, Letters and Fine Arts of Belgium for his outstanding contribution to the fields of allergology and molecular pharmacology. Namely, the international prize rewards his work on major allergens in dust mites and the mode of activation and regulation of G protein-coupled receptors (GPCRs), cellular membrane proteins that have emerged as promising therapeutic targets for a broad spectrum of diseases, including inflammatory and autoimmune disorders but also for many cancers. Established in 1969, the “Prix du Fonds Léon et Henri Fredericq” is awarded to researchers having particularly distinguished themselves through original research in the field of physiology or related sciences, such as molecular biology, biochemistry, biophysics and pharmacodynamics.

Dr Torsten Bohn,
NutriHealth Group leader at DoPH and one of the most cited global scientists in Clarivate's 2020 "Highly Cited Researchers" ranking

Dr Torsten Bohn among the world's most highly cited researchers

In November 2020, the business intelligence company Clarivate™ released its annual "Highly Cited Researchers" report, recognising the pioneers in the fields of science and technology who produced multiple highly-cited papers ranking in the top 1% by citations in Web of Science™. For the second consecutive year, Dr Torsten Bohn, Group leader of the Nutrition and Health Research (NutriHealth) team of the LIH Department of Population Health (DoPH), was featured in the list of the most cited global scientists in the field of Agricultural Sciences of this prestigious international ranking. Over the past decade, Dr Bohn has published 119 papers indexed in Web of Science™ and obtained a total of 5,477 citations. His research focuses on nutrition and its health impact, with special attention to nutrient and secondary plant bioactives bioavailability, dietary patterns, inflammation and oxidative stress. He is currently developing the public health and nutrition research activities at LIH, in line with the institute's translational and transversal vision, to explore the connection between nutrient intake and availability and various health aspects, including cardiometabolic diseases, cancer, the gut microbiome, immunity and genetic background. Dr Bohn was one of only three Luxembourg researchers to have been included in the 2020 edition of the report.

SCAN ME

View video
/Torsten/

Dr Meiser and Dr Golebiewska at the Legs Kanning award ceremony, January 28th 2020

Legs Kanning Prize awarded to DONC researchers

In January 2020, Dr Anna Golebiewska, Group Leader of the NORLUX Neuro-Oncology laboratory, and Dr Johannes Meiser, Group Leader of the Cancer Metabolism Group at the LIH Department of Oncology (DONC), were awarded the Legs Kanning Prize from the association "Action Lions Vaincre le Cancer". The prize, which amounts to EUR 7,500 for each awardee, rewards the scientific achievement of researchers who devote their career to cancer research in Luxembourg. Specifically, it supports Dr Golebiewska's work on glioblastoma (GBM), one of the deadliest types of brain cancers, and Dr Meiser's research on the metabolic alterations occurring in cancer cells, which play an important role in their survival, growth, motility and in metastasis formation. The award was conferred during the 15th Legs Kanning conference, which took place at the headquarters of the Banque Internationale à Luxembourg (BIL) on January 28th, in the presence of Mr Raoul Stefanetti, Head of Private Banking Luxembourg at BIL, and Prof Marc Diederich, president of "Action Lions Vaincre la Cancer".

SCAN ME

View video /Anna &Johannes/

Dr Danielle Perez Bercoff received a Rotary donation for her COVID-19 neutralisation study "NEUTRACOV" in June 2020

Dr Danielle Perez Bercoff supported by Luxembourg's Rotary Clubs

The four Rotary Clubs of the Grand Duchy joined forces in support of Luxembourg's research on the novel coronavirus, raising a special fund. In this context, Dr Danielle Perez Bercoff, Senior Scientist within the Clinical and Translational HIV Research Unit of the LIH Department of Infection and Immunity (DII), received a generous donation of EUR 30,000 for her project "NEUTRACOV" (A Novel High Throughput Assay To Measure Plasma NEUTRAlizing Activity Against SARS-CoV-2) in June 2020. The aim of the project is to develop a high-throughput assay to measure the ability of plasma and antibodies to effectively neutralise SARS-CoV-2. The test can be used to assist the Centre Hospitalier de Luxembourg (CHL) in identifying plasma from recovered patients with the highest neutralising activity to treat patients with severe or critical COVID-19 by plasmapheresis. The test was also used to identify neutralising antibodies in patients with different illness severity, thereby providing a rationale to predict patient outcome. With the deployment of vaccines and the emergence of new SARS-CoV-2 strains, the test is now particularly useful to evaluate the effectiveness, duration and waning of neutralising antibodies in recovered and vaccinated individuals. The "NEUTRACOV" project had been funded in April 2020 by the Luxembourg National Research Fund (FNR) through a EUR 50,000 grant under the new "COVID-19 Fast Track Call" funding scheme.

Dr Danielle Perez Bercoff received a Rotary donation for her COVID-19 neutralisation study "NEUTRACOV" in June 2020

SCAN ME

View video
/Danielle/

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

LIH leukaemia research supported by Plooschter Projet donation

In January 2020, the Luxembourgish non-profit association Plooschter Projet renewed its financial support to leukemia research through a generous EUR 30,000 donation to the Tumour Stroma Interactions (TSI) group of the LIH Department of Oncology (DONC). The grant supports TSI Group Leaders Dr Etienne Moussay and Dr Jérôme Paggetti's project in characterising in detail the identity and features of cells from the tumour microenvironment in chronic lymphocytic leukaemia (CLL). This will be achieved by using a high-throughput imaging technique known as Imaging Mass Cytometry (IMC, Hyperion), in collaboration with Sorbonne University (Paris, France). A better understanding of T cell subtypes, their localisation and of the way their functions are subverted by tumour immune escape mechanisms will provide hints as to potential targets for new innovative immunotherapies.

