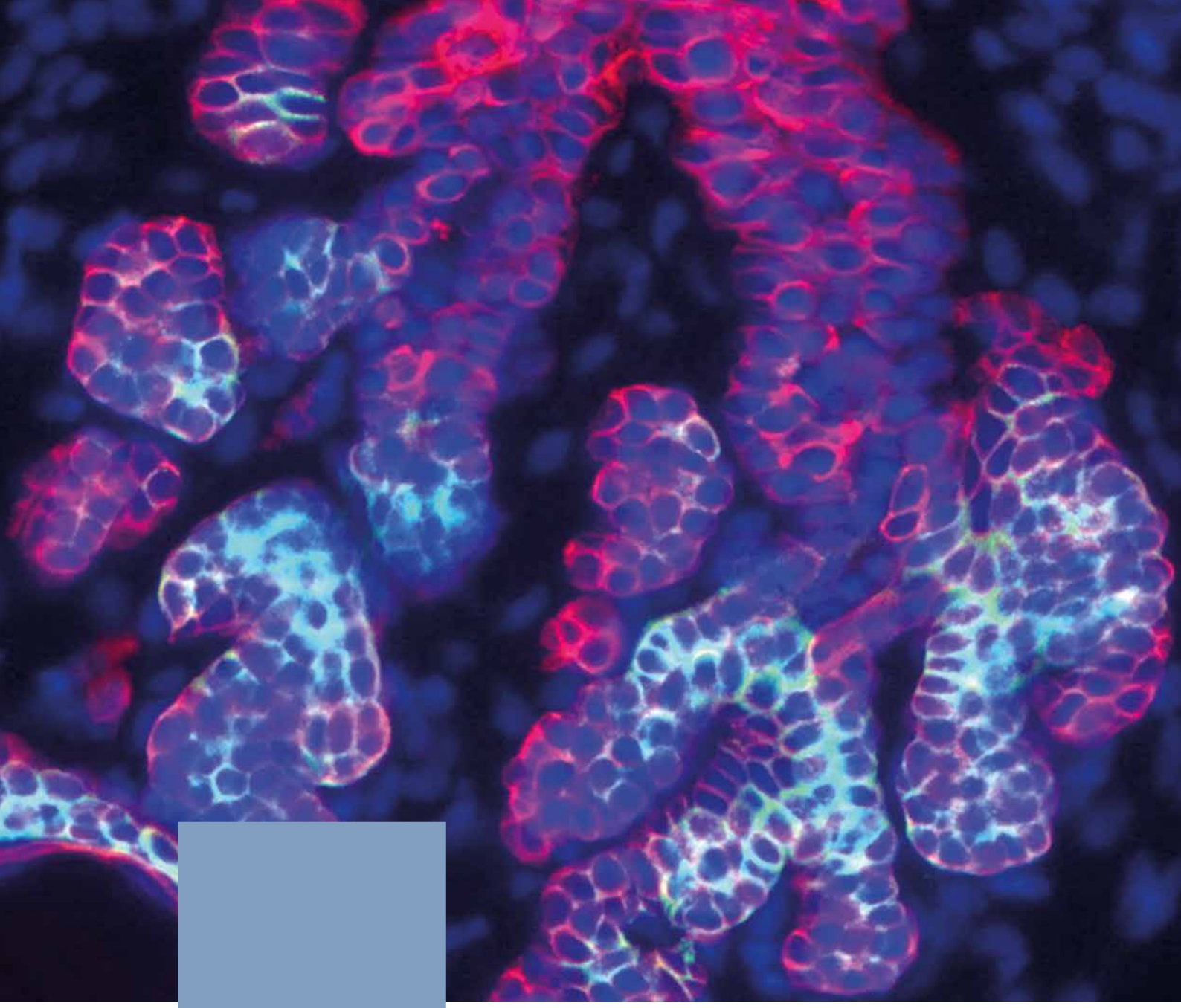
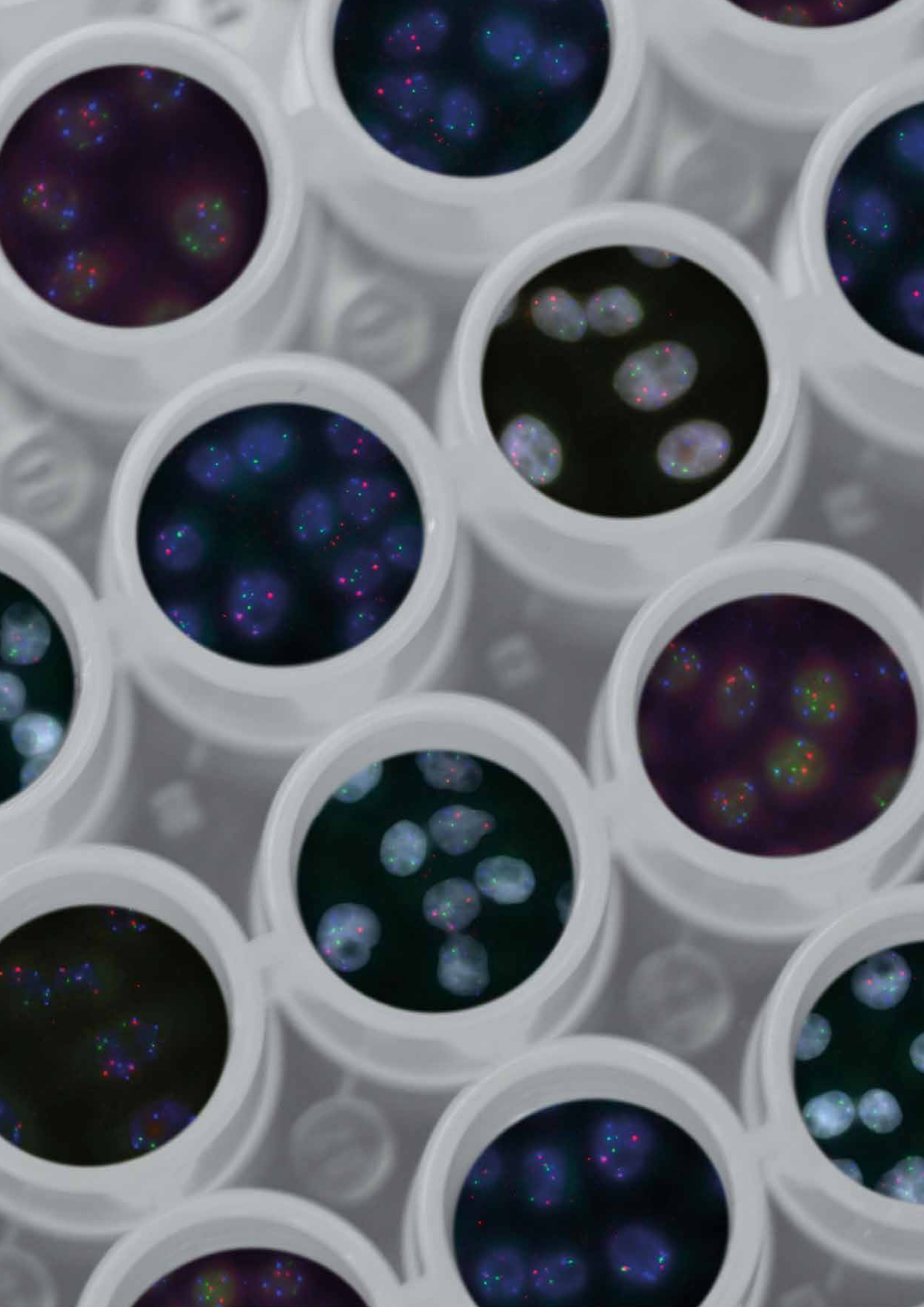


