

From Research to Impact

The WEL Research
Institute's Commitment
to Excellence

2023

Annual Report



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The WEL (Walloon Excellence) Research Institute or WELRI, formerly known as WELBIO, is an inter-university research institute subsidised by the Walloon region Government. With the aim of being a world-renowned research institute, it is committed to strategic research of excellence and the translation of the resulting discoveries into social and economic impact.

The WEL Research Institute's activities are channelled through two main departments:

- WELBIO: Life sciences research dedicated to the advancement of medical, pharmaceutical, and veterinary biotechnology.
- WEL-T: Research in engineering, chemistry and physics dedicated to advancing sustainable transition.

Strategic developments in 2023

A new department, WEL-T, was established in 2023 based on the decision of the Walloon government to support strategic research to generate breakthrough innovations in sustainable transition. With annual funding of €9.75 million, the first call for the selection of researchers for this new department was launched at the end of 2022.

On 1 October 2023, the 14 selected Investigators started their WEL-T programmes in the fields of sustainable energy, circular materials, new materials and sustainable production methods. We look forward to their scientific discoveries in the years to come. They join the 37 investigators of our historic WELBIO division.

Commitment to scientific excellence with a social and economic impact

Investigators for the WEL Research Institute are selected by an international scientific committee on the basis of a 4-year research programme submitted in response to calls for proposals. The organisation of the annual calls, which alternate between the WELBIO and WEL-T funding instruments, and the financial management of the research contracts are entrusted to the FRFS, a specialised fund of the FNRS.

Investigators receive funding on the basis of a 4-year research programme.

Through the WELBIO and WEL-T funding instruments, the Walloon Region allocates significant resources – over several years – to the Investigators within the WEL Research Institute to develop ambitious

research programmes and achieve major scientific breakthroughs. These programmes are a pillar of the Investigators' laboratory and are flexible so that the scope of the research can be adapted over time as needed. This funding strategy enables researchers to develop ambitious programmes that address critical unmet needs in their fields.

Two funding categories have been established to support Investigators based on their career progression:

- Advanced Investigators are established researchers with a proven track record of significant achievements and are recognised leaders in their field due to the originality and significance of their research contributions.
- Starting Investigators are in the process of establishing their own independent research teams. With less than 12 years of postdoctoral experience, they demonstrated scientific independence and are initiating ground-breaking research programmes.

Our Investigators are selected for their scientific excellence, their awareness of unmet needs in their field of research, and their willingness to translate research discoveries into applications with social and economic impact. This commitment is underpinned by a robust intellectual property valorisation process and individualised support provided to our Investigators, in collaboration with representatives from the Knowledge Transfer Office (KTO) of our partner universities.

Institutional framework & governance

- University partnerships: The Institute works closely with five universities in the Wallonia-Brussels Federation: UCLouvain, ULB, ULiège, UNamur and UMONS. The researchers of the WEL Research Institute are affiliated to these universities, which reinforces the dual nature of their research commitment.
- Governance and management: Governed by a General Assembly and a Board of Directors, the Institute's leadership includes representatives from industry, academia and the Walloon Region, ensuring effective oversight of all key stakeholders.



CHAPTER

Highlights of 2023



Philippe Denoël, Head of External Vaccines R&D at GSK takes over from Jean Stéphenne as chairman.

Chairman of the Board

After a 12-year mandate, Jean Stéphenne chaired his last Board meeting at the WEL Research Institute in June 2023. We deeply appreciate Jean Stéphenne's visionary leadership and his support for innovation within the Walloon ecosystem, which has significantly shaped the Institute since its inception.

Philippe Denoël, Head of External Vaccines R&D at GSK, has succeeded Jean Stéphenne as Chairman of the Board. Industry support for basic research, a hallmark of Jean's presidency and now continued under Philippe, remains a cornerstone of our institution.

Growth of the Scientific Teams

In 2023, the WEL Research Institute consisted of 51 Investigators, including about a third of whom were in the Starting category, which provides a springboard for scientists at the beginning of their careers. The number of Investigators in our Institute has grown dramatically in recent years, thanks to Walloon government's decision in 2021 to significantly increase its support for strategic research as part of the Walloon Recovery Plan.

- The first phase more than doubled the annual funding for the existing WELBIO funding instrument to €15 million from 2021. This led to a significant expansion in the number of Investigators in the WELBIO department in 2022.
- The subsequent phase, announced in October 2022, aimed to replicate this model by creating the WEL-T strategic axis in disruptive technologies, with a focus on sustainable transition and annual funding

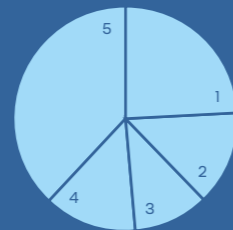
of €9.75 million. This led to the selection of 14 additional Investigators who joined the newly created WEL-T department within our Institute in 2023.

The 7th call for WELBIO Investigator Programmes was launched on 12 September 2023 with a total of 68 applications received.

51 Investigators with an active programme in 2023

2023 Highlights

Strategic research in fields of major importance for our society



- 1/ Cardiovascular, Metabolic & Genetic Diseases
- 2/ Immunology & Inflammation
- 3/ Microbiology & Infectious Diseases
- 4/ Neurosciences
- 5/ Oncology