View video /Etienne &Jérôme/

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Additional 2020 highlights

More news, events, awards and nominations

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3

JANUARY

1

New Board of Directors for LIH

The new Board of Directors for LIH was appointed in January 2020 for a term of 5 years. Namely, Dr Gregor Baertz (Medical Director, Hôpitaux Robert Schuman) was appointed President and Xavier Poos (Deputy Administrative Director, Health Directorate of the Ministry of Health) Vice-president of the Board of Directors, while Mr Pierre Misteri (Advisor to the Ministry of Higher Education and Research) was appointed to the position of Government Commissioner at LIH. The Board of Directors is nominated by the Government and is composed of nine external members of different professional backgrounds. Its mission is to oversee the activities at LIH. It is responsible for the general organisation, for defining internal rules, for budget control, for framework contracts with partner organisations and for approving new strategies.

MARCH

2

Framework agreement between IPIL and LIH

LIH CEO Prof Dr Ulf Nehrbass, LIH CFAO Marc Grabowski and Dr Serge Quazzotti signed a framework agreement between the Luxembourg Institute of Health and the Institut de la Propriété Intellectuelle Luxembourg (IPIL). This agreement will help develop a cooperation between the two institutions in the field of intellectual property. The collaboration will apply to activities including patent database queries, intellectual property training, intellectual property events for researchers, and the development of new tools to better integrate intellectual property into research activities in Luxembourg.

Photo: Dr Serge Quazzotti (IPIL) and Prof Dr Ulf Nehrbass (LIH CEO)

3

LaoLuxLab at the Institut Pasteur du Laos serves as back-up for COVID-19 diagnosis

In March 2020, four staff members of the LaoLuxLab, which is financially supported by the *"Direction de la coopération au développement et de l'action humanitaire"* of the Luxembourg Ministry of Foreign and European Affairs in the context of the Luxembourg-Laos Partnership for Research and Capacity Building in Infectious Disease Surveillance (PaReCIDS) project, volunteered to provide additional support for COVID-19 diagnosis in case of need. PaReCIDS is managed by the Clinical and Applied Virology group of the LIH Department of Infection and Immunity, in collaboration with the LaoLuxLab at the Institut Pasteur du Laos (IPL). In order to prepare for increased testing, the LaoLuxLab scientists Siriphone Virachith and Vilaysone Khounvisith and the technicians Bounta Vongphachanh and Latdavone Khenkha were trained to provide additional support to the IPL Virology team.

Photo: LaoLuxLab staff at the Institut Pasteur du Laos supporting COVID-19 diagnosis.

4

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4

2020 Career Launchpad Award for LIH post-doctoral fellow

Dr Nicole Kiweler, post-doctoral fellow within the Cancer Metabolism Group of the LIH Department of Oncology (DONC), was awarded a EUR 10,000 grant under the LIH Wolfgang Baertz Career Launchpad Award (Legs W. Baertz) programme at the end of March 2020. The funding will allow her to finalise her high-potential research project on cancer metabolism and metastatic progression, in view of submitting the findings for publication. Moreover, the funds allowed her to attend a Lab Leadership course in Heidelberg, organised by the European Molecular Biology Organisation (EMBO), which enabled her to strengthen the critical soft skills necessary to manage a team as a Principle Investigator.

Photo: Dr Nicole Kiweler, post-doctoral fellow, Cancer Metabolism Group, LIH Department of Oncology

APRIL

5

Launch of Research Luxembourg website and COVID-19 national platform

In April 2020, Research Luxembourg launched its official website. In addition to being a platform to promote Luxembourg research to an international audience, the site also features a dedicated section about the COVID-19 Taskforce. In parallel, Research Luxembourg also launched a national COVID-19 platform to coordinate research projects and collaborations, support the research community, and facilitate exchange and the identification of synergies. The different sections of the platform allow researchers to submit project ideas, browse ongoing projects and submitted open ideas, share and discuss new ideas, as well as browsing COVID-19 literature curated by the members of the dedicated COVID-19 Taskforce Work Package.

6

First PhD defence under CANBIO PRIDE training programme

The first PhD defence under the CANBIO doctoral research and training programme, which was also the first virtual PhD defence to be have been conducted, took place on April 27th 2020. Doctoral candidate Ines Kozar from the Department of Life Science and Medicine (DLSM) of the University of Luxembourg was the first student to graduate under the programme, following a "virtual" defence and graduation ceremony. She defended her thesis on the mechanisms underlying drug resistance in melanoma, providing deeper insights into the genetic alterations that characterise these tumours and opening up new therapeutic avenues. The Cancer Biology "CANBIO" PhD training programme, launched by LIH, the University of Luxembourg and the Laboratoire National de Santé (LNS) in 2016 and coordinated by Prof Simone Niclou, aims to provide state-of-the-art training in cancer biology to young scientists, leading to the development of more effective therapies and fostering translational research. It is funded by the Luxembourg National Research Fund (FNR) through the competitive PRIDE programme and by intramural funds from the Luxembourg Ministry of Higher Education and Research (MESR).

Photo: Dr Ines Kozar, first CANBIO graduate

MAY

7

The Grand Ducal couple visits LIH

On Monday May 4th 2020, LIH had the honour of welcoming Their Royal Highnesses the Grand Duke and the Grand Duchess of Luxembourg to the laboratories of the House of BioHealth in Esch-sur-Alzette, in the presence of Mrs Anne Calteux, First Government Advisor, Mr Claude Meisch, Minister of Higher Education and Research, Léon Diederich, First Government Advisor at the Ministry of Higher Education and Research and Government Commissioner for the LIH Board of Directors, Dr Gregor Baertz, President of the LIH Board of Directors and Mr Xavier Poos, Deputy Administrative Director, Health Directorate of the Ministry of Health and Vice-President of the LIH Board of Directors. The visit was an opportunity for the Grand Ducal couple to access the "behind the scenes" of Luxembourg research and meet the scientists involved in the fight against COVID-19, as well as getting acquainted with the teams working on different priority areas, from oncology to immunology.

Photo: Their Royal Highnesses the Grand Duke and the Grand Duchess of Luxembourg visiting the LIH laboratories in Esch-sur-Alzette on May 4th 2020.