ANNUAL REPORT 2020

welbio
Walloon Excellence in Life sciences



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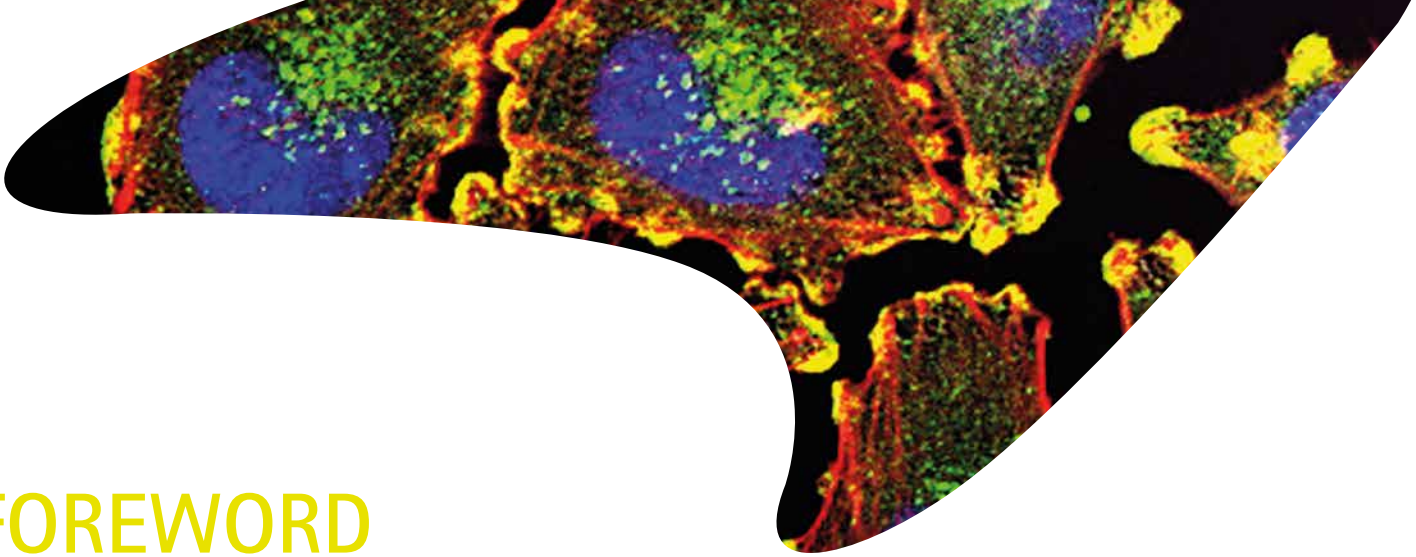


FOREWORD

WELBIO is an inter-university research institute subsidized by Wallonia.
Its missions are to support fundamental research in life sciences and to promote the industrial valorization of scientific discoveries into biomedical applications.

10TH ANNIVERSARY OF SCIENTIFIC EXCELLENCE

2020 marks the 10th anniversary of our first call for projects. Reflecting upon the last decade, we saw WELBIO grow from a virtual concept into a well-established inter-university institution in the French Community of Belgium. A total of 5 biannual calls for projects have been organized, resulting in the support of 65 projects. WELBIO Principal Investigators and their teams published numerous articles in the most prestigious journals, including Cell, Nature, Neuron, Gut and Blood. Their scientific excellence has been recognized by numerous awards and honors, and attracted additional competitive national and European funding, including from the European Research Council. With a Starting Grant category, WELBIO has also been a spring board for early career development.

TRANSLATING SCIENTIFIC DISCOVERIES INTO HUMAN APPLICATIONS

To promote the industrial valorization of scientific discoveries, WELBIO took the stance from inception to meet regularly with the WELBIO Principal Investigators and members of the Technology Transfer Offices from their respective academic institution to discuss scientific progresses. This aims at early detection of intellectual property and facilitating the translation of scientific discoveries into human applications. This resulted in a progressive build of valorization opportunities that are taking many forms including projects supported by the competitiveness clusters and SPW Research in Wallonia, licensing agreements, industry partnerships, and spin-off creation.

FACING A NEW VIRUS

2020 will also be remembered for an unprecedented global pandemic. Like many around the globe, WELBIO scientists had to adapt, prioritize lab activities and adjust to major delays including in hiring internationally. Down time in the lab however didn't equate to down time in activity. WELBIO scientists took this opportunity to contribute their expertise to the fight against the new virus.

LAST BUT NOT LEAST

Many thanks to Pierre Van Renterghem who led the Institute from 2015 to 2020 with dedication and enthusiasm. Welcome back to Vinciane Gaussin who was the initial Managing Director and is resuming her role after 5 years spent in the United States.

welbio
Walloon Excellence in Life sciences

KEY FIGURES FOR THE LAST DECADE

78 M€
INVESTED IN RESEARCH SINCE 2011

5
CALLS FOR PROJECTS

SCIENTIFIC EXCELLENCE

560
PUBLICATIONS INCLUDING

210
ARTICLES IN HIGH IMPACT FACTOR JOURNALS

12
ERC GRANTS

RESEARCH PROJECTS

65
RESEARCH PROJECTS

47
PRINCIPAL INVESTIGATORS

INCLUDING
19
EARLY-CAREER INVESTIGATORS

4
UNIVERSITIES

TRANSLATION OF SCIENTIFIC DISCOVERIES INTO APPLICATIONS

PATENT APPLICATIONS FOR
17
INVENTIONS

(BIO)PHARMACY
2 SPIN OFFS
1 LICENCE
2 CLINICAL TRIALS

IN VITRO DIAGNOSTIC
1 WALINNOV PROJECT

CELL PLATFORM FOR DRUG DISCOVERY
1 BIOWIN PROJECT

BIOMANUFACTURING
1 JOINT RESEARCH GROUP

SCIENTIFIC EXCELLENCE

Our researchers published 80 articles in 2020; including 45% in the most prestigious journals such as Nature, Blood, Cell Metabolism, Gut, Science Translational Medicine, Nature Communications and the Journal of Clinical Investigation. Here is a selection of articles to illustrate the internationally recognized groundbreaking work conducted by WELBIO Principal Investigators in several fields of life sciences.

ONCOLOGY

Heterotypic cell–cell communication regulates glandular stem cell multipotency

In this study that made the cover of Nature, researchers led by Cédric Blanpain (ULB) uncovered that communication between basal and luminal cells restricted multipotency in the mammary gland and the prostate. They identified the signaling pathways that restricted multipotency in normal conditions and that activated basal stem cell multipotency in regenerative conditions. Understanding the molecular mechanisms that control multipotency in different tissues could have important implications in cancer formation.

Centonze et al, 2020, Nature

Cover image @Alessia Centonze

Tumor driver promoting metastasis and resistance to therapy

It has been proposed that epithelial-to-mesenchymal transition (EMT), a process in which epithelial cells detach from their neighboring cells and acquire mesenchymal migrating properties, is important in the initiation of tumor metastasis. Cédric Blanpain's team (ULB) discovered that loss of function of FAT1, one of the most frequently mutated driver genes in a broad range of human cancers, promoted hybrid EMT phenotype in tumor cells. They demonstrated that this hybrid EMT state occurring following FAT1 loss-of-function promoted metastasis and was associated with poor clinical outcome in patients with lung cancers.

Pastushenko et al, 2020, Nature

RNF113A: a new therapeutic target in lung cancer

Lung cancer remains challenging to treat, at least because of intrinsic or acquired resistance of lung cancer cells to targeted therapies. Alain Chariot (ULiège) and his team focused on RNF113A, a subunit of the spliceosome that promotes the splicing of multiple pro-survival candidates including MCL-1. They showed that inhibition of RNF113A re-sensitized lung cancer cells with some acquired resistance to Cisplatin-dependent cell death. Their study defines RNF113A as a new potential therapeutic target for combination therapies in lung cancer.