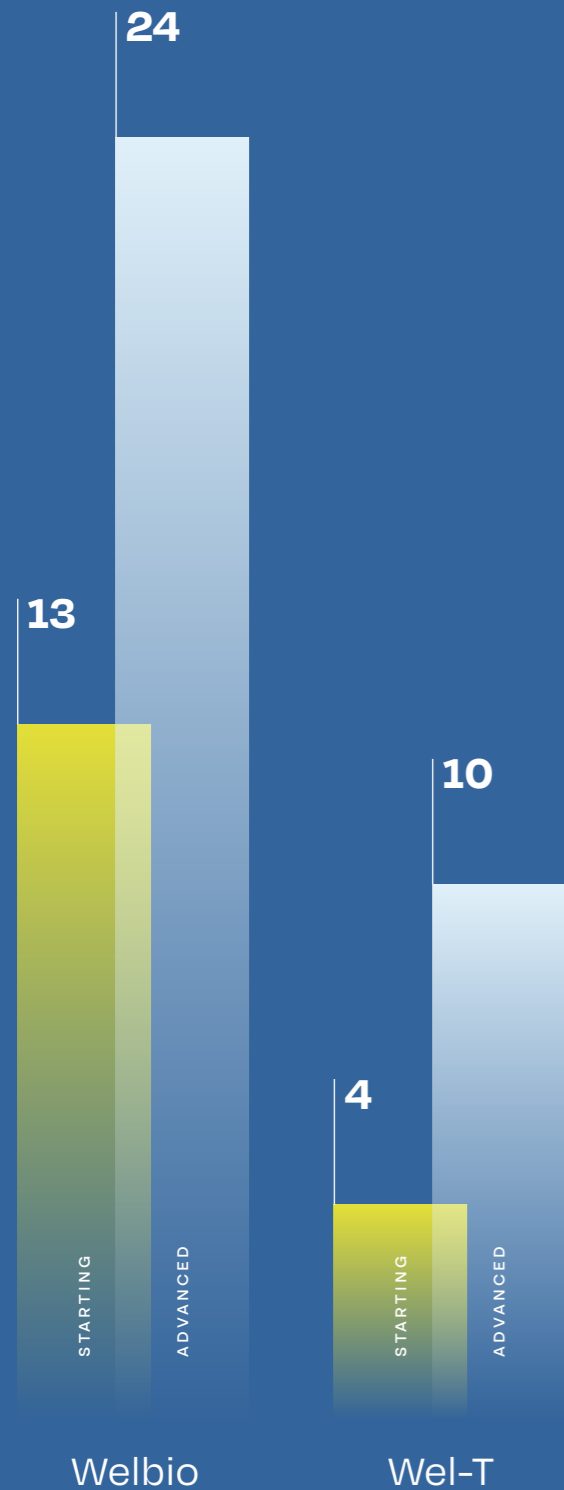


- 1/ Sustainable Energy Systems
- 2/ Circular Materials
- 3/ New Materials
- 4/ Agile and Safe Production Methods

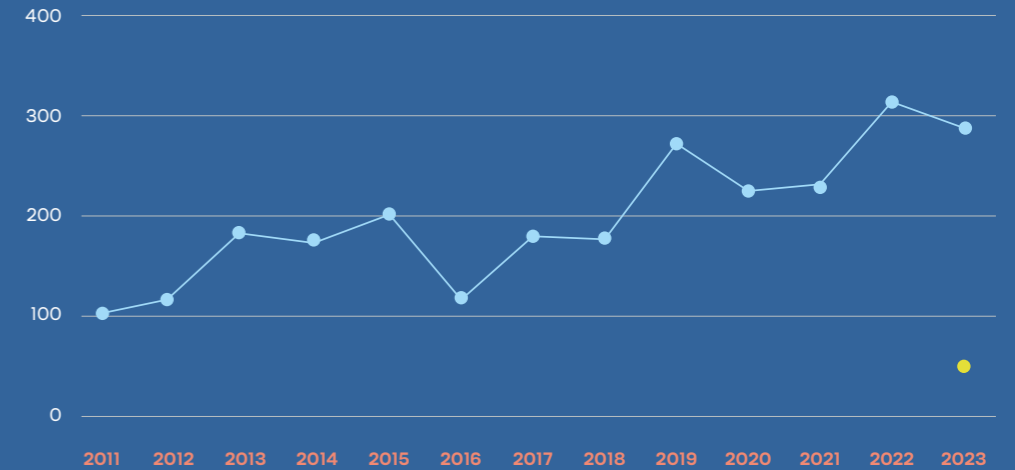
Annual funding increased to

With the addition of the WEL-T strategic axis in disruptive technologies (€ 9,75 Mio/year) to the existing WELBIO axis in life sciences (€ 15 Mio/year), the Walloon region has considerably increased the resources allocated to strategic research.

€24.75 Mio

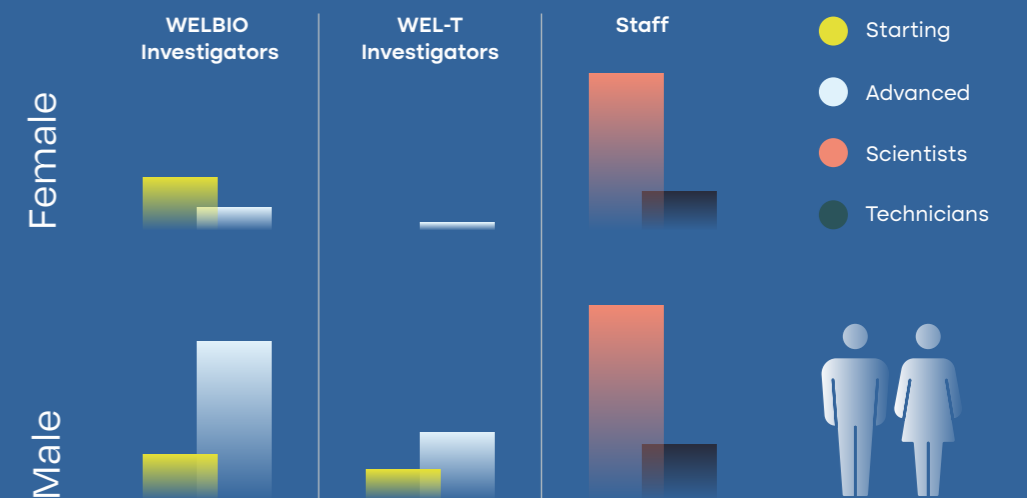


Growth of the scientific teams



Supported staff in 2023

Our Governing Board is committed to attracting junior talents and promoting gender balance among Investigators at the WEL Research Institute.



Scientific excellence

Fundamental research is driven by sheer scientific curiosity and its results lead to a better understanding of the natural world and create new knowledge. As the World Economic Forum states (when asked about the value of funding fundamental research):

"The history of innovation shows that freedom for researchers to pursue their creative ideas, without strings attached, has been vital for countless discoveries, many of which have led to breakthrough technologies with enormous benefits for society and that have boosted the economy."¹

Investigators at the WEL Research Institute conduct cutting-edge research programmes, the results of which are published in top-tier journals like Nature or Science, or in more specialised journals or conference proceedings in their field. In 2023, 60 articles were published, bringing the total number of publications since the creation of the Institute to 814, with an average of 40% in prestigious journals. These publications, coming mainly from our more established WELBIO department as the new WEL-T department was only created in 2023, have advanced our understanding in fields of major importance for our society such as oncology; cardiovascular, metabolic & genetic diseases; immunology & inflammation; neurosciences; and microbiology & infectious diseases.

