ANNUAL REPORT 2022

wel Research Institute

CONTENTS

FROM "WELBIO" TO "WEL RESEARCH INSTITUTE"

The WEL Research Institute, formerly called WELBIO, is an inter-university research institute subsidized by Wallonia which supports strategic research of excellence within its departments and the translation of disruptive innovations for an impact in health and sustainable transition.

SIGNIFICANTLY INCREASED SUPPORT FOR STRATEGIC RESEARCH

The Walloon Government, on the proposal of the Minister of the Economy Willy Borsus, decided to significantly increase its support to strategic research within the framework of the Walloon Recovery Plan in two phases. The first, announced in 2021, more than doubled the funding for the existing WELBIO initiative in life sciences (€15 million/year) with a revised granting strategy, based on funding research teams rather than one-off projects, with an ambitious perspective of valorising results. The second, announced in October 2022, aimed at replicating the model by funding a second strategic axis (€9.75 million/year) in the area of disruptive technologies for an impact in sustainable transition.

In this context, the Walloon Government decided to restructure and rename our non-profit organisation WELBIO into the non-profit organisation WEL Research Institute, which now comprises two departments:

- **WELBIO** (Walloon Excellence in Life Sciences and Biotechnology): strategic research in the life sciences to translate discoveries into industrial applications in the health sector.
- **WEL-T** (Walloon Excellence in Technology): strategic research in engineering, chemistry and physics to translate breakthrough innovations into industrial applications aimed at sustainable transition.

KEY FIGURES
SINCE FIRST CALL IN 2010

€ 112M
INVESTED IN RESEARCH
IN LIFE SCIENCES

6
CALLS FOR RESEARCH
PROGRAMMES

88
RESEARCH PROGRAMMES

60
PRINCIPAL
INVESTIGATORS

INCLUDING
27
EARLY-CAREER
INVESTIGATORS

4
UNIVERSITIES

SCIENTIFIC
EXCELLENCE

730
PUBLICATIONS
INCLUDING

280
ARTICLES
IN PRESTIGIOUS
JOURNALS

20
EUROPEAN GRANTS
FOR €36M

TRANSLATION OF
SCIENTIFIC DISCOVERIES
INTO APPLICATIONS

PATENT APPLICATIONS
FOR
37
INVENTIONS

5
SPIN OFFS

1
LICENCE

11
INDUSTRIAL
COLLABORATIONS

WELBIO DEPARTMENT: EXTENDED TO 37 PROGRAMMES

CALL FOR WELBIO INVESTIGATOR PROGRAMMES

The revised funding strategy mentioned above was at the core of the 6th call launched in October 2021. A record number of applications was received compared to previous calls, with 85 proposals from universities from the Wallonia-Brussels Federation. The selection was carried out by an international and independent scientific committee organized in partnership with the FNRS. The results were announced in May 2022 with the funding of 23 new programmes, adding to 14 programmes still in progress. About a third of currently active WELBIO programmes are Starting grants aimed at supporting promising scientists at the start of their career (maximum 12 years post-PhD at the time of funding application).

HOMECOMING CEREMONY FOR WELBIO INVESTIGATORS

A ceremony was held on October 7th, 2022 at the "Moulins de Beez" to introduce the new WELBIO research programmes.

This was the occasion for our institution to present its strategy and its main development axes, with speeches by Jean Stéphenne, President, Vinciane Gaussin, Managing Director, as well as from Anne-Sophie Nyssen, President of the FNRS, Véronique Halloin, Secretary General of the FNRS, and Vinciane Grimard, representative of the office of the Minister Borsus.

The ceremony was also the opportunity to present some research programmes in different fields and at different stages of evolution. The enthusiastic testimonies of six WELBIO Investigators emphasized the importance of seizing opportunities to translate scientific discoveries in a societal impact and of receiving the support, in this process, from representatives of the WEL Research Institute in collaboration with host university technology transfer offices.

WELBIO INVESTIGATORS

ONCOLOGY

Advanced grants

BLANPAIN Cédric • Mechanisms controlling epithelial–mesenchymal transition related tumor heterogeneity.

CHARIOT Alain • tRNA modifying enzymes and their targets in immunity and cancer.

CLOSE Pierre • tRNA epitranscriptomics: a new vulnerability in cancer.