8

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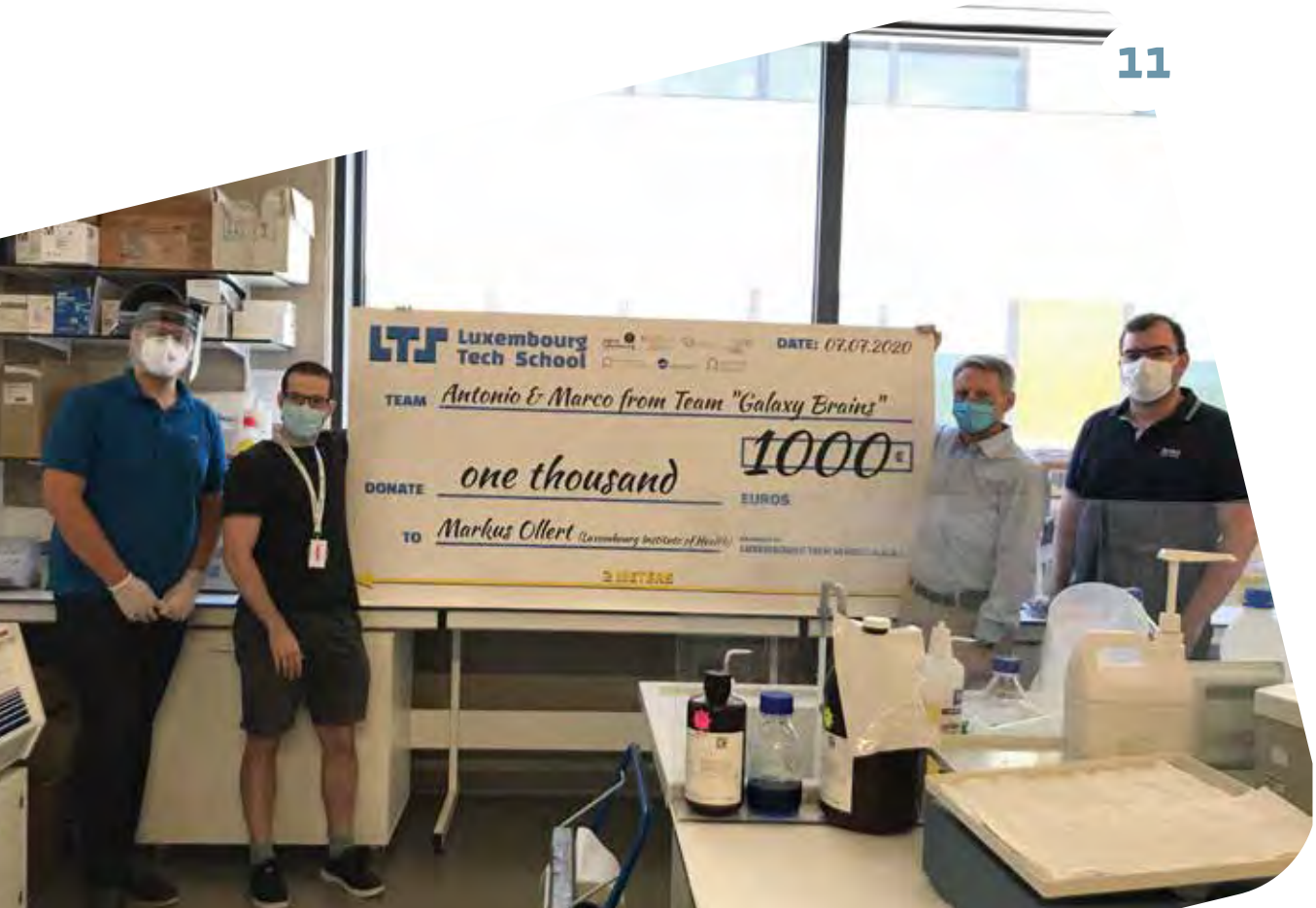

LTS Luxembourg Tech School
DATE: 07.07.2020
TEAM Antonio & Marco from Team "Galaxy Brains"
DONATE one thousand
1000 €
EUROS
TO Markus Ollert

11

8

IBBL 2020 Biospecimen Proficiency Testing Programme

In June 2020, IBBL launched its 2020 Biospecimen Proficiency Testing (PT) Programme. The PT programme is an internationally-recognised external quality assessment tool offering laboratories working with biospecimens the opportunity to verify the accuracy, precision and efficiency of their routine methods and benchmark their performance to that of other expert laboratories. The 2020 edition of the PT programme featured a new processing scheme – namely "Dual DNA/RNA Extraction from Frozen Tissue" – bringing the total offering to 20. 131 participants from 30 different countries registered for the 2020 PT Programme, for a total of 452 schemes subscribed.

9

New ISO 21899 biobanking standard published

ISO 21899, a new biobanking standard to which IBBL contributed extensively, was officially published in June 2020. The norm was developed by Working Group 2 of the ISO technical committee 276 'Biotechnology' to define the specific requirements for the validation and verification of processing methods, with the aim of assisting biobank laboratories in performing biological sample processing. It will act as a complementary standard to ISO 20387 (General requirements for biobanking), further reinforcing the progressive standardisation of biobanking activities at the international level.

10

Full Professorship in Immunology & Genetics at LCSB and LIH for Dirk Brenner

On June 15th 2020, Prof Dirk Brenner, Head of Experimental & Molecular Immunology at LIH, was appointed joint Professor in Immunology & Genetics at both the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg and at LIH. This new position will reinforce the already very dynamic immunology research in Luxembourg and develop synergies between the two institutions by bringing together the LIH expertise in immunology and the systems biology approach of the LCSB. This integrated "systems immunology" approach will be used to tackle new concepts in the regulation of the immune system and metabolism and to investigate and interfere with disease mechanisms using in vivo and patient-derived models. Furthermore, the new joint programme will allow the elucidation of the role of immunity in diseases that are not usually associated with the immune system, notably Parkinson's disease.