Research freedom drives innovation, resulting in societal & economic benefits.



National and international recognition through awards and grants are also key measures of scientific excellence.

In 2023, our Investigators were honoured with 9 scientific awards and secured 22 M€ in European (ERC, H2020, Marie Skłodowska-Curie Actions) and other international grants. Since the creation of the Institute, the Investigators have been awarded a total of 43 M€ in European and other international grants.

¹ World Economic Forum: Quote from <https://www.weforum.org/agenda/2023/01/here-s-why-fund-fundamental-scientific-research-davos2023/>

Societal and economic impact

The WEL Research Institute is committed to developing an environment, and providing support, to facilitate the transition of research from the laboratory to the marketplace. This is why the WEL Research Institute prioritises regular meetings with its Investigators, in close collaboration with the universities of the Wallonia-Brussels Federation and their Knowledge Transfer Offices (KTOs). The aim is to identify and protect unexpected results that could lead to innovation, and to develop strategies for transferring intellectual property to industry for the ultimate benefit of society.

- A total of 42 patent applications had been filed by 2023, including 1 new application within the year, of which 31 patent families were still active. Half of these are in the field of oncology, an area historically strongly represented in our WELBIO department.
- One new spin-off was created in 2023, an oncology drug discovery company. This brings the total number of spin-offs created based on results generated by programmes within the WEL Research Institute to 6. These spin-offs are based in the Walloon region and have secured a total of €84 million in funding and created 32 jobs.
- Research impacted patients with the announcement in 2023 that AbbVie had advanced ABBV-151 (ARGX-115) into Phase 2 trials for solid tumours. This antibody, designed to block GARP and boost the immune response against tumours, is based on research by Pierre Coulie and Sophie Lucas at UCLouvain and was co-developed with Argenx through the preclinical validation phases.

The intellectual property emerging from fundamental research may not have the necessary levels of technological maturity before being transferred to an industrial partner. The Bridge Fund is a funding instrument managed by the WEL Research Institute with the sole purpose of supporting the next critical research steps that will significantly increase the likelihood of commercialisation of this intellectual property.

- By the end of 2023, a total of 7 Bridge Fund awards had been made for a total of €913,610, including an award of €150,000 in 2023, in the field of oncology.

Patents

42

A TOTAL OF 42 PATENT APPLICATIONS HAD BEEN FILED BY 2023

Articles

814

NUMBER OF PUBLICATIONS SINCE THE CREATION OF THE INSTITUTE

CHAPTER

Scientific excellence

The cutting-edge work carried out by the Investigators and their teams is internationally recognised, as evidenced by the publication of their ground-breaking results in leading scientific journals.

The scientific advances achieved by WELRI Investigators are the culmination of many years of research and form the basis for securing highly competitive grants at both European and international levels. The excellence of their work is further underlined by numerous prestigious scientific awards received by the WELRI Investigators.

In 2023:

- 60 articles were published, with around 40% appearing in prestigious journals such as Nature and Nature Communications.
- The Investigators secured around €22 million in European and international grants, including approximately €13 million from the European Research Council (ERC) and €5 million from other European funding initiatives such as Horizon 2020 and the Marie Skłodowska-Curie Actions.

- The excellence of the work led by the Investigators and their teams has been recognised by 9 major national and international scientific distinctions.

The following sections present a selection of scientific highlights to illustrate the internationally recognised ground-breaking work being carried out by WELRI Investigators in various fields of life sciences and technology.

01 WELBIO

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Life sciences
for impact in
health

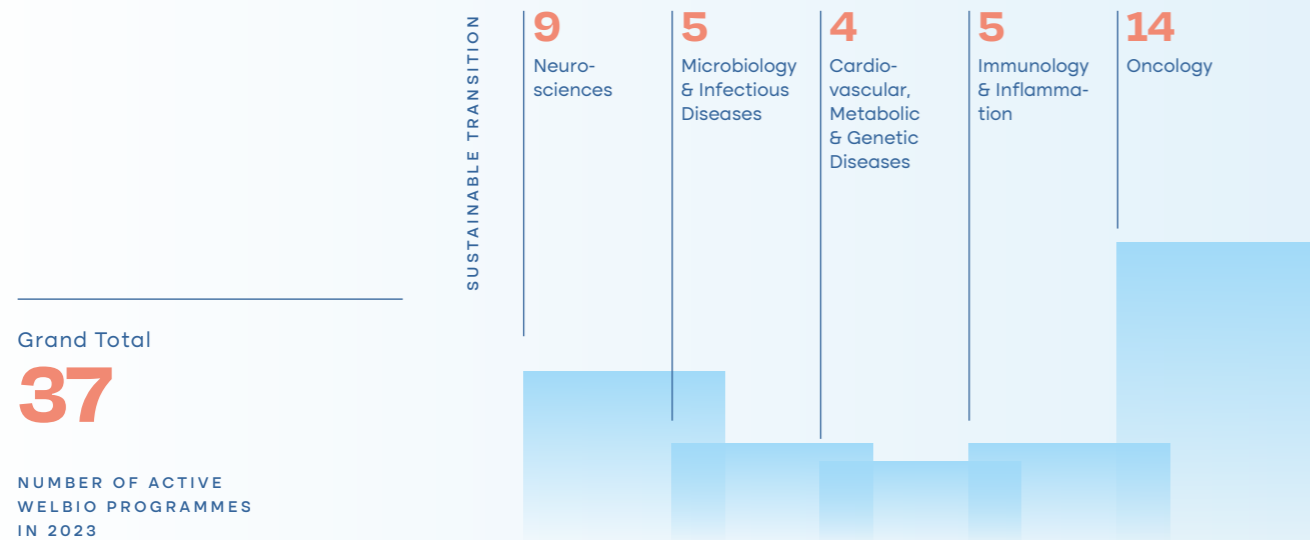
WELRI

WELLBIO

The WELBIO department

In 2023, the major societal challenges addressed by the 37 active programmes in the WELBIO (Walloon Excellence in Life Sciences) department were oncology (~40%), cardiovascular, metabolic & genetic diseases, immunology & inflammation, neurosciences, and microbiology & infectious diseases.

Number of active WELBIO programmes in 2023



As of 2023, the WEL Research Institute has supported a cumulative total of 88 WELBIO research programmes. Oncology represents ~40% of the total portfolio of programmes supported to date.