CONSTANTINESCU Stefan • Targeting mechanisms of pathogenic dimerization and activation of thrombopoietin receptor by mutant calreticulins and by JAK2 V617F in myeloproliferative neoplasms.

FERON Olivier • Tumor acidosis: a new lens to study drug-tolerant persister cancer cells and associated ferroptosis sensitivity.

MARINI Anna Maria • Mep-Amt-Rh transport proteins: control of membrane permeability to ammonium and proliferation.

NOEL Agnes • Innovative roles of uPARAP in lymphatic vessel morphogenesis and functions.

SONVEAUX Pierre • Understanding the metabolic control of brain-specific cancer metastasis.

VAN DEN EYNDE Benoît • Identification and characterization of new cancer immunotherapy targets discovered by in vivo genomic pool screening.

Starting grants

BINDELS Laure • Harnessing bacterial amino acid metabolites to tackle muscle wasting in cancer.

GURZOV Esteban • Early diagnosis: can protein tyrosine phosphatase activity predict obesity-induced hepatocellular carcinoma?

PASTUSHENKO Ievgeniia • Uncovering the role of H3K36 and H3K4 methyltransferases in cancer.

RAPINO Francesca • Translating into cancer: tRNA actors' role in cancer stem cells establishment.

VAN GASTEL Nick • Defining the Metabolic drivers of Clonal Hematopoiesis through Integrative single cell Profiling.

IMMUNOLOGY & INFLAMMATION

Advanced grants

GEORGES Michel • Systematic eQTL and CMap based identification of IBD predisposing genes and interacting drugs.

LUCAS Sophie • Targeting TGF-β1, β2 or β3 activation in auto-immunity and graft-versus-host disease.

MARICHAL Thomas • Deciphering the contribution of the myeloid-epithelial crosstalk to viral-induced exacerbations of chronic airway diseases: an inescapable path towards precision medicine and improved quality of life.

VERMIJLEN David • The third way of immune protection in human: development and function of γδ T cells in early life.

Starting grant

BELOQUI GARCIA Ana • Oral delivery of biologics for the treatment of gastrointestinal diseases.

NEUROSCIENCES

Advanced grants

DE KERCHOVE D'EXAERDE Alban • Maged1 in the thalamus, a key gateway to understand drug addiction and improve its treatment.

NGUYEN Laurent • Cell migration shapes cerebral cortex morphogenesis and function.

Starting grants

BOMMER Guido • Novel biochemical aspects of neurodegeneration in Parkinson's disease.

EL TAHRY Riem • Optimize VNS for refractory Epilepsy.

HANSEEUW Bernard • Beyond amyloid and tau pathology: On the road towards clinical trials modulating synaptic function in preclinical and symptomatic Alzheimer's disease.

MICROBIOLOGY & INFECTIOUS DISEASES

Advanced grants

COLLET Jean-François • Exploring the cell envelope of Escherichia coli, a compartment that is an attractive target for innovative biotechnological and biopharmaceutical approaches.
VANDERPLASSCHEN Alain • The use of Herpesvirus-fish models to unravel host-pathogen-environment interactions: a new paradigm in disease mitigation for aquaculture.

Starting grants

ALSTEENS David • Deciphering the molecular mechanisms of reovirus and rotavirus entry at the nanoscale.
HALLEZ Régis • Molecular characterization of the cellular processes targeted by the second messenger (p)ppGpp in bacteria.

CARDIOVASCULAR & METABOLIC/GENETIC DISEASES

Advanced grants

BALLIGAND Jean-Luc • Structural and functional characterization of Aquaporin-1 as a "peroxiporin" in cardiovascular tissue.
BERTRAND Luc • CARdiovascular DIseases and o-GlcnAcylatioN: the case of cardiac hypertrophy.
CANI Patrice • Identifying novel gut microbes and their active compounds to tackle diseases.
EIZIRIK Decio • Beta cell splicing signature in diabetes.
GILON Patrick • Study of the control of glucagon secretion and of its dysregulation in diabetes, and search for new therapeutic targets to restore a normal control in diabetes.
GOVAERTS Cédric • Capturing alternatives conformers of CFTR with nanobodies to understand pathogenesis of Cystic Fibrosis at the molecular level and to delineate new therapeutic routes.
VIKKULA Miikka • Towards novel treatments for primary lymphedema: from identification of genetic causes to in vivo modelling and preclinical trials.