Shostak et al, 2020, Nature Communications

Combining immunotherapies to increase the efficacy of treatments against cancer

Cancer immunotherapy consists in manipulating immune cells in patients to fight cancer. Sophie Lucas (UCLouvain) and her team showed in a murine model that selective blockade of TGF-β1 production by Tregs with antibodies against GARP:TGF-β1 complexes, initially described in Science in 2018, induced regressions of tumors otherwise resistant to anti-PD-1 immunotherapy. These results support the clinical evaluation of blocking anti-GARP:TGF-β1 mAbs, alone or in combination to treat patients with cancer resistant to currently available immunotherapies.

de Streel et al, 2020, Nature Communications

MPL mutations in essential thrombocythemia

Several activating mutations in the transmembrane/juxtamembrane (JM) domains of the thrombopoietin receptor (TpoR) are causing human myeloproliferative neoplasms. Stefan Constantinescu (UCLouvain) and his laboratory demonstrated that the classical S505N and W515 mutations, and new set around H499, depended on one extracellular tryptophan residue W491, which stabilized the active receptor and could be a target for therapy.

Levy et al, 2020, Blood

IMMUNOLOGY & INFLAMMATION

Understanding the molecular mechanism by which VEGFA promotes psoriasis

Psoriasis is a common skin inflammatory disorder affecting 3% of the population. Despite the well-known role of VEGFA in promoting psoriasis, it remains unclear whether VEGFA acts directly on the skin epidermis or only on blood vessels, mediating recruitment of inflammatory cells and resulting in defective epidermis differentiation. Using different psoriasis mouse models, the team of Cédric Blanpain (ULB) provided evidence that targeting VEGFA signaling specifically in the epidermis prevented psoriasis development.

Benhadou et al, 2020, Science Advances

CARDIOMETABOLIC DISEASES

Inspiration from plant biology to tackle cardiac diseases

Cardiovascular disease remains the world's number one killer and advanced heart failure is a major contributor. The team of Jean-Luc Balligand (UCLouvain) demonstrated that Aquaporin-1 (AQP1), expressed at the membrane of cardiac myocytes, is a «bona fide» peroxiporin. Blockade of AQP1 with an extract of Brahmi, a plant used for centuries in traditional Ayurvedic medicine, prevented adverse myocardial remodeling in vitro and in vivo, without affecting contractility, opening new therapeutic possibilities for hypertrophic cardiomyopathies.

Montiel et al, 2020, Science Translational Medicine

Discovery of a novel gene involved in primary lymphedema

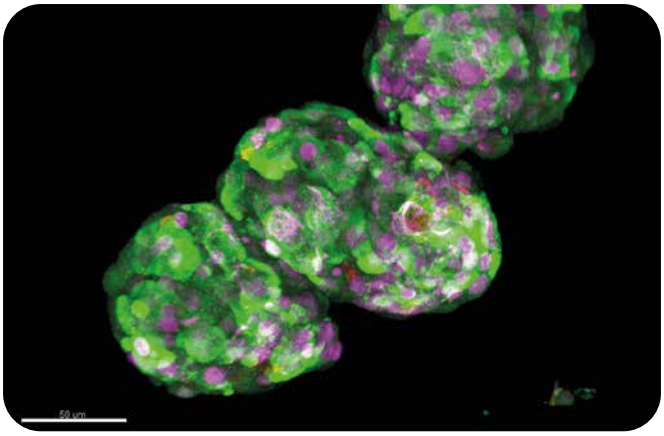
Lymphedema is a strongly invalidating chronic disease resulting from abnormal development or function of the lymphatic system. Today many people with the disease are still not diagnosed. The team of Miikka Vikkula discovered mutations in a gene called ANGPT2 in five families with occurrence of lymphedema and characterized the impact of these mutations on the function of ANGPT2. This work puts the ANGPT2/TIE signaling into the core of underlying pathophysiological mechanisms of primary lymphedema.

Leppänen et al, 2020, Science Translational Medicine

GDF15: a new target for Type 1 Diabetes Intervention

Type 1 diabetes results from the progressive loss of pancreatic β cells, a process propagated by pro-inflammatory cytokine signaling. To identify proteins involved in this process, Decio Eizirik (ULB) and his team performed comprehensive proteomics of stressed human pancreatic islets. This novel proteomics approach provided a unique resource for the identification of the human islet proteins regulated by cytokines and was effective in discovering a potential target for type 1 diabetes therapy, namely GDF15.

Nakayasu et al, 2020, Cell Metabolism



@Miriam Cnop

How interferon-α impacts human pancreatic β-cells

Type 1 diabetes is a chronic autoimmune disease leading to pancreatic islet inflammation (insulitis) and progressive beta cell loss. Decio Eizirik (ULB) and his team used an innovative "multi-omics" approach combining genomic, transcriptomic

and proteomic techniques with advanced bioinformatic tools to analyze the initial changes present in human beta cells exposed to the cytokine IFNα, a cytokine that plays an important role in the early stages of type 1 diabetes. Data mining of this multi-omics analysis identified two compound classes that antagonize IFNα effects on human beta cells and have potential as a future therapeutics for diabetes.

Colli et al, 2020, Nature Communications

YIPF5 mutations cause neonatal diabetes

Neonatal diabetes develops before 6 months of age and is caused by single gene mutations reducing pancreatic β cell number or impairing β cell function. To date, 30 genetic causes have been described. The laboratory of Decio Eizirik (ULB) reported recessive YIPF5 mutations as the genetic cause of a novel syndrome of microcephaly, epilepsy and neonatal/early-onset diabetes, highlighting a critical role of YIPF5 in beta-cells and neurons. This is the first report of mutations disrupting the ER-to-Golgi trafficking resulting in diabetes.

De Franco et al, 2020, J Clin Invest

Hazem Ibrahim, Jonna Saarimäki-Vire and Hassam Montaser

Targeting our second brain (the gut) to fight type 2 diabetes

The enteric nervous system is a mesh-like system of neurons that governs the function of the gastrointestinal tract. In type 2 diabetes, duodenal hypercontractility disrupts the gut-brain axis considered as a major actor in the control of glycemia, contributing to insulin resistance. Using a combination of nutritional and pharmacological approaches, Patrice Cani (UCLouvain) and Claude Knauf (INSERM) identified a new signaling pathway whereby gut microbiota could modify the actions of enteric neurons. The identification of specific targets, such as the enteric neuronal population, could pave the road for the development of new treatment for type 2 diabetes with fewer side effects than existing ones.

Abot et al, 2020, Gut

MICROBIOLOGY & INFECTIOUS DISEASES

Molecular interaction and inhibition of SARS-CoV-2 binding to the ACE2 receptor

David Alsteens (UCLouvain) and his team used atomic force microscopy to investigate the mechanisms by which the S-glycoprotein of SARS-CoV-2 binds to the ACE2 receptor. The laboratory demonstrated, both on model surfaces and on living cells, that the receptor binding domain served as the binding interface within the S-glycoprotein with the ACE2 receptor and extracted the kinetic and thermodynamic properties of this binding pocket. Altogether, these results provided a picture of the established interaction on living cells. The team also tested several binding inhibitor peptides targeting the virus early attachment stages, offering new perspectives in the treatment of the SARS-CoV-2 infection.

Yang et al, 2020, Nature Communication

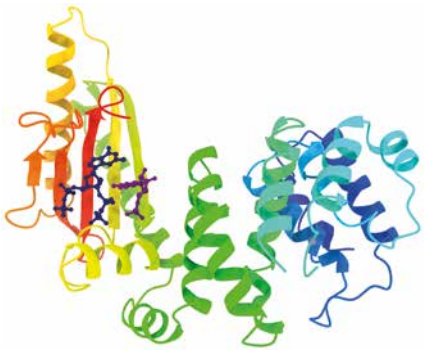
Understanding the defense mechanisms of bacteria

The resistance of bacteria to antibiotics is a major health problem. The beta-barrel protein BamA, in the outer membrane of Gram-negative bacteria, plays an essential role in antibiotic resistance but its mechanism of action remains poorly understood. By solving the structure of BamA, in complex with its lipoprotein substrate RcsF, the team of Jean-François Collet (UCLouvain) shed new light on the BAM machinery and how it exports lipoproteins to the surface. Their work paves the way for the design of new antibacterial strategies targeting BAM.