Oncology

Oncology focuses on understanding the possible causes of various types of cancer, with the aim of discovering new treatments, enhancing diagnosis, and improving patient outcomes.

Investigators

Advanced

BLANPAIN Cédric - ULB

Mechanisms controlling epithelial-mesenchymal transition related tumour heterogeneity

CHARIOT Alain - ULiège

tRNA modifying enzymes and their targets in immunity and cancer

CLOSE Pierre - ULiège

tRNA epitranscriptomics: a new vulnerability in cancer

CONSTANTINESCU Stefan - UCLouvain

Calreticulin and TpoR in Myeloid cancer

FERON Olivier - UCLouvain

Tumour acidosis: a new lens to study drug-tolerant persister cancer cells and associated ferroptosis sensitivity

MARINI Anna Maria - ULB

Mep-Amt-Rh transport proteins: control of membrane permeability to ammonium and proliferation

NOEL Agnes - ULiège

Innovative roles of uPARAP in lymphatic vessel morphogenesis and functions.

SONVEAUX Pierre - UCLouvain

Understanding the metabolic control of brain-specific cancer metastasis

Starting

VAN DEN EYNDE Benoît - UCLouvain

Identification and characterisation of new cancer immunotherapy targets discovered by in vivo genomic pool screening

BINDELS Laure - UCLouvain

Harnessing bacterial amino acid metabolites to tackle muscle wasting in cancer

GURZOV Esteban - ULB

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

PASTUSHENKO Ievgeniia - ULB

Uncovering the role of H3K36 and H3K4 methyltransferases in cancer

RAPINO Francesca - ULiège

Translating into cancer: tRNA actors role in cancer stem cells establishment

VAN GASTEL Nick - UCLouvain

Defining the metabolic drivers of clonal hematopoiesis through integrative single cell profiling

Representative publications

RHOJ: CONTROLLING RESISTANCE TO CHEMOTHERAPY

Chemotherapy resistance is one of the main causes of treatment failure in cancer patients. The team of **Cédric Blanpain** showed that RHOJ expression was particularly high in chemotherapy-resistant cells and that silencing RHOJ restores the sensitivity of cancer cells to chemotherapy. The team then explored the mechanism of action and discovered that RHOJ can activate the DNA damage repair pathway induced by chemotherapy, allowing cancer cells to repair the DNA lesions and escape cell death.

Debaugnies et al (2023) Nature

ELUCIDATING HOW MUTATIONS IN CALRETICULIN INDUCE BLOOD CANCER

Since 2000, **Stefan Constantinescu's** research team has been mapping the molecular basis of myeloproliferative neoplasms, a group of blood cancers associated with complications such as thrombosis and leukaemia. In 2013, the group discovered that a mutant form of calreticulin, a protein that normally found inside the cells, is secreted into the blood and can then bind and activate the thrombopoietin receptor (TpoR) in an uncontrolled manner thereby causing a form of myeloproliferative neoplasm. Here, the team provided an extremely precise mapping of the binding sites between the mutated calreticulin and the TpoR receptor, answering a question that had puzzled scientists for many years: why does mutated calreticulin bind to the thrombopoietin receptor and not to any other proteins?

Papadopoulos et al (2023) Nat Commun

AN INNOVATIVE APPROACH THAT COULD IMPROVE THE EFFECTIVENESS OF CANCER IMMUNOTHERAPY

Immune checkpoint inhibitors have changed the landscape in cancer therapy with their ability to promote tumour rejection and provide long-term clinical benefit in a number of cancer patients. However, most patients do not respond. New research by **Benoit Van den Eynde's** team has revealed that drugs previously used to treat hypertension could offer an interesting way to fight cancers that are resistant to immunotherapy. These molecules can also stimulate macrophages in their role as T-lymphocyte informants, making T lymphocytes more reactive and more effective in rejecting cancer cells, particularly in cancer models resistant to standard immunotherapy. This new approach could therefore "boost" the clinical immunotherapy process, particularly for the many cases of cancer for which this treatment is still of limited efficacy.

Zhu et al (2023) Nature

INHIBITION OF NETRIN TO SENSITISE CANCER TO CHEMOTHERAPY AND IMMUNOTHERAPIES: FROM BENCH TO BEDSIDE

Netrin-1 is expressed by cancer cells and the tumour microenvironment in a large proportion of human neoplasms. A netrin-1-blocking humanised monoclonal antibody (NP137) developed by Netris Pharma is currently in clinical trials in solid tumours (ClinicalTrials.gov identifier NCT02977195). The laboratory of **Cédric Blanpain** investigated the role of netrin during epithelial-mesenchymal transition (EMT), a process by which cancer cells detach from their neighbouring cells, acquire invasive properties, and contribute to the development of resistance to cancer treatments. Using a mouse model of skin tumours that spontaneously undergo EMT, the researchers found that pharmacological inhibition of netrin-1 by administration of NP137 reduced the proportion of EMT tumour cells in mouse skin, decreased the number of metastases and increased the sensitivity of tumour cells to chemotherapy. In biopsies obtained from the on-going clinical trial in collaboration with the group of Patrick Mehlen (University of Lyon, France), the researchers showed that NP137 not only reduced the number of tumour cells but also induced inhibition of EMT features. These results showed that blockade of netrin with NP137 reduces resistance to cancer treatments through a mechanism involving EMT inhibition, providing a strong scientific rationale for the on-going combination clinical trial with NP137.

Lengrand et al (2023) Nature

Cassier et al (2023) Nature

ROLE OF THE EXTRACELLULAR ENVIRONMENT IN CANCER FORMATION

Oncogenic mutations alone are not sufficient to induce cancer formation and other factors, such as the extracellular environment, influence the progression of oncogene-expressing cells to invasive tumours. In animal models, researchers led by **Cédric Blanpain** studied the ability of oncogene-expressing cells to develop basal cell carcinoma (BCC) tumours in different skin locations (ear and back) at a single cell resolution. Surprisingly, they found that cells expressing the oncogene in the ear, but not in the skin of the back, gave rise to the typical appearance of invasive BCC. The team found that the extracellular matrix of the dermis is characterised by increased rigidity and a denser collagen network in the skin of the back than in the ear. By enzymatically reducing collagen density, the team demonstrated that collagen abundance is a key factor in limiting the invasion and formation of tumours in the skin of the back. This study provides a better understanding of cancer formation in humans, with BCC originating preferentially in certain areas of the body such as the ears and nose, which have different levels of collagen to other parts of the body.