Photo: Prof Dirk Brenner

11

Luxembourg Tech School students support COVID-19 efforts at LIH

On July 31st 2020, two students of the Luxembourg Tech School (LTS) donated the sum of EUR 1,000 to Prof Markus Ollert's team at the LIH Department of Infection and Immunity (DII), in support of its COVID-19 vaccine development activities. The donation was made by students Antonio del Rio and Marco Brunacci, who had been awarded the second prize of the LTS game development contest 'GameDev Challenge 2020'. Specifically, the donation will support the DII study "RD-Vac SARS-CoV-2" (Rapid Development and Initial Preclinical Evaluation of an Effective Candidate Vaccine against SARS-CoV-2), which aims to develop a vaccine based on the expression of recombinant SARS-CoV-2 antigenic variants in a novel trimeric form, combined with CpG oligodinucleotides adjuvant.

Photo: From left to right: Antonio del Rio, Guillem Montamat (PhD candidate, Allergy and Clinical Immunology, LIH), Prof Markus Ollert (LIH) and Dr Christophe Trefois (LTS representative; LCSB).

12

LIH-ULiège: University Certificate in Clinical Trials

Through the Clinical and Epidemiological Investigation Centre (CIEC) of the Department of Population Health (DoPH), LIH partnered with the University of Liège (ULiège) to launch an innovative University Certificate in Clinical Trials for health professionals in Luxembourg and Belgium. Lessons began in September 2020 and will take place until June 2021. The course entails over 80 hours of teaching by clinical research professionals; 40 hours of internship in a centre specialised in the implementation of clinical trials; a visit to a clinical pharmacology unit, a pharmaceutical industry and a biobank; and a unique final certificate in Belgium and Luxembourg. The course aims to familiarise healthcare professionals with clinical trial methodology and design, as well as with the complex procedures for the implementation of clinical trials to evaluate new drugs before they are placed on the market.

13

ESMO Virtual Congress 2020

The 2020 edition of the European Society for Medical Oncology (ESMO) Congress went fully virtual for the first time. Spread over two weekends, the Science Weekend of the Congress took place between September 19th 2020 and September 21st, while the Education Weekend took place between October 16th and October 18th 2020. The event introduced promising new developments to improve cancer patient care and included a dedicated COVID-19 and cancer research track. Prof Simone Niclou, Director of the LIH Department of Oncology (DONC), was part of the Scientific Advisory Board of the Central Nervous System (CNS) tumour session that was held on September 20th 2020, and acted as its co-chair. She was also an invited discussant, invited to critically review, discuss and contextualise the previously presented abstracts of the session during a dedicated presentation.

14

National PhD Welcome day 2020

The 5th annual National PhD Welcome Day took place on October 28th 2020 in a fully virtual format. The event provides all first-year PhD candidates in Luxembourg with the opportunity to network with their peers, acquiring the tools needed for a successful PhD during "tool kit" sessions led by Luxembourg actors in doctoral education, researcher networks and student associations. Moreover, the event allows new doctoral students to pick up tips and best practices from 3rd and 4th year PhD candidates. The 2020 virtual edition also entailed a "fun" online quiz about Luxembourg, with a prize for the most knowledgeable candidate. The National PhD Welcome Day 2020 was organised under the lead of the Luxembourg Institute of Science and Technology (LIST), in partnership with the University of Luxembourg, LIH, LISER, MPI, LuxDoc, EURAXESS and FNR.

Photo: National PhD Welcome day 2020

15


LUXEMBOURG
INSTITUTE
OF HEALTH
LIST
www.lih.lu

17


MBD
MEDICAL & BIO DECISION
LIH/IBBL - MBD
Collaborative Laboratory
LUXEMBOURG
INSTITUTE
OF HEALTH
IBBL

16

15

Bilateral cooperation agreement signed with the University of Luxembourg

In November 2020, Prof Ulf Nehrbass signed a mutual bilateral cooperation agreement with the University of Luxembourg, in the presence of Claude Meisch, Minister for Higher Education and Research. The scope of the agreement covers research cooperation through participation in joint research projects, development of common research platforms, the creation of inter-institutional research groups and co-affiliation of staff via Honorary, Affiliated or Joint Professorships. One example of collaboration around inter-institutional research platforms includes the University-LIH joint Disease Modelling & Screening Platform (DMSP). DMSP is currently led by Dr Yong-Jun Kwon, Head of Disease Modelling & Screening Platform, who supervises the implementation of several drug screening programmes on the LIH side, while Prof Dr Rejko Krüger, joint professor for Neuroscience at the University and Director of TTM at LIH, has been involved in the platform since its early conception.

16

André Losch Foundation visits LIH

On November 26th 2020, LIH welcomed Mrs Daniela Ragni, Director of the André Losch Foundation, to its premises in Strassen for a visit of the LIH Clinical and Epidemiological Investigation Centre (CIEC). Mrs Ragni was received by Prof Ulf Nehrbass, CEO of LIH, Dr Frank Glod, Chief of Scientific Operations, Prof Rejko Krüger, Director of Transversal Translational Medicine (TTM), Prof Markus Ollert, Director of the LIH Department of Infection and Immunity, Dr Guy Fagherazzi, Director of the LIH Department of Population Health (DoPH), and Dr Manon Gantenbein, Head of CIEC. The event also provided an opportunity to discuss the status of the COVID-19 projects CON-VINCE and Predi-COVID, coordinated by LIH and financially supported by the André Losch Foundation through a generous donation.

Photo: Mrs Daniela Ragni (Director, André Losch Foundation) visits LIH

17

Establishment of joint MBD-LIH lab for personalised cancer treatment

On December 9th 2020, South Korean biotech company Medical & Bio Decision (MBD), LIH and IBBL announced the establishment of a joint laboratory for precision medicine tailored to cancer patients. The joint MBD-LIH/IBBL lab, which was set up at the premises of IBBL in Dudelange, Luxembourg, will focus on performing translational oncology research. Specifically, the lab will test the sensitivity, efficacy and toxicity of anticancer drugs leveraging MDB's proprietary 3D cell culture platform technology, which allows the identification the most effective anticancer drug using cancer cells derived directly from patients across Europe. The lab will also benefit from IBBL's state-of-the-art biological sample storage facilities. The joint lab holds the potential to advance the treatment of various types of cancers, including Glioblastoma, gastric and colorectal cancers.