Rodríguez-Alonso et al, 2020, Nature Chemical Biology

A nucleotide-switch mechanism mediates opposing catalytic activities of Rel enzymes

Many of the infectious diseases that are difficult to treat with antibiotics are caused by highly tolerant pathogens that can switch to a dormant-state to withstand stress. The alarmone (p)ppGpp is one of the effector molecules underlying the stress response.



@Abel Garcia-Pino

Its synthesis and degradation are regulated by the bifunctional Rel enzymes. Abel Garcia-Pino (ULB) and his team combined structural biology, biochemistry and biophysical approaches to gain further insight into the regulation of the opposing activities of Rel enzymes. They identified an allosteric mechanism that safeguarded against futile cycles of alarmone synthesis and degradation to control the levels of alarmone in the cell.

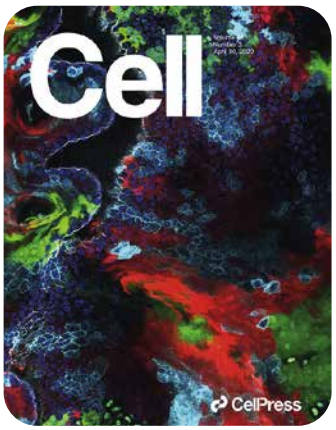
Tamman et al, 2020, Nature Chemical Biology

CELLULAR & MOLECULAR BIOLOGY

Defining the design principles of postnatal skin growth

During postnatal growth, an excess of cell production over cell loss is required to ensure tissue expansion while maintaining tissue function. This study led Cédric Blanpain and his team, that made the cover of Cell, unraveled the mechanisms that mediate postnatal skin expansion. The team found that a unique developmental stem cell population mediates tissue expansion by a constant self-duplication throughout postnatal development.

Dekoninck et al, 2020, Cell



Cover image @Sophie Dekoninck

Mechanisms of stretch-mediated skin expansion at single-cell resolution.

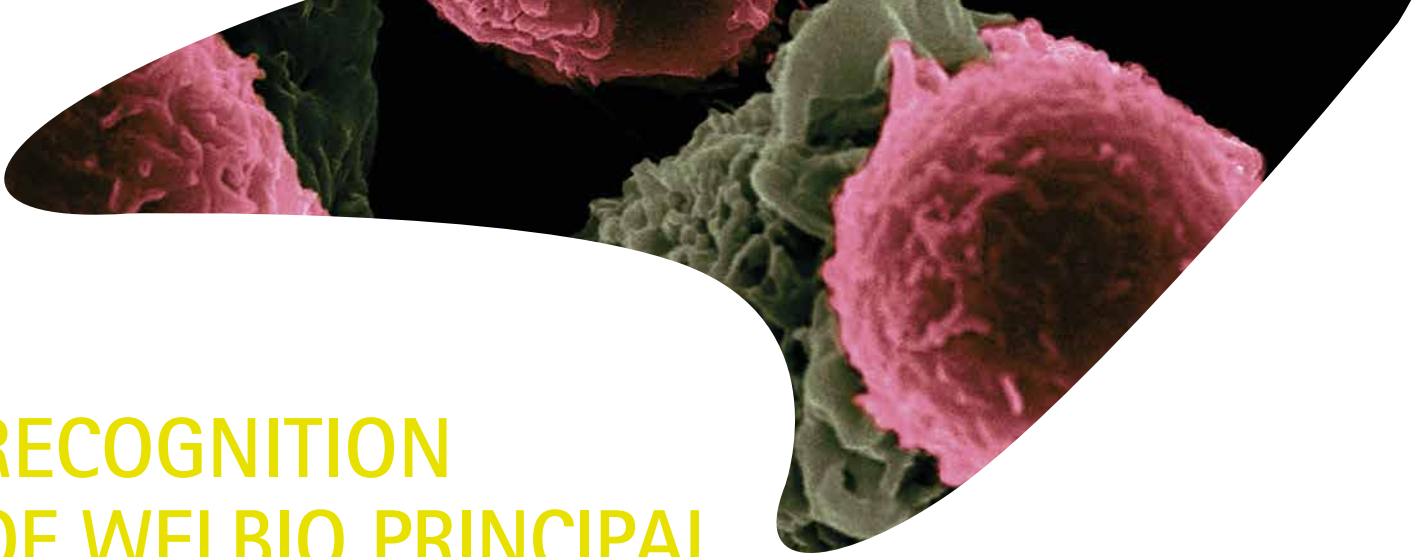
The ability of the skin to grow in response to stretching has been exploited in reconstructive surgery, but the underlying mechanisms in vivo are still poorly understood. In this study, researchers led by Cédric Blanpain (ULB), in collaboration with Benjamin D. Simons (University of Cambridge) demonstrated that stretching resulted in skin expansion by inducing self-renewal of epidermal stem cells. They uncovered the signaling pathways responsible for stretch-induced stem cell activation and renewal at the single cell resolution.

Aragona et al, 2020, Nature

5hmC as a timely maintainer of the balance between pluripotency and lineage-priming factors in mouse embryonic stem cells

A balance between pluripotency and lineage-priming factors must be maintained to ensure the orderly differentiation of embryonic stem cells (ESCs). Here, François Fuks' laboratory (ULB) provided evidence of an additional level of regulation of the ESC self-renewal network. They proposed a stepwise working model whereby 5hmC mRNA modification acted as an essential regulatory layer to safeguard efficient, timely, authentic downregulation of lineage-specific genes. This would ensure adequate repression of lineage-specific factors and critically prepare ESCs to rapidly respond to differentiation stimuli.

Lan et al, 2020, Nature Communications



RECOGNITION OF WELBIO PRINCIPAL INVESTIGATORS

Scientific advances achieved by WELBIO Principal Investigators are the results of many years of research. The fact that WELBIO investigators have received prestigious scientific awards year after year, and attracted competitive international European funding, is a testimony to the excellence of their work. In 2020,

Jean-Luc Balligand (UCLouvain) was invited to present the Dirk Brutsaert Lecture at the Heart Failure Association Winter Meeting on Translational Heart Failure Research.

Luc Bertrand (UCLouvain) received the Dr. Léon Dumont Prize of the Belgian Heart Foundation and King Baudouin Foundation, as well as the Lambertine-Lacroix Prize.

Pierre Close (ULiège) received the Quinquennial Prize of the Royal Academy of Medicine of Belgium in Biomedical Sciences.

Jean-François Collet (UCLouvain) received the Quinquennial Prize of the Scientific Research Fund (FNRS) in Basic Biomedical Sciences (Scientific Prize Joseph Maisin).

Stefan Constantinescu (UCLouvain) was nominated Vice-President of the Royal Academy of Medicine of Belgium and President-elect for the Federation of European Academies of Medicine (FEAM).

Pierre van der Bruggen (UCLouvain) was awarded the Fund Maurange from the King Baudouin Foundation.

Benoit Vanhollebeke (ULB) was awarded the Ernest Solvay prize from the Queen Elisabeth Medical Foundation.

Mikka Vikkula (UCLouvain) received a 2-year renewal of the prestigious Generet Prize for Rare Disease Research, originally awarded in 2018 for the first time in Belgium by the King Baudouin Foundation. He was also invited to serve as a Member at Large to the board of the International Society for the Study of Vascular Anomalies (ISSVA).

4 running ERC grants to WELBIO Principal Investigators:

Thomas Marichal (ULiège): ERC Starting grant (2018)

Abel Garcia-Pino (ULB): ERC Consolidator grant (2019)

Benoît Vanhollebeke (ULB): ERC Consolidator grant (2019)

Cédric Blanpain (ULB): ERC Advanced grant (2019)

Cédric Blanpain (ULB) was awarded the Francqui-Collen Prize 2020, sometimes referred to as the "Belgian Nobel Prize", for his fundamental research in cancer and stem cells biology. Cédric Blanpain's laboratory studies stem cells during embryonic development, homeostasis and tissue repair as well as their connection with the development and progression of cancers. The team made several groundbreaking discoveries published in the most prestigious journals.