Bansaccal et al (2023) Nature

Awards



**CÉDRIC
BLANPAIN**

WEL RESEARCH
INSTITUTE - ULB

Cédric Blanpain pursues research in stem cell biology and oncology to decipher the roles of cancer stem cells in the development, progression and metastasis of skin, breast and brain cancers. Cédric holds an **ERC Advanced grant** (2020-2025) to define the different tumour states at the single-cell level using a multidisciplinary approach. In 2023, Cédric received the **Momentum Award from the International Society for Stem Cell Research** (USA) for his innovative research in cancer stem cell research.



**IEVGENIIA
PASTUSHENKO**

WEL RESEARCH
INSTITUTE - ULB

Ievgeniia Pastushenko conducts research in cancer biology, in particular related to the cellular and molecular mechanisms behind cancer metastasis and therapeutic resistance. In 2023, Ievgeniia was elected **member of the Collegium of the Royal Academy of Belgium**. The Collegium, a young body of the Royal Academy of Belgium, brings together young researchers under the age of 40 from Wallonia-Brussels who have particularly distinguished themselves in their careers.



Immunology and Inflammation

Immunology and Inflammation study the body's immune response and the complex processes underlying inflammation in order to develop treatments for autoimmune and inflammatory diseases, as well as immunotherapies against cancer.

Investigators

Advanced

GEORGES Michel - ULiège

Systematic eQTL and CMap based identification of IBD predisposing genes and interacting drugs

LUCAS Sophie - UCLouvain

Targeting TGF- β 1, β 2 or β 3 activation in auto-immunity and graft-versus-host disease

MARICHAL Thomas - ULiège

Deciphering the contribution of the myeloid-epithelial crosstalk to viral-induced exacerbations of chronic airway diseases (asthma or COPD)

VERMIJLEN David - ULB

The third way of immune protection in human: development and function of $\gamma\delta$ T cells in early life

Representative publications

UNEXPECTED PROLIFERATIVE CAPACITY OF BLOOD MONOCYTES

An unexpected discovery by the team of **Thomas Marichal** has challenged our common understanding that most cells in a living organism are derived from stem cells. The team showed that blood monocytes, previously considered differentiated cells, are capable of proliferating and forming a pool of monocytes in tissues to give rise to macrophages. This study paves the way for further investigations into the possibility of controlling monocyte proliferation for therapeutic purposes.

Vanneste et al (2023) Nature Immunol

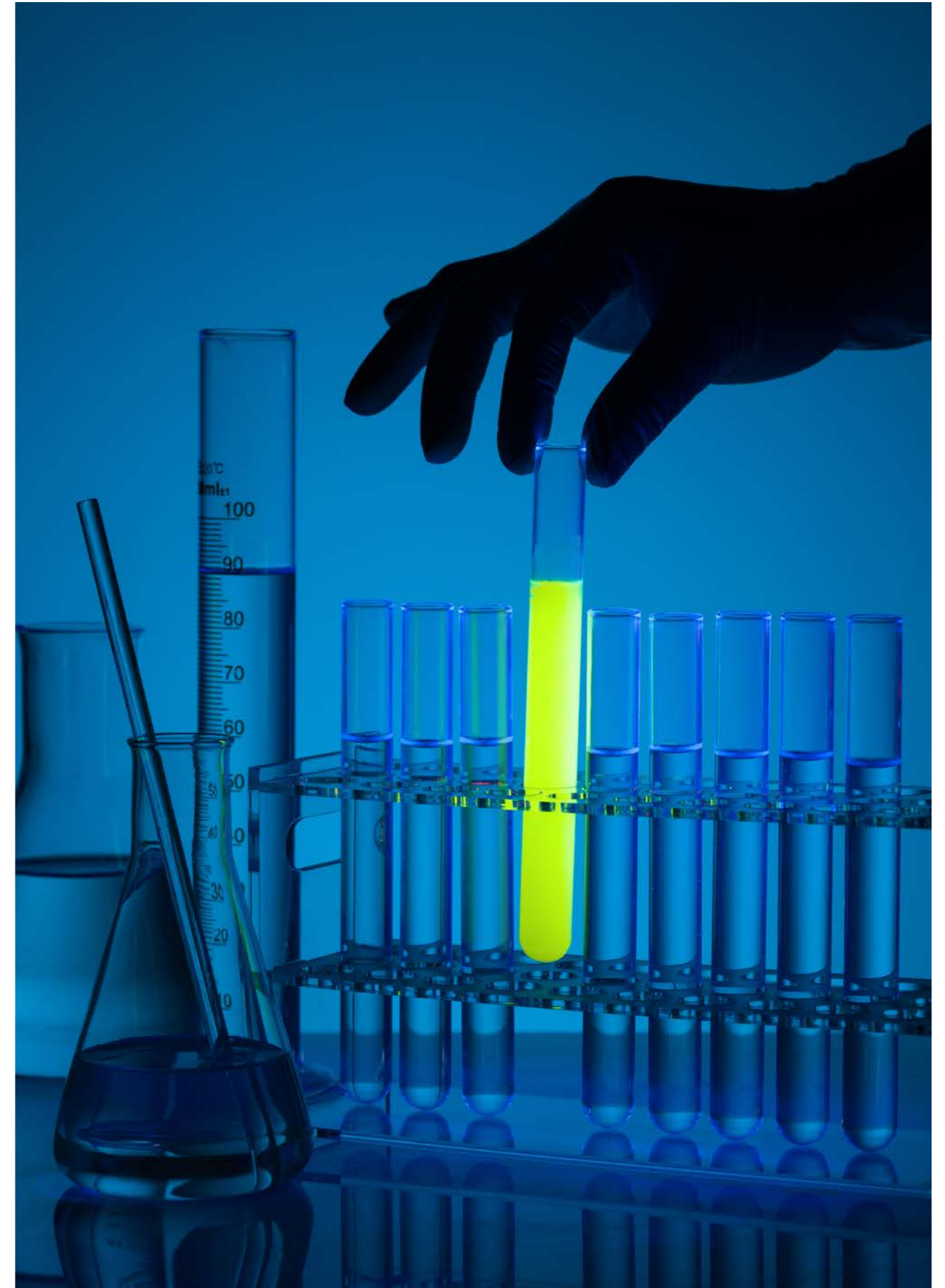
Awards



THOMAS MARICHAL

WEL RESEARCH
INSTITUTE –
ULIÈGE

Thomas Marichal focuses on research in immunological responses and diseases, with a particular emphasis on advancing our understanding of the environmental triggers of asthma and allergies. In 2023, Thomas was awarded an **ERC Consolidator Grant** to continue his research into the mechanisms of lung regeneration following respiratory infections such as Covid-19 or influenza.