Photo: The MBD-LIH/IBBL collaborative lab

Institutional organisation and figures

BOARDS

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

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

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

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

BOARD OF DIRECTORS

TRANSVERSAL ACTIVITIES & PLATFORMS

DEPARTMENT OF INFECTION & IMMUNITY

DEPARTMENT OF ONCOLOGY

DEPARTMENT OF POPULATION HEALTH

CEO LIH
Prof Ulf Nehrbass

RESEARCH DEPARTMENTS

RESEARCH SUPPORT SERVICES

CFAO
Marc Grabowski

ADMINISTRATIVE DEPARTMENT & CORE SERVICES

CEO IBBL
Prof Ulf Nehrbass

INSTITUTE IBBL

KEY FACTS 2020*

232
New agreements signed**

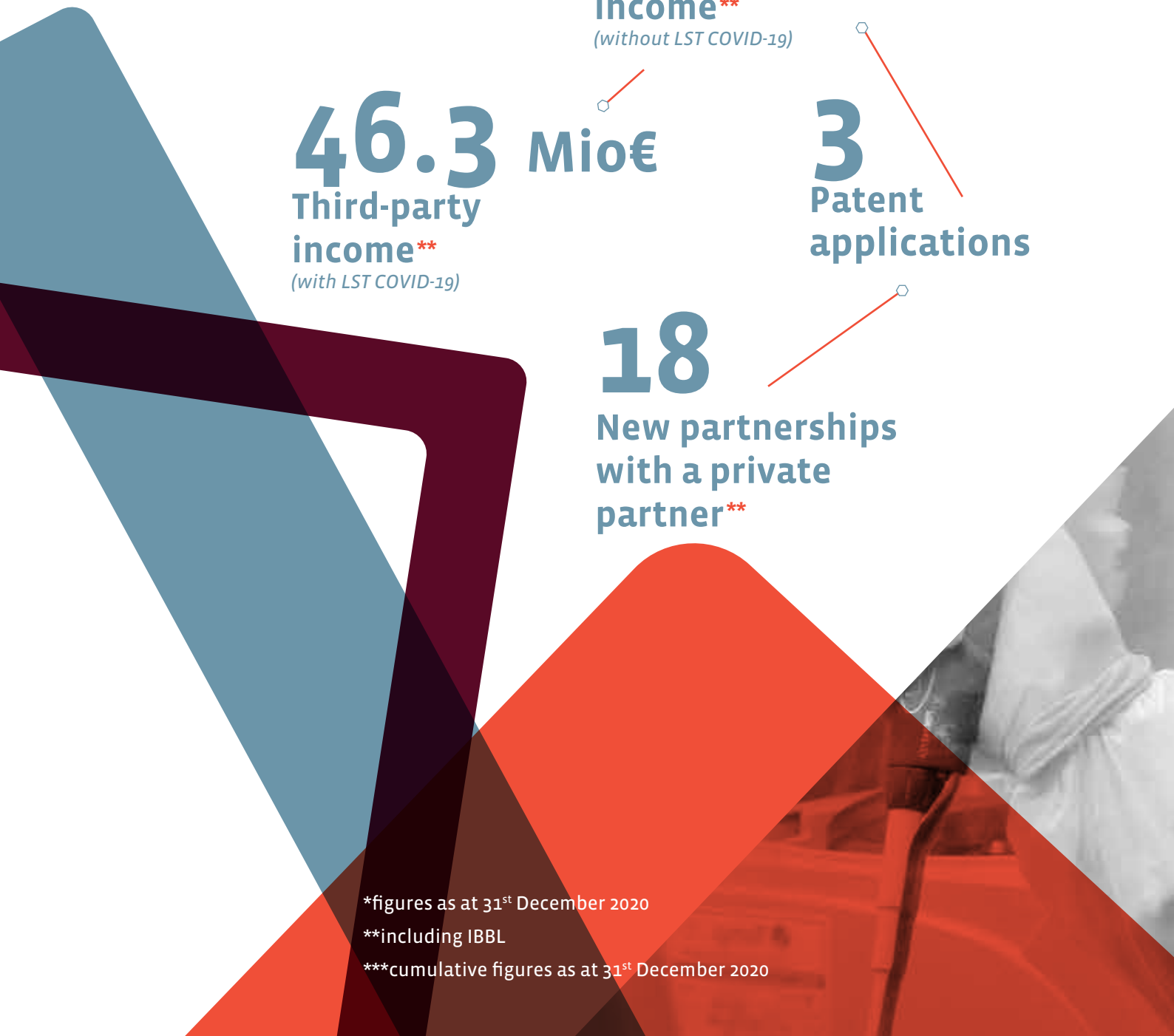
314
Publications**

16.6 Mio€
Third-party income**
(without LST COVID-19)

46.3 Mio€
Third-party income**
(with LST COVID-19)

3
Patent applications

18
New partnerships with a private partner**



*figures as at 31st December 2020
**including IBBL
***cumulative figures as at 31st December 2020

419
Employees**

321
Ongoing projects

221
Scientists**

9
Clinical trials with LIH leading role

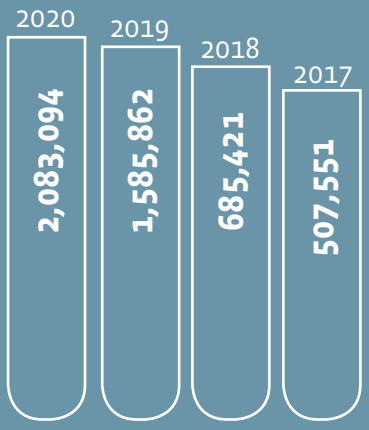
2.1 million
Total samples collected and aliquots created*** (IBBL)

109,675
Total samples distributed*** (IBBL)