TRANSLATION OF SCIENTIFIC DISCOVERIES INTO HUMAN APPLICATIONS

GENERATING INTELLECTUAL PROPERTY

WELBIO meets regularly with the WELBIO Principal Investigators and members of the Technology Transfer Offices from their respective academic institution to discuss scientific progresses. This aims at early detection of intellectual property. In 2020, 5 new patent applications were filed, bringing the total of active patent applications generated by WELBIO research projects to 17. The following have been published:

WO/2014/037460:
Immobilised Cyclindependent Kinase 4 Fusion proteins and uses thereof

WO/2015/015003:
Anti-GARP protein and uses thereof

WO/2017/198685:
Method for determining sensitivity to a CDK4/6 inhibitor

WO/2018/138358:
PERK and IRE-1A inhibitors against neuro-developmental disorders

WO/2018/167312:
Detection, quantification and/or isolation of circulating tumour cells based on the expression of CD321 marker

WO/2019/175380:
Antigenic peptides deriving from Secretogranin V and uses thereof for the diagnosis and treatment of type-1 diabetes

WO/2019/202149:
sglt2 inhibitors for the treatment of neutropenia

WO/2019/207057:
Combination of metformin and cyclophosphamide as an adjuvant in cancer immunotherapy

WO/2020/011856:
Dysosmobacter, a novel bacterial genus of the gastrointestinal microbiota and uses thereof

WO/2020/083982:
Guanabenz as an adjuvant for immunotherapy

WO/2020/221888:
Cystic Fibrosis Transmembrane Conductance Regulators Stabilizing Agents

CREATION OF A SECOND SPIN OFF: GEPECERON

Gepeceron was created in April 2020 as a spin-off of the Université Libre de Bruxelles, by Theodorus IV and ABBM Asbl, representing the academic founders. The mission of the company is to develop novel therapeutic approaches for solid cancers and inflammatory diseases, with a focus on small molecules targeting selected G protein-coupled receptors. The activities are built on the knowhow developed by Marc Parmentier, WELBIO investigator since 2013, and his team at the Institute of Interdisciplinary Research of ULB (IRIBHM). Gepeceron is supported by the Butterfly Fund and ABBM, and received a grant from the Walloon Region for the initial stage of its development.

GEPECERON

@Mireille Roobaert

FROM FUNDAMENTAL RESEARCH ON BACTERIAL STRESS TO THE PRODUCTION OF BIOMEDICINES

This story started by a meeting in 2013 between a basic scientist with in-depth knowledge about bacteria and two industries, leaders in biomedicine development and production...

The laboratory of Jean-François Collet, a WELBIO Principal Investigator since 2010 (UCLouvain, De Duve Institute), conducts fundamental research to better understand how bacteria respond to different stress to which they are exposed, including antibiotics. This fundamental work has the potential to identify new targets for the development of new antibiotics. A publication in Cell in 2014, that described how the protein RcsF was involved in bacterial defense mechanisms against antibiotics, firmly established Jean-François Collet as a leader in the field. (Cho et al, 2014, Cell)

Eurogentec is a world leader in the production of biomedicines. The use of biomedicines is disrupting current medicine and offers new prospects for the treatment of diseases. Unlike chemical molecules, biomedicines must be produced by living cells. Bacteria are among the organisms of choice for producing biomedicines. Eurogentec is the Walloon subsidiary of Kaneka, which has 50 years of experience in the development of biotechnologies in fields as varied as food supplements, pharmaceuticals and biodegradable polymers.

In 2020, Kaneka and its Walloon subsidiary, Kaneka Eurogentec S.A., entered into a 3-year renewable partnership with Jean-François Collet's laboratory by funding a new joint research group at the Duve Institute of University of Louvain (UClouvain). The group will consist of up to 15 people. This mixed university-company group will develop optimized bacterial strains for the production of biomedicines.

SUCCESSFUL CLINICAL TRANSLATION OF A FUNDAMENTAL DISCOVERY TO TREAT A RARE METABOLIC DISEASE

In the rare metabolic disease known as glycogen storage disease type 1B (GSD-1b), a decrease in the number of neutrophils (neutropenia) and neutrophil dysfunction cause serious infections and inflammatory bowel disease.

Fundamental research in metabolism, led by the team of Emile Van Schaftingen (WELBIO Principal Investigator 2011-2019) and Maria Veiga-da-Cunha, shed light on the underlying mechanism. The team (UCLouvain, De Duve Institute) showed that genetic mutation in GSD-1b caused an accumulation of a non-classical and toxic metabolite in neutrophils leading to neutrophil dysfunction and apoptosis. Lowering blood concentration of the precursor (1,5AG) of this toxic metabolite in a mouse model of the disease was sufficient to increase their neutrophil counts. This new mechanism of action was published in 2019. (Veiga-da-Cunha et al, 2019, Proc Natl Acad Sci U S A)

To translate this fundamental discovery to the clinical setting, the team proposed to repurpose the widely used antidiabetic drug empagliflozin in GSD-1b patients. The aim was to increase the elimination of 1,5AG via the urine to lower its blood concentration. Three children under the age of 6 years old and a 21-year old adult, bearing the GSD-1b mutation, presented recurrent infections of the mouth, intestine and/or skin, with the impossibility for some of them to eat normally, with persistent diarrhea and/or superinfected wounds that did not heal. Administration of the antidiabetic drug empagliflozin resolved clinical symptoms of frequent infections, mucosal lesions, and inflammatory bowel disease. The results of this clinical study conducted by the UCLouvain-St-Luc team in collaboration with clinicians from Austria, the United States and the Netherlands were published in Blood. (Wortmann et al, 2020, Blood).

This work underlines the importance of fundamental research to further our understanding of biological mechanisms. Over the years, bench-to-bedside translation of scientific discoveries may lead to new therapeutic approaches for the treatment of diseases with unmet needs.

COVID-19: HIGHLIGHTING HOW RESEARCH IS ESSENTIAL IN THE FIGHT AGAINST DISEASE

2020 is a year like no other, characterized by a global pandemic and unprecedented sanitary crisis. The sudden appearance of a new virus that took the lives of millions of people brought the spotlight on the importance of fundamental research to decipher the biological mechanisms involved in health and diseases. Many scientists around the world gathered together to decode this new virus and identify targets of interest for the subsequent development of vaccines and therapeutics. Here are some of the contributions by the WELBIO investigators:

Excessive lung release of neutrophil DNA traps may explain severe complications in Covid-19 patients

In an article published in the Journal of Experimental Medicine, Thomas Marichal (ULiège) and colleagues have detected massive amounts of neutrophil extracellular traps (NETs) in distinct compartments of the lungs of patients who died from severe Covid-19. These NETs are released massively into the airways, the lung tissue and the blood vessels, which could be a major contributor to severe disease complications leading to in-hospital death.

Radermecker et al, 2020, The Journal of Experimental Medicine

A biological profile for diagnosis and outcome of COVID-19 patients

Stefan Constantinescu (UCLouvain) collaborated to a study highlighting the key and early changes in the biologic profiles of COVID-19 patients. Biomarkers for COVID19 were identified and separated in two severity groups, non-ICU and ICU (Intensive Care unit). Early markers lymphopenia and eisonopenia were separated from later markers such as neutrophilia and anaemia. Overall, this study led the background for sequencing of severe cases with no co-morbidities in order to identify genetic predisposition to severe COVID19.