Neurosciences

Neurosciences explore the intricate workings of the brain and nervous system to advance our understanding of neurological disorders, with the aim of developing treatment and diagnostic strategies for conditions such as Alzheimer's disease, Parkinson's disease and drug addiction.

Investigators

Advanced

DE KERCHOVE D'EXAERDE Alban - ULB

Maged1 in the thalamus, a key gateway to understanding drug addiction and improving its treatment

NGUYEN Laurent - ULiège

Cell migration shapes cerebral cortex morphogenesis and function

Starting

BOMMER Guido - UCLouvain

Novel biochemical aspects of neurodegeneration in Parkinson's disease

EL TAHRY Riem - UCLouvain

Optimisation of VNS in refractory epilepsy

HANSEEUW Bernard - UCLouvain

Beyond amyloid and tau pathology: Towards clinical trials modulating synaptic function in preclinical and symptomatic Alzheimer's disease

Representative publications

HOW DOES THE STRIATUM CONTROL OUR MOVEMENTS?

Proper control of movement relies primarily on the correct functioning of the striatum, a subcortical brain region adjacent to the basal ganglia. Alterations in its function are at the heart of several neuropsychiatric disorders such as Parkinson's disease, autism spectrum disorders and schizophrenia. The striatum is mainly composed of two populations of spiny projection neurons (SPNs): one population forming the direct pathway (dSPN) and the other population forming the indirect pathway (iSPN). **Alban de Kerchove** d'Exaerde's team resolved a paradox regarding the precise organisation of neuronal activity in the striatum by combining artificial.

intelligence with recordings of SNP activity using calcium imaging. The laboratory demonstrated that the concerted and cooperative activity of dSPNs and iSPNs is necessary for the correct initiation and execution of actions, accompanied by complementary neuronal activation and inactivation profiles to select which movements to perform.

Varin et al (2023) Nat Commun

TOWARDS A MORE RELIABLE DIAGNOSIS OF ALZHEIMER'S DISEASE IN PATIENTS

Among neurodegenerative diseases, tauopathies (including Alzheimer's disease) are characterised by the abnormal accumulation of aggregates of the tau protein in neuronal cells. The tau protein exists in different isoforms, so-called 3R or 4R. In Alzheimer's disease, all the isoforms are diseased and aggregate. In other tauopathies, it is either the 3R or 4R isoforms that accumulate. At present, the only reliable diagnostic method for distinguishing between 3R and 4R isoform aggregates is autopsy, which is too late to optimise treatment for the patient. Whereas most biochemists work on the aggregate forms of the tau protein, **Bernard Hanseeuw's** team took a new approach to analyse the soluble (non-aggregated) form of the tau protein in cerebral autopsy material. They discovered that modifications to the soluble proteins could potentially be used as a surrogate to determine the type of isoforms that aggregate. For the researchers, this is a great encouragement to continue this research, this time using cerebrospinal fluid, which can be taken directly from the patient.

Kyalu Ngoie Zola et al (2023) Nat Commun

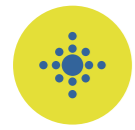
Awards



LAURENT NGUYEN

WEL RESEARCH
INSTITUTE –
ULIÈGE

Laurent Nguyen specialises in the molecular mechanisms underlying brain development and neurological disorders, with a focus on how neural circuitry is organised during developmental conditions. In 2023, Laurent was awarded an **ERC Synergy grant** (2023-2028) to lead an interdisciplinary project bringing together 4 European laboratories. The aim is to study the mechanisms underlying the mechanical folding of the cerebral cortex during embryonic development and the correspondence with the functional organisation of the brain.



Cardiovascular, Metabolic & Genetic Diseases

This area investigates the underlying physiological and/or genetic factors that contribute to cardiovascular, metabolic and genetic diseases, with the aim of developing treatment strategies for conditions such as heart failure, diabetes and cystic fibrosis.

Investigators

Advanced

BALLIGAND Jean-Luc - UCLouvain

Structural and functional characterisation of Aquaporin-1 as a "peroxiporin" in cardiovascular tissue

BERTRAND Luc - UCLouvain

Cardiovascular diseases and o-GlcNAcylation: the case of cardiac hypertrophy

CANI Patrice - UCLouvain

Identifying novel gut microbes and their active compounds to tackle diseases

EIZIRIK Decio - ULB

Beta cell splicing signature in diabetes

GILON Patrick - UCLouvain

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 - ULB

Capturing alternatives conformers of CFTR with nanobodies to understand the pathogenesis of Cystic Fibrosis at the molecular level and to delineate new therapeutic routes

VIKKULA Miikka - UCLouvain

Towards novel treatments for primary lymphoedema: from identification of genetic causes to in vivo modelling and preclinical trials

Starting

BELOQUI GARCIA Ana - UCLouvain

Oral delivery of biologics for the treatment of gastrointestinal diseases

EVERARD Amandine - UCLouvain

Identification of gut microbes and metabolites involved in the gut-to-brain axis controlling the hedonic and reward system during food intake

MARTIN Maud - ULB

Mechanistic understanding of microtubule function during angiogenesis

Representative publications

ORAL FORMULATION WITH LIPID NANOPARTICLES : AN ALTERNATIVE TO INJECTIONS?

GLP-1 agonists, used in the treatment of type 2 diabetes and under clinical investigation for non-alcoholic fatty liver disease, require one or more daily subcutaneous injections. **Ana Beloqui Garcia** and her team developed an oral formulation of a GLP-1 analogue based on lipid nanoparticles. In two mouse models of non-alcoholic fatty liver disease, the group demonstrated that oral administration of this GLP-1 formulation was more effective in slowing down the progression of the disease to more severe states than subcutaneous injection of the same analogue. This oral mode of administration offers a promising strategy to overcome current treatment limitations, including overcoming the lack of patient compliance due to the inconvenience of daily injections.