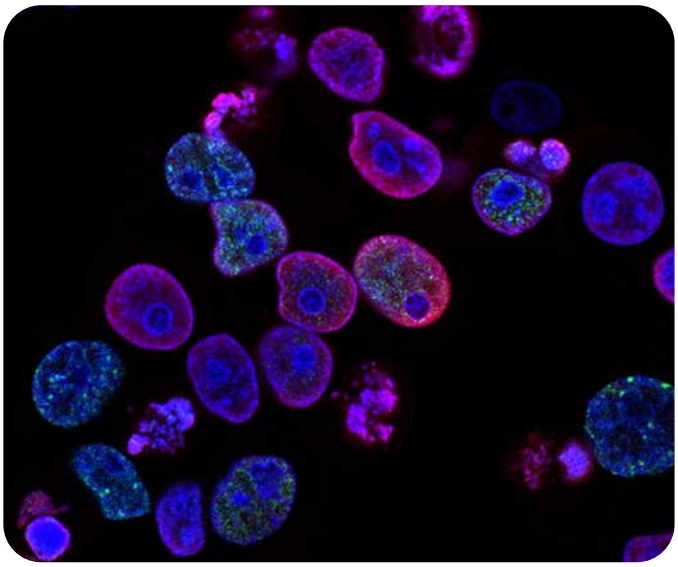
Starting grants

EVERARD Amandine • Identification of gut microbes and metabolites involved in the gut-to-brain axis controlling hedonic and reward system during food intake.
MARTIN Maud • Mechanistic understanding of microtubule function during angiogenesis.

WEL-T DEPARTMENT: SELECTION OF INITIAL PROGRAMMES

CALL FOR WEL-T INVESTIGATOR PROGRAMMES

The first call for "WEL-T Investigator Programmes" was launched on December 15, 2022. Results will be published in June 2023, after selection by an international and independent scientific committee organized in partnership with the FNRS. Selected WEL-T Investigators should demonstrate a combination of scientific excellence, an awareness of unmet needs in sustainable transition in their field, and a willingness of seeking opportunities to translate breakthrough discoveries into potential industrial applications.



SCIENTIFIC EXCELLENCE

ADVANCING KNOWLEDGE

WELBIO Investigators published 127 articles in 2022; including about a third in the most prestigious journals such as Nature, Blood, Gut, Science, Nature Communications and Science Advances. Here is a selection of articles to illustrate the internationally recognized groundbreaking work conducted by WELBIO Investigators in several fields of life sciences.

ONCOLOGY

GARP: from solid to liquid tumors

In 2009, Sophie Lucas and her team identified GARP as a novel immuno-oncology target expressed on immunosuppressive regulatory T-lymphocytes (Tregs). This led, a decade later, to the initiation of a clinical trial, currently underway, in solid tumors with an industrial partner. Here, Sophie Lucas teamed up with another WELBIO Investigator, Stefan Constantinescu, to demonstrate that the anti-GARP antibodies developed in the laboratory were also effective against some blood cancers. The group had indeed known for long that GARP was also expressed on platelets and megakaryocytes which are abnormally abundant in myeloproliferative neoplasms. In mice modeling this liquid tumor, the researchers found tumor burden reduction in response to GARP blockade. Unexpectedly, this effect depended on GARP on Tregs but not on tumoral megakaryocytes or platelets.

Lecomte et al, 2022, Blood

GARP: a long history of research with an impact in immuno-oncology

2004: Sophie Lucas and Pierre Coulie initiate a project to understand the functioning of regulatory T-lymphocytes (Tregs) which block immune responses in the event of cancer.

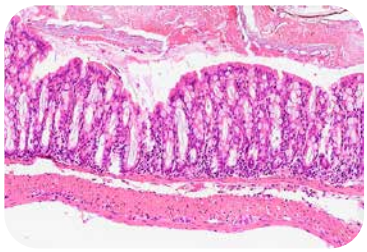
2009: Discovery of GARP expressed at the surface of Tregs.

2018: Understanding the role of GARP: the molecule acts as a messenger for Tregs, sending signals that sabotage immune responses against tumours. Sophie Lucas then succeeded in developing anti-GARP antibodies able to neutralize the blocking effect of GARP on the immune system. This important discovery was published in Science (Liénart et al, 2018, Science).