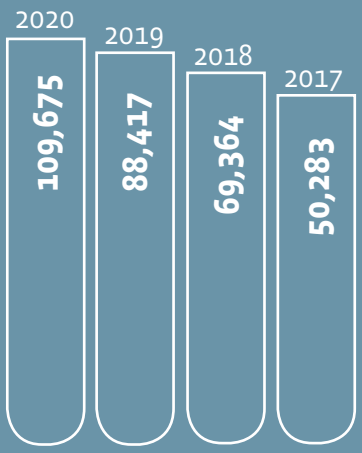
2,189
Mentions of LIH/IBBL in the press (736 national and 1,453 international)**
> Of which 1,274 COVID-19 related

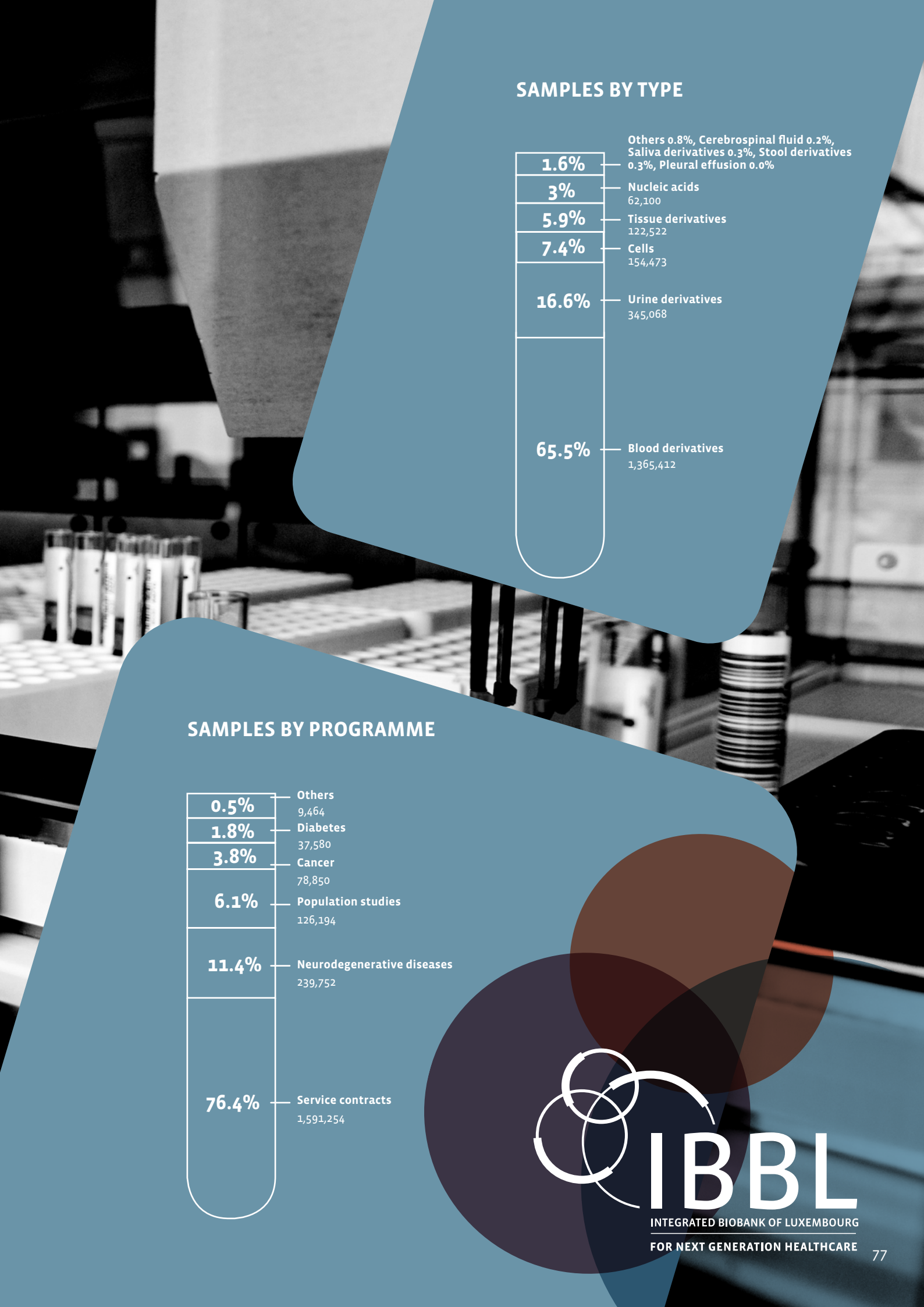
Collection statistics

TOTAL SAMPLES COLLECTED AND ALIQUOTS CREATED



DISTRIBUTED



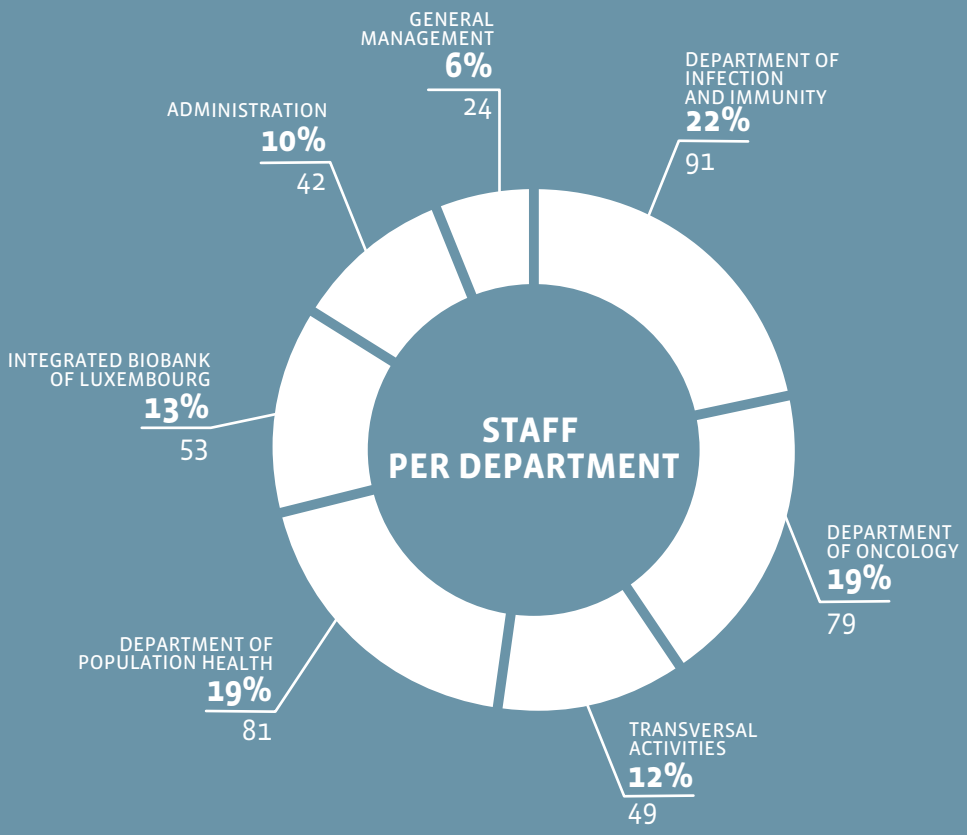


SAMPLES BY TYPE

SAMPLES BY PROGRAMME

IBBL
INTEGRATED BIOBANK OF LUXEMBOURG
FOR NEXT GENERATION HEALTHCARE

Human Resources