Domingues et al (2023) J. Control. Release

ALTERED HEPATIC AHR SIGNALLING IN CANCER CACHEXIA IMPACTS LIVER METABOLISM

Cancer cachexia is a serious and common complication of cancer disease, characterised by involuntary weight loss, muscle wasting and immune system impairment, and often associated with chronic inflammation. **Laure Bindels'** laboratory found that the activity of the aromatic hydrocarbon receptor (AHR) was profoundly altered in multiple mouse models of cancer cachexia and in patient biopsies, independent of food intake. This alteration contributed to the hepatic inflammation and metabolic disorders characteristic of cancer cachexia. The researchers also showed that pharmacological activation of AHR was sufficient to ameliorate liver inflammation and glycaemic disorders in a cachectic mouse model. As there is currently no treatment available, these findings may pave the way for future therapeutic approaches to tackle cancer cachexia.

Dolly et al (2023) J. Cachexia Sarcopenia Muscle

ALTERED HEPATIC AHR SIGNALLING IN CANCER CACHEXIA IMPACTS LIVER METABOLISM

Considered a rare disease, lymphatic malformations can cause deformities, severe pain, functional impotence, muscle weakness and bleeding. Several studies in the laboratory of **Miikka Vikkula** highlighted the properties of Sirolimus, a drug used to treat cancer, in the treatment of low-flow vascular malformations such as lymphatic malformations. Based on this scientific knowledge, in 2016, the team of Laurence Boon at the Cliniques Universitaires Saint-Luc became the first in the world to treat a vascular malformation in utero with Sirolimus administered directly to the mother during pregnancy. The foetus had a large lymphatic malformation in the cervical region and was suffering from respiratory failure, putting the pregnancy at risk. After treatment, the size of the lesion diminished considerably, and the delivery proceeded normally. The baby's treatment continued for several years. Now aged 6, the child is doing well and growing normally. This medical achievement is the result of a multidisciplinary collaboration between several clinicians and researchers.

Seront et al (2023) Nat Cardiovasc Res

Awards



ANA BELOQUI
GARCIA

WEL RESEARCH
INSTITUTE -
UCLOUVAIN

Ana Beloqui Garcia focuses on the development of oral delivery methods for biological drugs, a more patient-friendly approach than the daily intravenous injections usually required to administer biological drugs. For her research, Ana was awarded the 2023 **FNRS Endocrinology, Diabetes and Metabolism Award** and the 2023 **Simonart Foundation Prize**.



DECIO L.
EIZIRIK

WEL RESEARCH
INSTITUTE -
ULB

Decio L. Eizirik leads research in the field of diabetes, specifically focusing on the molecular mechanisms and genetic factors that contribute to beta-cell dysfunction and the pathogenesis of type 1 diabetes. In 2023, Decio received the prestigious **George Eisenbarth Memorial Lecture Award** (USA) delivered at the 15th annual Network for Pancreatic Organ Donors with Diabetes (nPOD) meeting held in Florida, USA.



MIIKKA
VIKKULA

WEL RESEARCH
INSTITUTE -
UCLOUVAIN

Miikka Vikkula focuses on understanding the genetic and molecular bases of lymphatic and vascular anomalies, with the goal to move from bench-to-bedside and provide patients with viable and tangible knowledge-based improvements in their healthcare. In 2023, Miikka received the prestigious **Earl P. Benditt Award** (USA) delivered at the North American Vascular Biology Organization (NAVBO) meeting in Rhode Island, USA.



PATRICE
CANI

WEL RESEARCH
INSTITUTE -
UCLOUVAIN

Patrice Cani leads research to understand the role of our intestinal bacteria in the development of various diseases, including type 2 diabetes associated with overweight and obesity, and certain cancers. For the 8th consecutive year, Patrice has been named **Highly Cited Researchers** in 2023 by Clarivate.com in recognition of the significant and widespread influence of his work in this field of research.



AMANDINE
EVERARD

WEL RESEARCH
INSTITUTE -
UCLOUVAIN

Amandine Everard studies how our intestinal bacteria can influence our eating behaviour and the role of this gut-brain axis in eating disorders, such as binge-eating. Amandine has been named **Highly Cited Researchers** in 2023 by Clarivate.com for her publications ranked in the top 1% of citations in this field of research over the last decade.



Microbiology & Infectious Diseases

Research in Microbiology and Infectious Diseases investigates the mechanisms of pathogens, such as bacteria and viruses, and host responses, with a focus on the treatment of infectious diseases to improve global health outcomes.

Investigators

Advanced

COLLET Jean-François - UCLouvain

Exploring the cell envelope of Escherichia coli, a compartment that is an attractive target for innovative biotechnological and biopharmaceutical approaches

VANDERPLASSCHEN Alain - ULiège

The use of Herpesvirus-fish models to unravel host-pathogen-environment interactions: a new paradigm in disease mitigation for aquaculture

Starting

ALSTEENS David - UCLouvain

Deciphering the molecular mechanisms of reovirus and rotavirus entry at the nanoscale

HALLEZ Régis - UNamur

Molecular characterisation of the cellular processes targeted by the second messenger (p)ppGpp in bacteria

Representative publications

CNOX: AN UNEXPECTED PARTNER FOR GROEL

Chaperones ensure the correct folding of proteins in cells. GroEL is a textbook example of a chaperone, and scientists thought they knew everything about it... until **Jean-François Collet** and colleagues discovered that GroEL requires a partner, CnoX, to function properly. CnoX is a chaperedoxin that controls the redox quality of GroEL substrates. The team was able to photograph the interaction between GroEL and its previously unknown partner CnoX.

Dupuy et al (2023) Cell

"Z" FOR ZALPHA

Since the early 2000s, carp farms (koi and common carp) have been decimated by a virus, the Cyprinid herpesvirus 3, with serious economic consequences. **Alain Vanderplasschen** and his team deciphered the role of the Zalpha domain, a specific protein domain of the virus, in the mechanism of viral infection in carp. They showed that the Zalpha domain binds to double-stranded DNA or RNA in a specific conformation known as a "left-handed double helix" (as opposed to the well-known right-handed double helix conformation of DNA described by Watson and Crick). This binding affects the concentration gradient of certain proteins in the cytoplasm of infected cells, and acts as a protective shield that prevents the infected cell from detecting the viral infection.

Diallo et al (2023) Nucleic Acids Research

Awards



DAVID ALSTEENS

WEL RESEARCH
INSTITUTE –
UCLouvain

David Alsteens pursues research on nano-biophysics of the cell surface machinery, focusing on the interactions at a nanoscale level between biological molecules and viruses to improve our understanding of the cellular mechanisms of viral infections. David is pursuing an **ERC Consolidator Grant** (2022-2027) to bring nanotechnology to the field of virology and decipher the complex interaction between a virus and a cell.