2020: The lab showed that anti-GARP antibodies in mouse models induced regressions of mouse tumors otherwise resistant to anti-PD-1 immunotherapy. These results were published in Nature Communications (de Streel et al, 2020, Nature Commun) and marked the launch of a phase I clinical trial, currently underway, with an industrial partner in patients with locally advanced or metastatic solid tumors (ClinicalTrials.gov: NCT03821935).

2022: The group demonstrated that the anti-GARP antibodies were also effective against some "liquid" tumors as a monotherapy (Lecomte et al, 2022, Blood).

Role of ELP3 in macrophage polarization



Macrophages are critical in anti-microbial and inflammatory activity in host defense as well as in the resolution of inflammation and wound healing. Their plasticity helps macrophages to acquire tailored activities within tissues and is often addressed through the concept of macrophage polarization. Alain Chariot and his team reported that translational reprogramming linked to macrophage polarization relies on Elp3, a tRNA-modifying enzyme involved in mRNA translation. Mechanistically, Elp3 promoted mRNA translation of multiples candidates, including Ric8b, a mTORC2 activator, and the synthesis of several mitochondrial proteins, with important consequences in metabolic reprogramming linked to macrophage polarization.

Chen et al, 2022, EMBO J

Secreted mutant calreticulins as rogue cytokines in myeloproliferative neoplasms

Calreticulin (CALR) resides in the endoplasmic reticulum and is involved in a spectrum of cellular processes. Mutant CALR proteins carry a novel C terminal amino-acid sequence and drive the development of myeloproliferative neoplasms. Mutant CALRs were shown to activate the thrombopoietin receptor (TpoR/MPL) in an autocrine fashion. Here, the lab of Stefan Constantinescu reported that mutant CALR proteins were secreted and could be found in patient plasma at levels up to 160ng/mL. Such secreted CALR mutant proteins activated TpoR/JAK-STAT signaling in cell lines and patient primary cells. The team proposed a model where mutant CALR proteins are secreted from CALR-mutated cells and can act as "rogue" cytokine to enhance the activation of TpoR of a nearby CALR-mutated cell in a paracrine fashion.

Petit et al, 2022, Cancer Immunol Res

T Cell–Mediated Targeted Delivery of Anti–PD-L1 Nanobodies

Monoclonal antibodies blocking immune checkpoints such as programmed death ligand 1 (PD-L1) have yielded strong clinical benefits in many cancer types. Still, current limitations are the lack of clinical response in many patients and the development of immune-related adverse events in some. As an alternative to PD-L1–specific antibody injection, the team of Benoit Van den Eynde developed an approach based on the engineering of tumor-targeting T cells to deliver intratumorally an anti–PD-L1 nanobody. In the MC38-OVA model, locally delivered anti–PD-L1 nanobody improved PD-L1 blocking at the tumor site while avoiding systemic exposure. This approach appears promising to overcome the limitations of immunotherapy based on PD-L1–specific antibodies.

Jeschke et al, 2021, Nature Cancer

Programming anti-cancer properties in T cells during their development

Within the immune system, γδT cells possess several characteristics that make them attractive cellular targets for immunotherapy in cancer. Using state-of-the-art single-cell technologies, the team of David Vermijlen identified pathways leading to the acquisition of anti-cancer properties during the development of these cells. These insights could pave the way for strategies targeting these cells to improve their anti-cancer properties.

Sanchez Sanchez et al, 2022, Nat Commun

NEUROSCIENCES

A link between sugar metabolism and Parkinson's disease

Guido Bommer's team discovered a highly reactive compound, cyclic 1,3-phosphoglycerate, generated during glycolysis and which has the potential to damage proteins and metabolites. They also found that the enzyme PARK7, present in most of our cells, can destroy this reactive compound, thereby preventing the damage from occurring. They observed that inactivation of PARK7 caused damages to accumulate in systems as diverse as human cells, mice and even flies. Some cases of Parkinson's disease are due to genetic inactivation of the PARK7 enzyme. Altogether, these findings offer a mechanistic explanation of how PARK7 deficiency may cause Parkinson's disease.