Khourssaji et al, 2020, Clinical Chemistry and Laboratory Medicine

Study of the variability of the T cell response in patients with COVID-19

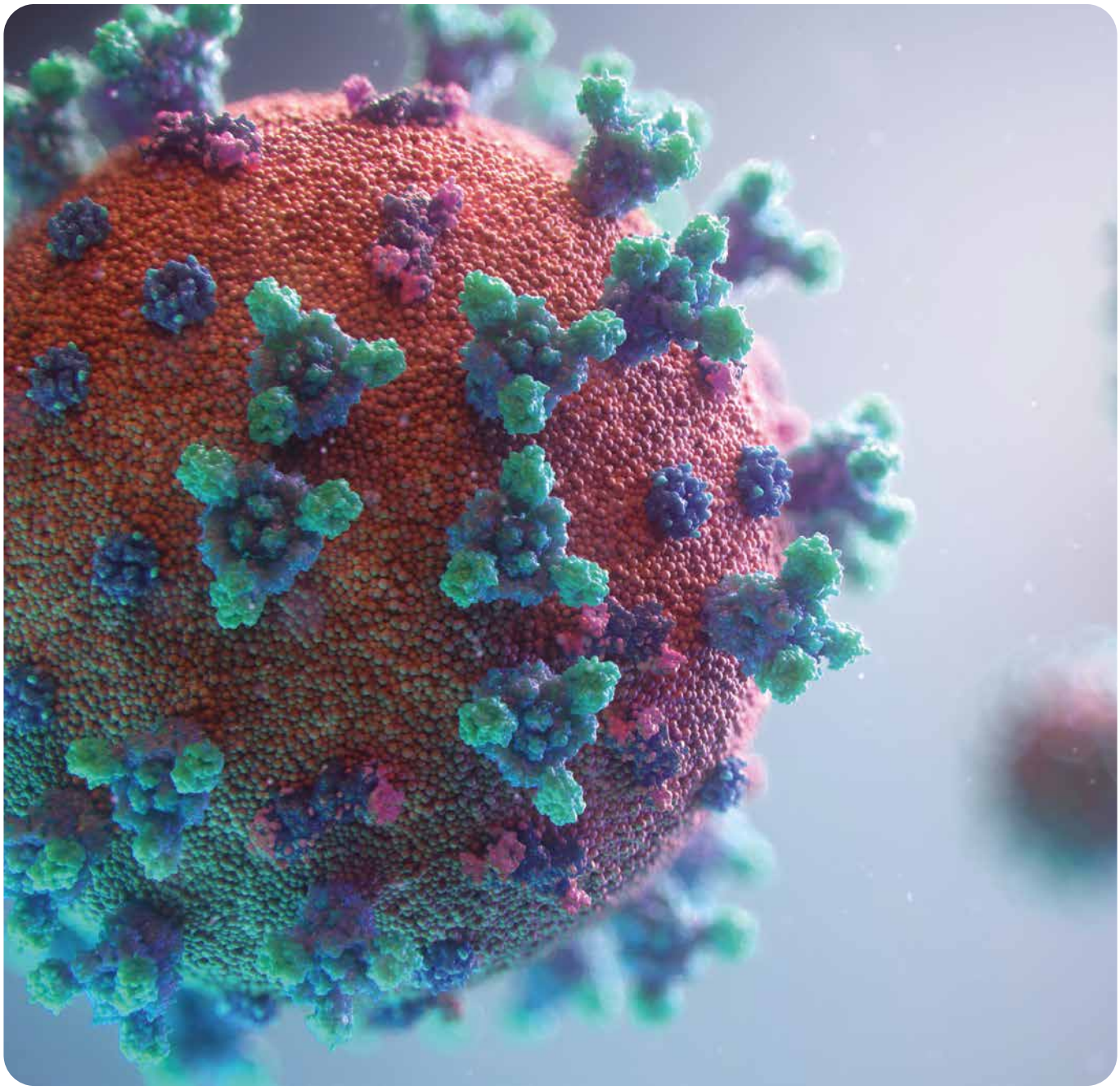
Pierre van der Bruggen (UCLouvain) received a "Crédit urgent de recherche" from the Scientific Research Fund (FNRS) to better understand the exacerbated and prolonged immune response in the case of SARS-Cov-2. The goal is to identify potential avenues for therapeutic management to reduce the side effects resulting from the sudden exposure of anti-viral T lymphocytes to a large amount of viral antigen.

Genetic variants contributing to severe COVID-19 evolution

Stefan Constantinescu (UCLouvain) co-directed with Prof. Antoine Froidure, Cliniques universitaires Saint-Luc a study on genetic variants contributing to severe COVID-19 evolution. This study was later invited to join the COVID Human Genetics Effort (COVIDHGE) as a sequencing hub. COVIDHGE is an international consortium aiming at discovering the human genetic and immunological bases of the various clinical forms of SARS-CoV-2 infection.

Clinical trials to study a potential link between COVID19 and cardiovascular diseases

Jean-Luc Balligand (UCLouvain) carried out (with Virginie Montiel) a clinical study to research a potential link between COVID19, vascular oxidative stress, and vascular nitric oxide bioavailability measured as nitrosylated hemoglobin by Electron Paramagnetic Resonance spectroscopy. This study could shed light on the mechanism underlying the coagulopathy and thrombo-embolic disease currently observed in the course of the COVID-19 disease.



WELBIO PRINCIPAL INVESTIGATORS AND THEIR TEAMS

STARTING GRANTS

Starting grants support talented early-career scientist (maximum 12 years post-PhD at the time of funding application). With this funding category, WELBIO aims at jump starting career development for promising junior scientists. About a third of currently active WELBIO projects are Starting grants:

David Alsteens (UCLouvain): Deciphering the molecular mechanisms of reovirus and rotavirus entry at the nanoscale.

Benjamin Beck (ULB): Characterization of the molecular core of esophageal cancer.

Guido Bommer (UCLouvain): Novel biochemical aspects of neurodegeneration in Parkinson's disease.

Pierre Close (ULiège): Translation reprogramming through wobble tRNA modification in cancer.

Amandine Everard (UCLouvain): Identification of gut microbes and metabolites involved in the gut-to-brain axis controlling hedonic and reward system during food intake.

Abel Garcia-Pino (ULB): Cellular and molecular bases of the regulation of bacterial persistence by (p)ppGpp synthetases/hydrolases.

Esteban Gurzov (ULB): Early diagnosis: can protein tyrosine phosphatase activity predict obesity-induced hepatocellular carcinoma?

Régis Hallez (UNamur): Molecular characterization of the cellular processes targeted by the second messenger (p)ppGpp in bacteria.

Thomas Marichal (ULiège): Epithelial cells as master regulators of mucosal homeostasis: unraveling the regulatory role of Rab guanine nucleotide exchange factor-1 (RABGEF1).

Benoît Vanhollebeke (ULB): Deciphering the regulatory mechanisms of blood-brain barrier function.

ADVANCED GRANTS

Advanced grants support established investigators:

Jean-Luc Balligand (UCLouvain): Cardiac Aquaporin-1: a new regulator of myocardial remodeling.

Luc Bertrand (UCLouvain): CARdiovascular DIseases and o-GlcnAcylatioN: the case of cardiac hypertrophy.

Stefan Constantinescu (UCLouvain): Targeting mechanisms of pathogenic mutant calreticulin signaling via thrombopoietin receptor and JAK2 in myeloproliferative neoplasms.

Pierre Coulie (UCLouvain): Cytolytic CD8 T lymphocytes in severe forms of human autoimmune diseases, towards diagnostic markers and new therapeutic avenues.

François Fuks (ULB): Unravelling the role of RNA epigenetics in health and disease.

Sophie Lucas (UCLouvain): Targeting TGF-β1, β2 or β3 activation in auto-immunity and graft-versus-host disease.

Anna Maria Marini (ULB): Rh factors and the control of membrane permeability to ammonium.

Agnès Noël (ULiège): Innovative roles of uPARAP in lymphatic vessel morphogenesis and functions.

Pierre van der Bruggen (UCLouvain): At the crossroads of cancer and autoimmunity: novel therapeutic targets on exhausted human T cells.