STAFF BY FUNCTION

RESEARCHERS
53%
221

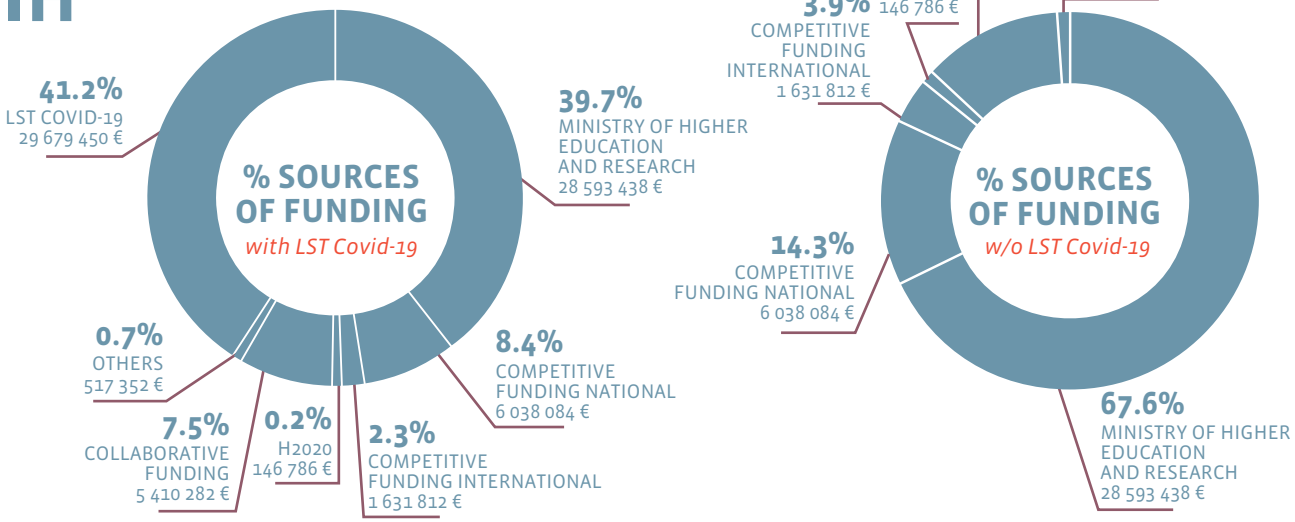
TECHNICIANS
24%
101

SUPPORT STAFF
23%
97

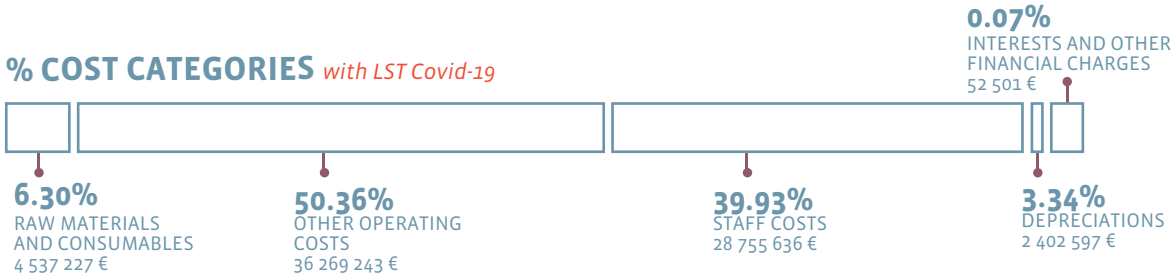

STAFF BY NATIONALITY
FRENCH
33% (140)
BELGIAN
14% (59)
LUXEMBOURGISH
14% (59)
GERMAN
12% (50)
OTHER EUROPEAN NATIONALITIES
16% (69)
NON-EUROPEAN NATIONALITIES
10% (42)
STAFF BY GENDER
263
FEMALE
156
MALE
EXTERNAL
1%
4
FIXED-TERM
34%
142
PERMANENT
65%
273
STAFF BY WORK CONTRACT TYPES