Heremans et al, 2022, Proc. Natl. Acad. Sci. USA

An innovative approach to treating brain diseases

The blood-brain barrier (BBB) is established during early embryogenesis and maintained throughout adulthood. The BBB regulates the exchange between the vascular system and central nervous system (CNS). Increased BBB permeability, due to age or injury, is involved in many neurological conditions through the leakage of harmful blood substances into the CNS. By studying the proteins controlling the formation of cerebral blood vessels during embryonic life, the team of Benoit Vanhollebeke identified the Gpr124/Reck membrane complex which enabled brain endothelial cells to selectively respond to Wnt7, thereby discriminating between multiple Wnt ligands (Science, 2018).

Here, the team showed that dysfunctional BBB in adult mice could be repaired by using the molecules that endogenously control its formation during embryogenesis. By modulating Gpr124/Reck in mouse models of brain pathologies, the researchers succeeded in restoring the BBB permeability, slowing down the progression of glioblastoma, or reducing the lesions following a stroke.

Martin et al, 2022, Science

The spin off NeuVasQ was founded in 2021 based on new insights into the molecular mechanisms maintaining the integrity of the blood-brain barrier (BBB) generated by the laboratory of Benoit Vanhollebeke (ULB). BBB dysfunction is a factor in many neurodegenerative disorders, such as Alzheimer's, as well as multiple acute neurological conditions like stroke and epilepsy.

With its EUR 20 million Series A, NeuVasQ aims at identifying the most promising indications for clinical trials, focusing on a range of neurodegenerative disorders and acute neurological disorders. As part of these exploratory studies, NeuVasQ will also consider various innovative therapeutic modalities, including gene and mRNA therapies.

CARDIOVASCULAR & METABOLIC / GENETIC DISEASES

Genetic cause identified for a severe form of lymphedema

Central Conducting Lymphatic Anomaly (CCLA) is a severe, rare disease in which lymph fluid accumulates in spaces around the lungs, the heart, as well as in the feet and legs. Signs and symptoms typically present in children and teenagers, but the disorder can also result in fetal or perinatal death. The cause remains unknown for most of the cases. The lab of Miikka Vikkula discovered that patients had mutations in a gene called MDFIC. By generating a novel mouse model, they were able to reveal a crucial role for this gene in the development of lymphatic vessel valves. The researchers also found how the genetic mutations lead to CCLA, by identifying the mechanism by which MDFIC controls collective cell migration, an important early event during the formation of lymphatic vessel valves. This work will improve the genetic diagnosis of CCLA and may ultimately lead to the development of novel therapeutics able to combat this life-threatening disease.

Byrne et al, 2022, Sci Transl Med

Diabetes: At the heart of the 'battle' leading to beta cell loss

Type 1 Diabetes (T1D) is caused by a misunderstanding from our immune system that attacks the insulin-producing pancreatic beta-cells. Pioneering research by Decio Eizirik and his team introduced a paradigm shift in the field: the distorted "dialogue" between the beta cells and the immune system could be caused by beta-cells' neoantigens generated by alternative splicing and their presentation in the context of HLA class I to the immune system. Here, the team discovered that the expression of the transcriptional regulator NLRC5 is increased in beta-cells from pancreas donors with T1D and that the cytokine IFNgamma up-regulates NLRC5 expression in human beta-cells. This double role of NLRC5 on HLA class I expression and regulation of alternative splicing suggests that this transcription factor plays a pivotal role both in the generation of neoantigens and in their presentation to the immune system.