CONTINUATION GRANTS

Continuation grants are awarded to WELBIO Principal Investigators whose Starting or Advanced grants led to identification of intellectual property and a plan towards its valorization.

Cédric Blanpain (ULB): Mechanisms controlling epithelial–mesenchymal transition related tumor heterogeneity.

Fabrice Bureau (ULiège): Lung regulatory macrophages: phenotype, function and therapeutic potential.

Patrice Cani (UCLouvain): Targeting NAPE-PLD, novel bioactive lipids and specific gut microbes to improve cardiometabolic disorders associated with obesity.

Alain Chariot (ULiège): tRNA modifying enzymes and their targets in immunity and cancer.

Jean-François Collet (UCLouvain): Exploring the cell envelope of Escherichia coli, a compartment that is an attractive target for innovative biotechnological and biopharmaceutical approaches.

Decio Eizirik (ULB): Beta cell splicing signature in diabetes.

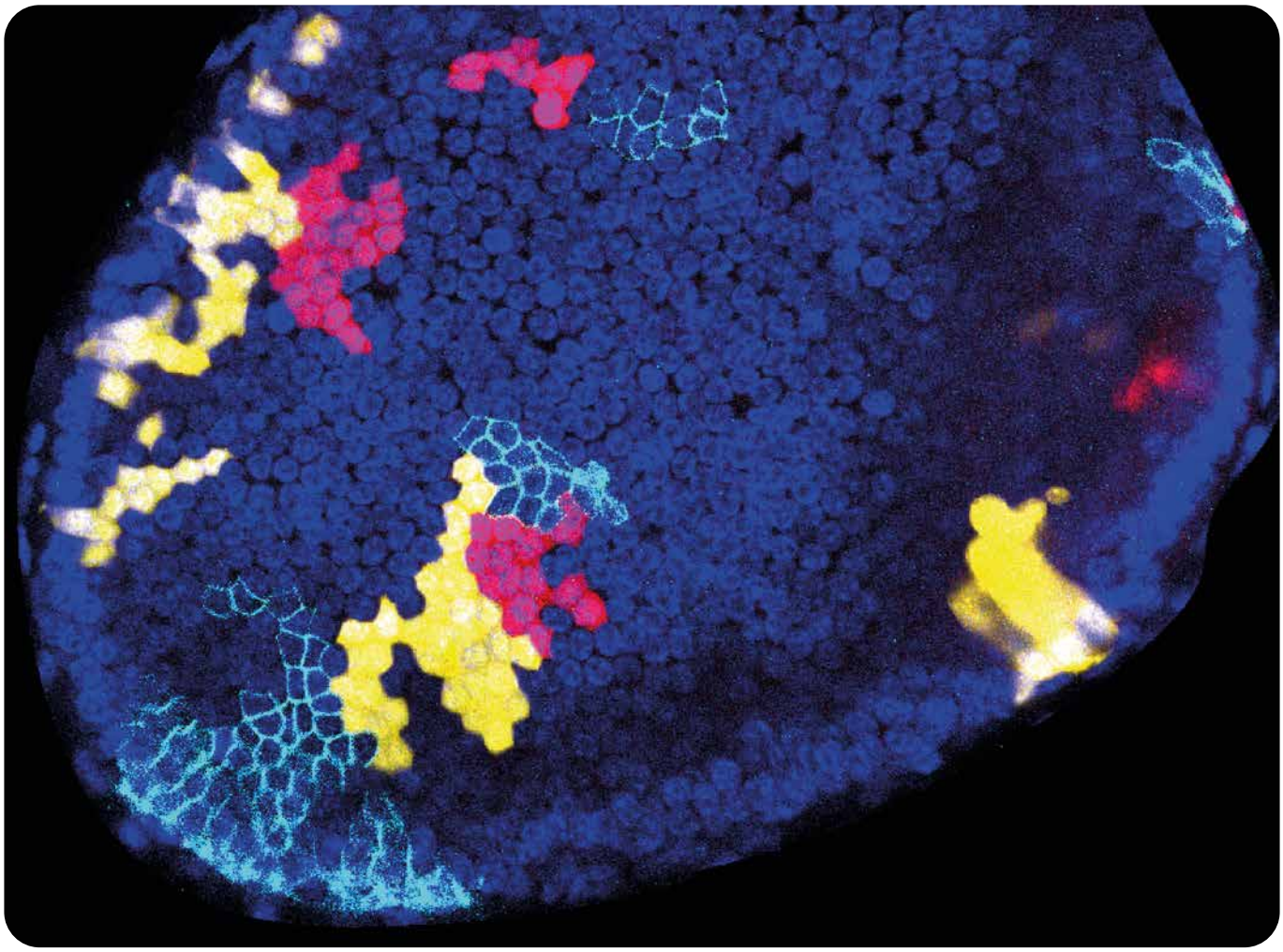
Marc Parmentier (ULB): Chemerin and its receptors in tumoral angiogenesis.

Benoît van den Eynde (UCLouvain): Identification and characterization of new cancer immunotherapy targets discovered by in vivo genomic pool screening.

Miikka Vikkula (UCLouvain): Towards novel treatments for primary lymphedema: from identification of genetic causes to in vivo modelling and preclinical trials.

RESEARCH TEAMS

Since inception of the initial WELBIO projects, the work and/or salary of a total of 630 team members, including 75% of scientists, have been supported through WELBIO funding to 47 WELBIO Principal Investigators. In 2020, the teams of the current 28 WELBIO Principal Investigators included 180 members (130 scientists and 50 lab technicians) supported through WELBIO funding.



ADMINISTRATIVE AND FINANCIAL RESOURCES

GOVERNANCE OF WELBIO ASBLL

The Board of Directors is composed of representatives from academia, industry and the government. The Board is chaired by Jean Stéphenne, with Pierre Lekeux as Vice Chair. The composition of the Board is as follows:

Representatives of the Walloon Government:

- **Christopher Sortino,** Research advisor, representing the Minister-President
- **Vinciane Grimard,** Advisor, representing the Minister for the Economy
- **Emmanuël Sérusiaux,** representing the Minister for Research and Innovation

Representatives of the economic and industrial sector with an interest in life sciences:

- **Jean Stéphenne,** Board member of several biotech companies
- **Jean-Christophe Tellier,** CEO, UCB
- **Philippe Denoël,** Head of External R&D, GSK Vaccines
- **Frédéric de Sauvage,** Vice-Président, Genentech

Academic experts who are internationally recognized in the field of life sciences:

- **Pierre Lekeux**, Professeur, ULiège
- **Emile Van Schaftingen,** Professeur, UCLouvain
- **Gilbert Vassart,** Professeur, ULB

Representatives from the universities in the French Community of Belgium:

- **Rudi Cloots,** Vice-Rector of Research, ULiège
- **Jean-Christophe Renauld,** Prorector of Research, UCLouvain
- **Oberdan Leo,** Vice-Rector of Research and Regional Development, ULB

Ex officio

- **Véronique Halloin,** General Secretary, Scientific Research Fund (FNRS)
- **Isabelle Quoilin,** Managing Director, Walloon Public Service for the Economy, Employment and Research (SPW EER)

WELBIO: THE LIFE SCIENCE AXIS FOR THE FUNDS FOR STRATEGIC FUNDAMENTAL RESEARCH

The decree of 4 December 2012 established a cross-collaboration between the French Community of Belgium and the Walloon region for the funding of strategic fundamental research. In 2016, in agreement with this decree, the FRFS (Strategic Fundamental Research Funds) was created at the FNRS and the WELBIO non-profit organization was integrated, as a delegate of Wallonia, as the strategic axis for life sciences.

The goal was to leverage the extensive expertise of the FNRS in the management of call for projects so the WELBIO non-profit organization could focus its activities on driving the translation of scientific discoveries into human applications.

MANAGEMENT REPORT

This report concerns the tenth fiscal year, which covers the period from 1 January 2020 to 31 December 2020.