FINANCES
STATUTORY EXPENSES

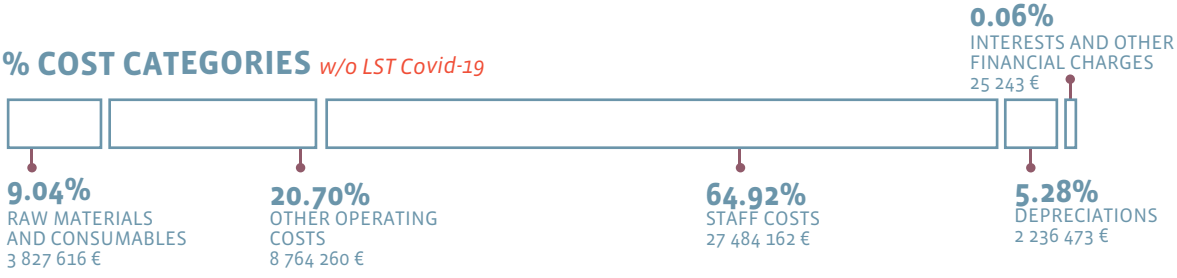
LIH



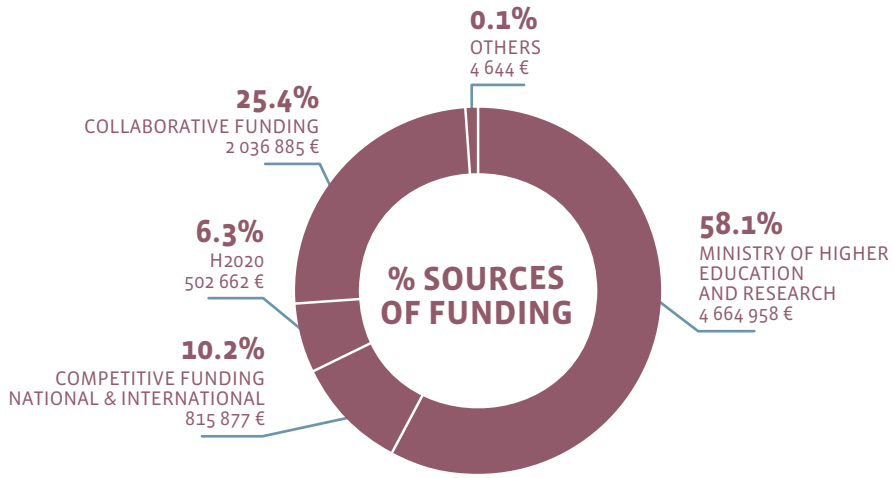
% COST CATEGORIES *with LST Covid-19*



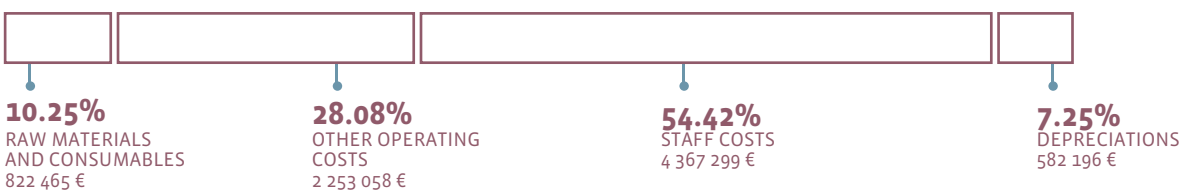
% COST CATEGORIES *w/o LST Covid-19*



IBBL



% COST CATEGORIES



PROFIT AND LOSS ACCOUNT (EUR)	2020 01.01 - 31.12.20	2019 01.01 - 31.12.19
A. CHARGES		
1. Use of merchandise, raw materials and consumable materials	5,359,692	4,662,365
2. Other expenses	38,522,301	12,075,743
3. Staff costs	33,122,934	30,457,858
4. Value adjustment on intangible, tangible assets and financial assets	2,922,580	3,123,539
5. Value adjustment on current assets	62,214	0
6. Interests payable and similar expenses	52,507	3,522
TOTAL CHARGES	**80,042,228**	**50,323,027**
B. INCOME		
1. Net turnover	3,441,243	2,961,987
2. Subsidies	75,933,814	46,577,022
3. Other income	126,953	272,050
4. Other interest receivable and similar income	12,550	22,392
5. Loss for the financial year	527,668	489,576
TOTAL INCOME	**80,042,228**	**50,323,027**

FINANCES
PROFIT AND LOSS ACCOUNT
(31st December 2020)

ASSETS (EUR)	2020 01.01 - 31.12.20	2019 01.01 - 31.12.19
FIXED ASSETS		
Intangible fixed assets	586,689	637,950
Tangible fixed assets	6,196,510	6,647,540
Financial fixed assets	1,380	1,380
TOTAL FIXED ASSETS	**6,784,579**	**7,286,870**
CURRENT ASSETS		
Stocks		
Raw materials and consumables	**633,730**	
Debtors		
1. Trade debtors	**2,367,235**	**1,631,081**
a. Becoming due and payable within one year	2,367,235	1,629,964
b. Becoming due and payable after more than one year	0	1,117
2. Other debtors	**922,981**	**2,765,657**
a. Becoming due and payable within one year	922,981	2,765,657
Cash at bank and in hand	**39,664,638**	**29,559,929**
TOTAL CURRENT ASSETS	**43,588,584**	**33,956,667**
Prepayments	**916,057**	**926,180**
TOTAL ASSETS	**51,289,220**	**42,169,717**

FINANCES
BALANCE SHEET
(31st December 2020)

CAPITAL, RESERVES AND LIABILITIES (EUR)	2020 01.01 - 31.12.20	2019 01.01 - 31.12.19
CAPITAL AND RESERVES		
Financial wealth	4,099,157	4,099,157
Reserves	1,486,881	1,486,881
Profit or loss brought forward	7,509,968	7,999,544
Profit or loss for the financial year	-527,668	-489,576
Capital investment subsidies	7,336,688	7,601,529
TOTAL CAPITAL AND RESERVES	**19,905,026**	**20,697,535**
Available reserve for projects	**24,101,854**	**16,105,399**
Provisions for risks and charges	**1,637,156**	**942,624**
CREDITORS		
1. Trade creditors	**2,402,971**	**3,361,390**
a. Becoming due and payable within one year	2,402,971	3,358,475
b. Becoming due and payable after more than one year	0	2,915
2. Tax and social security debts	**1,055,595**	**977,722**
a. Tax authorities	9,720	9,720
b. Social security authorities	1,045,875	968,002
3. Other creditors	**2,175,354**	**77,788**
a. Becoming due and payable within one year	2,175,354	77,788
TOTAL AVAILABLE RESERVE FOR PROJECTS, PROVISIONS AND CREDITORS	**31,372,930**	**21,464,923**
Deferred income	**11,264**	**7,259**
TOTAL CAPITAL, RESERVES AND LIABILITIES	**51,289,220**	**42,169,717**

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