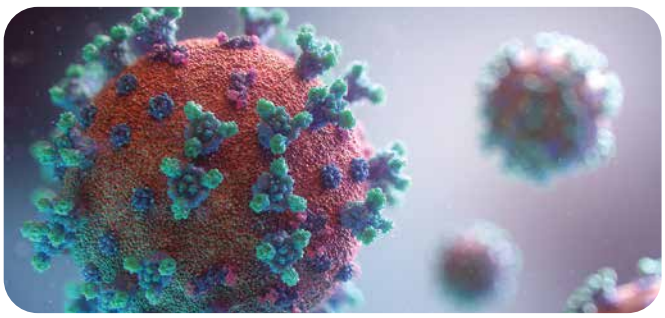
Szymczak et al, 2022, Science Advances

MICROBIOLOGY & INFECTIOUS DISEASES

Blocking spike captors to counter Covid

Sugar residues are present on the surface of our cells and play a role in cell recognition. Viruses leverage these sugars to facilitate their attachment and entry into their target cells thereby initiating their infection. David Alsteens and his team identified a variant of these sugars (9-O-acetylated) that interacted more strongly than other sugars with the S protein of SARS-CoV-2. The scientists developed multivalent structures (or glycoclusters) with multiple 9-O-acetylated sialic acids which can block in vitro both binding and infection by SARS-CoV-2. If the virus does not attach to cells, it cannot enter and therefore dies. Within the context of the Covid-19 pandemic, the various vaccines primarily addressed the SARS-CoV-2 mutations. Here, the glycoclusters developed by the team has the potential to act independently of the virus mutations.

Petitjean et al, 2022, Nat Commun



AWARDS & RECOGNITION

Scientific advances achieved by WELBIO Investigators are the results of many years of research. The fact that WELBIO Investigators have received prestigious scientific awards year after year is a testimony to the excellence of their work. In 2022...

Ana Beloqui Garcia (UCLouvain) received the Galien Prize awarded by the "Journal du Médecin" during a ceremony attended by the Minister of Social Affairs and Public Health, Frank Vandenbroucke, and the General Administrator of the Inami, Benoît Collin.

Luc Bertrand (UCLouvain) was elected Member of the Council of the European section of the International society for Heart Research (ISHR).

Laure Bindels (UCLouvain) was awarded the Collen-Francqui Research Professor Mandate (2022-2025), an opportunity provided by the Foundation to a researcher of an exceptionally high level to dedicate himself/herself to research, with a reduced teaching assignment.

Cédric Blanpain (ULB) was the winner of the 2022 Mike Price Gold Medal Award from the European Association for Cancer Research, a biennial award recognizing a senior researcher who has made exceptional contributions to the progress of cancer research in Europe.

Guido Bommer (UCLouvain) was awarded the 2022 Vicomtesse Valine de Spoelberch prize from the Queen Elisabeth Medical Foundation during a ceremony held in the presence of H.R.H. Princess Astrid. He was also the holder of the Bauchau Chair at the University of Namur in 2022.

Patrice Cani (UCLouvain) received the AstraZeneca Foundation Prize and the medal of the Royal Academy of Medicine of Belgium in honor of his seminal discoveries over 20 years of research on the intestinal microbiota, obesity and type 2 diabetes.

Pierre Close (ULiège) was the recipient of the 2022 Worldwide Cancer Research (WWCR) award.

Stefan Constantinescu (UCLouvain) was elected President of the Belgian Royal Academy of Medicine for the year 2022.

Decio Eizirik (ULB) was awarded the George Eisenbarth Memorial Lecture from the Network for Pancreatic Organ Donors with Diabetes (nPOD), an award recognizing researchers working to discover the causes of the disease and new therapies for type 1 diabetes. The lecture will be given at the annual meeting of the nPOD in Florida, USA, in February 2023.

Esteban Gurzov (ULB) received the 2022 Scientific Award from the AstraZeneca Foundation in the category "Gene editing as a therapeutic approach".

Bernard Hanseeuw (UCLouvain) received the René de Cooman Prize awarded to a Belgian researcher under 45-year-old having made a prominent contribution to the problem of aging.

Thomas Marichal (ULiège) received the Biomedical Prize from the Baillet Latour Fund, awarded for the first time in 2022, and aiming at supporting the careers of promising young researchers in the field of biomedical sciences for a period of five years.

Agnès Noël (ULiège) received a lifetime achievement recognition on the occasion of the 50th anniversary of the BSCDB (Belgian Society of Cell and Developmental Biology).

Francesca Rapino (ULiège) was elected at the collegium of the Royal Academy of Belgium as one of the first 16 members of this new organism. The collegium is composed of young (under 40-year-old) scientists, artists or prominent personalities in the Wallonia-Brussels Federation who will relay their research and work through the Academy's infrastructure.