Since 2015, funding from the Walloon region has been outsourced to the FNRS, within the framework of the FRFS (Strategic Fundamental Research Funds). To cover its operating costs of managing call for projects, the FNRS deduct up to 4% of the funding after which the WELBIO non-profit organization receives 10% to conduct its missions.

For the 2020 fiscal year, the Walloon region allocated €4,000,000 to the FRFS-WELBIO strategic axis and the WELBIO non-profit organization received €384,000 to cover operating costs.

ASSETS

- Financial fixed assets amounted to €3,450.00 and concerned the guarantee on rented offices in Wavre.
- Accounts receivable within one year amounted to €384,000 related to the 2020 grant to be received.
- Cash investments amounted to €2,080,939.33 in the form of two reserves to distribute the remaining liquidity of WELBIO as follow: €243,300.00 (operating costs 2021) and €1,837,639.33 (Bridge fund).
- A BPAID account has been created to cover various small expenses and the remaining balance is €199.21.
- Adjustment accounts amounted to €3,823.18 and concerned charges that were to be carried forward.
- Total assets amounted to €2,472,411.72.

LIABILITIES

- The balance as of December 31st, 2019, under the heading of "other allocated funds", amounted to €2,286,623.46.
- The result for the fiscal year was a profit of €139.243,47.
- The balance as of December 31st, 2020, for other allocated funds, amounted to €2,425,866.93.
- Supplier debts amounted to €5,875.15.
- The estimated tax liability for 2020 was €136.00.
- Tax for 2019 amounted to €158.55.
- The as-yet-undue withholding tax amounted to €9,300.22.
- The as-yet-undue ONSS amounted to €9,218.45.
- Salaries to be paid amounted to €31.16.
- Provisions for holiday payments amounted to €21,769.96.
- Other debts amounted to €50.00.
- Adjustment accounts amounted to €5.30.
- Total liabilities amounted to €2,472,411.72.

RESULT

- The grant for 2020 operating costs amounted to €384,000.00.
- Membership dues were received for a total amount of €125.00.
- Expense for the web platform Wal-CRIN were paid for a total of €19.360,00.
- Miscellaneous services and assets amounted to €56,058.63 and primarily concern operating costs, rent and fees.
- Salaries and social contributions amounted to €169,862.28.
- Depreciations amounted to €550.28.
- The estimated tax liability amounted to €136.00.
- Net bank interest, without withholding tax, amounted to €1,188.26.
- Financial charges amounted to €102.60.
- The result for the fiscal year is a profit of €139,243.47.

CONTACT

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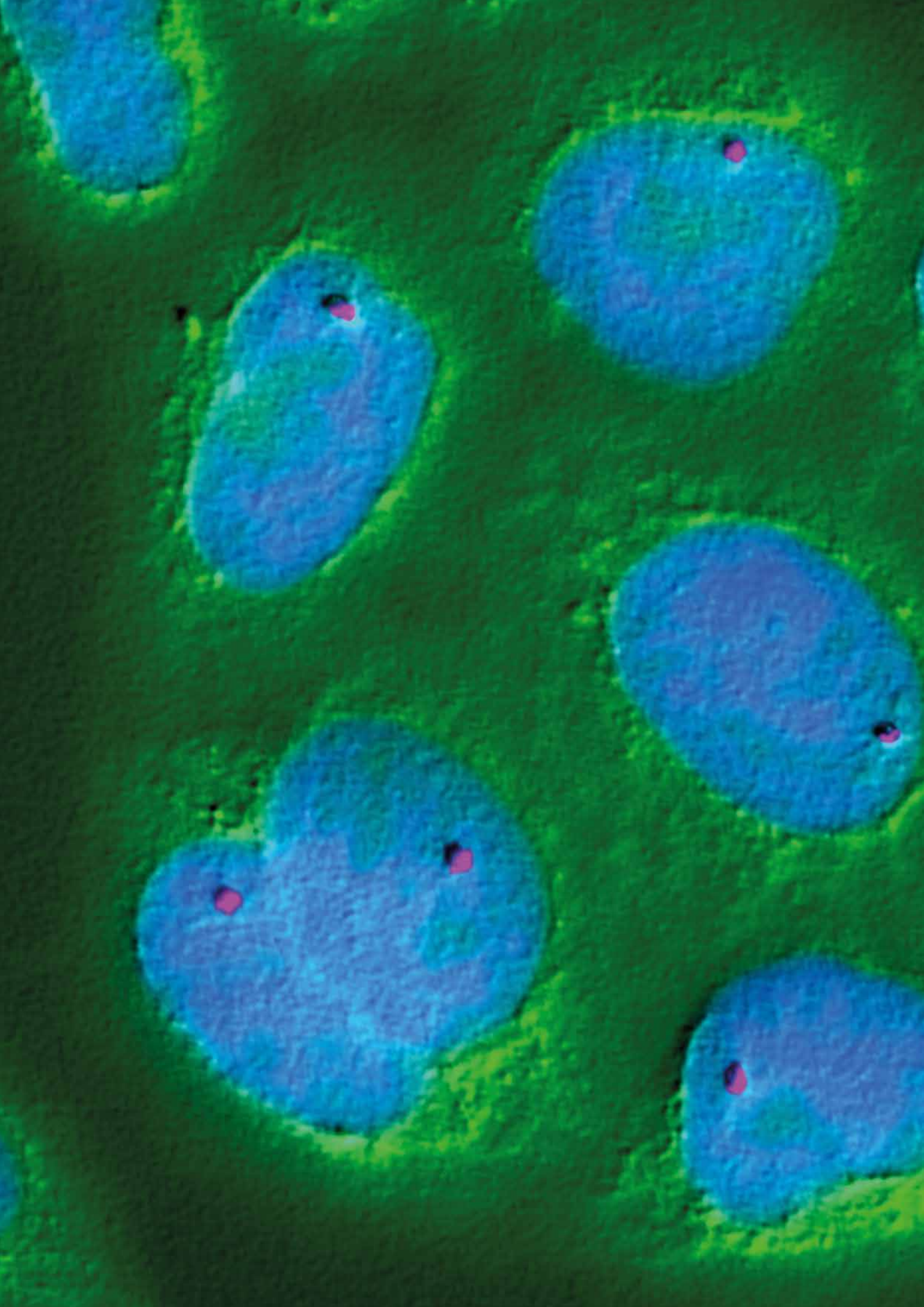

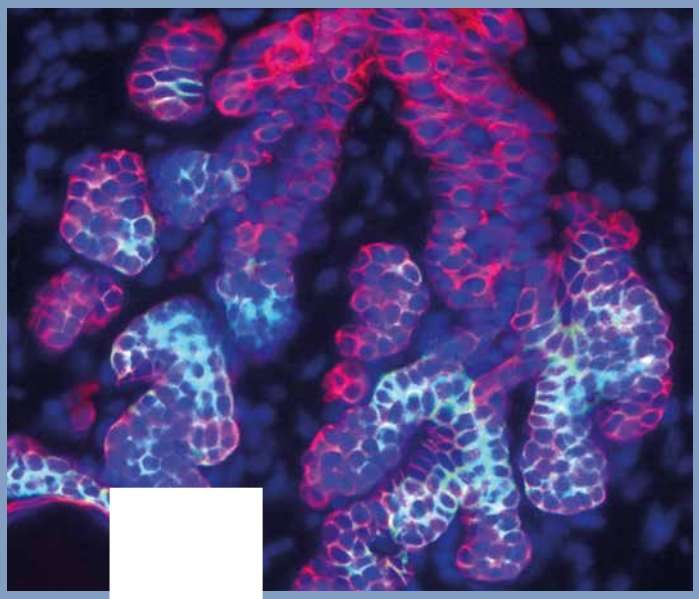

ANNUAL REPORT 2020

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welbio
Walloon Excellence in Life sciences

Avec le soutien de la Wallonie

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