SOCIETAL IMPACT

RESEARCH TEAMS

To date, a total of 88 research programmes led by 60 Principal Investigators have been, or are still being, supported by the WEL Research Institute. Principal Investigators receive significant support with up to 1.4 Mio EUR awarded for 4-year programmes that can be renewed by applying to subsequent calls for projects. This funding strategy provides the opportunity for researchers to develop ambitious research programmes that address important unmet needs in their fields, including, for the WELBIO department, in oncology, immunology & inflammation, cardio-metabolic diseases, neuroscience, microbiology & infectious diseases.

This funding also allows Principal Investigators to support scientific and technical staff in their teams. To date, approximately 620 scientists and 200 technicians have been supported directly (via their salaries) or indirectly (via operating costs).

INTELLECTUAL PROPERTY

The mission of the WEL Research Institute is to accelerate the translation of scientific discoveries into a societal impact. In cooperation with the host universities and their technology transfer offices, a whole chain of support for the Principal Investigators has been put in place to develop the potential of their research programme and the transfer of results emerging from this research towards the industry.

A total of 37 patent applications have been filed to date, including 8 in 2022. 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

WO/2020/254083:
Lipid nanocapsules charged with incretin mimetics

WO/2021/144473:
Genetically modified bacterium with altered envelop integrity and uses thereof

WO/2021/197574:
Rel/RelA/SpoT small molecules modulators and screening methods

WO/2021/214129:
Alpha-2 Adrenergic Receptor Agonists for the prevention and/or the treatment of cancer

WO/2021/214175:
Alpha-2 Adrenergic Receptor Agonists for the prevention and/or the treatment of spleen disorders

WO/2022/013328:
Method for determining sensitivity to an antineoplastic agent

WO/2022/207588:
Protein tyrosine phsophatases as biomarkers for hepatocellular carcinoma and uses thereof

@ULiège

VALUE CREATION IN THE WALLOON REGION

A total of 5 spin off have been created to date based on results that emerged from WELBIO research programmes. These spin offs are anchored in the Walloon region, including in the Brussels South Charleroi BioPark, Mont-Saint-Guibert and in Liège. They have raised a total of €45M in pre-seed and seed funding. They also generated employment for 21 full-time equivalents.

THERAtRAME: ARTIFICIAL INTELLIGENCE TO FIGHT CANCER

THERAtRAME SA, a new spin-off of the University of Liège and the WEL Research Institute, announced in September 2022 having secured €4.5M seed financing to develop novel cancer medicines in the field of tRNA epitranscriptomics.

The spin off, incubated at the Belgian start-up accelerator VentureLab since 2020, was founded based on new insights in tRNA epitranscriptomics resulting from over a decade of fundamental research in the laboratories of Alain Chariot, Pierre Close and Francesca Rapino, who are all three WELBIO Investigators at the GIGA Biomedical Research Institute (ULiège). Their work revealed that cancer cells could seize control of the protein synthesis process by making specific modifications in the tRNA, an essential component of the protein translation machinery, to support the cells' rapid growth, metastasis and resistance against existing drugs. This new discovery exposed previously underexplored vulnerabilities in cancer that are now being targeted by THERAtRAME's drug discovery platform to develop first-in-class small molecule therapeutics. In addition, THERAtRAME plans on leveraging its proprietary artificial intelligence (AI) algorithms to identify the most promising oncology indications for clinical studies.

ADMINISTRATIVE AND FINANCIAL RESOURCES

GOVERNANCE OF WELBIO ASBL

The Board of Directors of the non-profit organization (a.s.b.l.) WEL Research Institute comprises representatives from the industry, academia, and of Ministers of the Walloon Region.

Board of Directors

- President: Jean Stéphenne
- Vice-President: Pierre Lekeux

Representatives of Ministers of the Walloon Region:

- Vinciane Grimard, representing the Minister for the Economy
- Catherine Dath, representing the Minister for research
- Christopher Sortino, representing the Minister-President

Representatives of the financial and industrial sector

- Jean Stéphenne, Member of the board of several biotech companies
- Gwenaëlle De Keyser, Head of Public Private Partnerships, UCB BioPharma
- Joëlle Van Malderen, Head of AWA Benelux and Head of AWA Switzerland, AWA
- Marc Van Den Neste, Founder and administrator, EKOSYS

Academic experts

- Pierre Lekeux, Professor, ULiège
- Philippe Lambin, Professor, UNamur

Representatives from the universities in the French Community:

- Jean-Christophe Renauld, Prorecteur Recherche, UCLouvain
- Marius Gilbert, Vice-recteur à la Recherche et à la Valorisation, ULB
- Ruddy Wattiez, Vice-recteur à la Recherche, UMons

Secrétaire Général du Fonds de la Recherche Scientifique (F.R.S.-FNRS)

- Véronique Halloin, Secrétaire Générale

Representative of the Walloon Public Service

- Jean-François Heuse, Inspecteur Général

THE FUNDS FOR STRATEGIC FUNDAMENTAL RESEARCH (FRFS)

The Fund for Strategic Fundamental Research (FRFS) is an Associated Fund of the F.R.S.-FNRS. Its purpose, within the framework of a mission assigned by the Walloon region, is to fund fundamental research of excellence in strategic axes determined by the Walloon region. These strategic axes are "improved health" and "sustainable transition".

The Walloon Government established WELBIO ("improved health") and WEL-T ("sustainable transition") as both departments of the WEL Research Institute and strategic axes of the FRFS.

The WEL Research Institute and the FRFS complement each other in the implementation of the mission assigned by the Walloon region. The FRFS carries out the selection and financial management of the research programmes that make up the WELBIO and WEL-T departments. The WEL Research Institute establishes the overall strategy for the calls and drives the translation of scientific discoveries into applications with a societal impact.

MANAGEMENT REPORT

This report concerns the 12th fiscal year, which covers the period from 1 January 2022 to 31 December 2022.

For the financial year 2022, the agreement signed by the FNRS and WELRI on November 04, 2022 is applicable to the management of the funding allocated to WELRI as follows:

- The total "WELRI Amount" in 2022 amounts to €2,389,800.
- WELRI submitted a declaration of claims to the FNRS in the amount of €400,000.00 to cover the costs incurred during the period from 01/01/2022 to 31/12/2022.
- The "WELRI Balance", corresponding to the difference between the "WELRI Amount" and the claim declaration, amounts to €1,989,800. This balance, on the FNRS account, remains allocated in proportion to the original allocation attributed by the Walloon region between WELBIO and WEL-T.

WELBIO has published its annual accounts with the National Bank of Belgium since the 2017 financial year. Although WELBIO can be considered as a micro non-profit organization, it has not opted for a simplified accounting system and has decided to maintain the publication of its annual accounts with the National Bank of Belgium.

ASSETS

Tangible fixed assets amount to €3,538.29 and relate to computer equipment.

Financial fixed assets amounted to €7,497.00 and concerned the guarantee on rented offices in Wavre.

Accounts receivable within one year amounted to €400,000.00 and consist of a statement of claim due from the F.R.S. - FNRS.

Cash investments amounted to €2,107,274.09 in the form of two reserves to distribute the remaining liquidity of WELRI.

These liquid cash sums were allocated as follows:

Operating costs (2023)	€468,300.00
Bridge fund	€1,638,974.09
	€2,107,274.09

A BPAID account has been created to cover various small expenses and the remaining balance is €143.11.

Adjustment accounts amounted to €7,473.19 and concerned charges that were to be carried forward for the amount of €7,280.30.

Total assets amounted to €2,525,925.68.

LIABILITIES

The balance as of December 31st, 2021, under the heading of "other allocated funds", amounted to €2,473,432.25.

The result for the fiscal year was a profit of €9.113,10.

The balance as of December 31st, 2022, for other allocated funds, amounted to €2,482,545.35.

Supplier debts amount to €14,957.91 and consist of €14,957.91 of trade payables.

The estimated tax liability for 2022 is €204.18.

Provisions for holiday payments amount to €28,162.94.

Other debts amount to €50.00 and relate to an administrator current account of €50.00.

Adjustment accounts amount to €5.30 and relate to expenses to be charged.

Total liabilities amounted to €2,525,925.68.

RESULT

The grant for 2022 operating costs amounted to €400,000.00.

Membership dues were received for a total amount of €200.00.

Miscellaneous services and assets amounted to €96,600.17 and primarily concern operating costs, rent and fees.

Salaries and social contributions amounted to €226,039.21.

The estimated tax liability amounted to €204.18.

Net bank interest, after withholding tax, amounted to €275.98.

Financial charges amounted to €3,075.08.

The result for the fiscal year is a profit of €9,113.10.

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NOTES

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