Engineering
sciences, chemistry
and physics
for an impact
in sustainable
transition

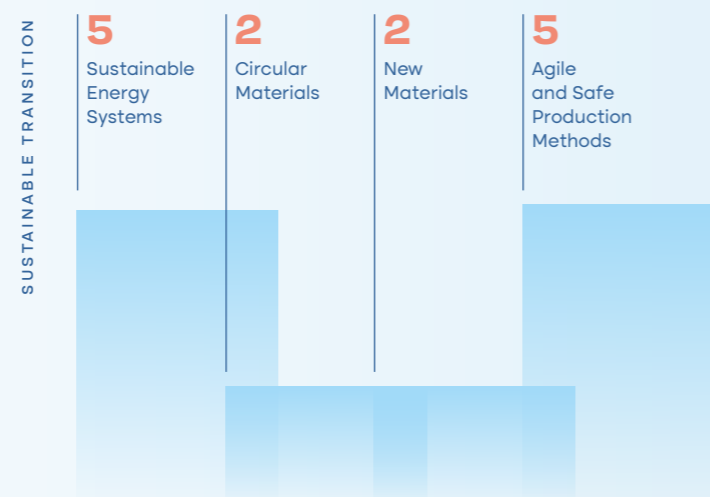
WELRI

WELRI

The WEL-T department

The overall objective of WEL-T is to promote breakthrough technologies for industrial applications, thus contributing to the Walloon Region's efforts towards sustainable transition. Targeting engineering, chemistry and physics, WEL-T (Walloon Excellence in Technology) is a strategic extension of Wallonia's commitment to cutting-edge research. It complements the successful WELBIO programme, which focuses on life sciences.

Number of active WEL-T programmes in 2023



Grand Total

14

NUMBER OF ACTIVE
WEL-T PROGRAMMES IN
2023



Sustainable Energy Systems

Research into sustainable energy systems plays a crucial role in advancing clean and renewable energy sources, while promoting energy efficiency and environmental sustainability.

Investigators

Advanced

BONAVENTURE Olivier - UCLouvain

Sleepable and energy-efficient Internet protocols

PARENTE Alessandro - ULB

Lifelong-learning digital twins for sustainable combustion technologies

Starting

CAUDRON Corentin - ULB

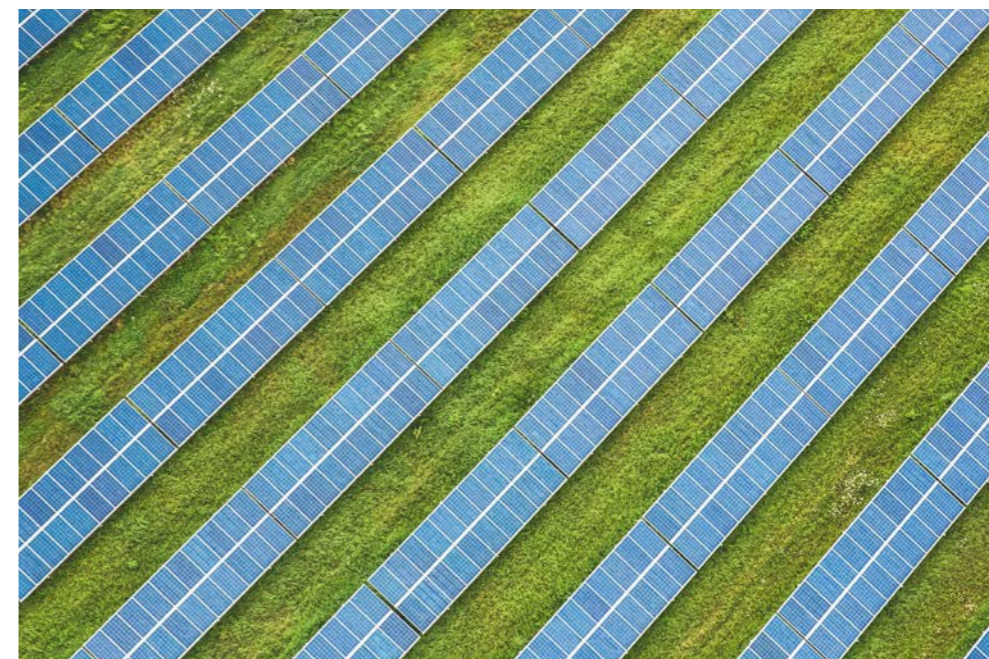
Towards 4D monitoring of geothermal operations in 4D using passive-based seismic approaches

FRANCI Alessio - ULiège

Embodied Excitability: a principle for designing neuromorphic adaptive agents

TROIAN-GAUTIER Ludovic - UCLouvain

Fe(II/III) photosensitizers for dye-sensitized photoelectrochemical cells (DSPECs) application



Circular Materials

Circular materials are designed to enable complete recycling of materials and novel synthesis strategies free from toxic precursors or by-products to regenerate raw materials.

Investigators

Advanced

RAQUEZ Jean-Marie - UMONS

Continuous solid-state modification of plastic waste via upcycling approach

SIMAR Aude - UCLouvain

Recycling healable aluminium waste by circular solid state additive manufacturing



New Materials

Thanks to their unique properties and superior performance, new materials can replace traditional materials and help protect the environment.

Investigators

Advanced

PARDOEN Thomas - UCLouvain

Novel nanolaminate coatings and ultra-miniaturised test instrumentation for extreme nuclear environments

Starting

PONCÉ Samuel - UCLouvain

Computationally-driven improvements in lead-free halide perovskite photovoltaics

Awards



**THOMAS
PARDOEN**

WEL-RESEARCH
INSTITUTE –
UCLouvain

Thomas Pardoën focuses on understanding and improving the durability and strength of materials used in the aerospace, energy, and electronics industries, with a strong emphasis on innovation in materials design and testing methodologies. In 2023, Thomas was the laureate of the "**Grande Médaille de la Société Française de Métallurgie et de Matériaux**" (France).



Agile and Safe Production Methods

Research to increase efficiency, reduce waste and identify areas for sustainable innovation across a range of manufacturing processes.

Investigators

Advanced

DETREMBLEUR Christophe - ULiège

Cascade exotherms to stimulate self-foaming of Isocyanate-free polyurethane formulations at ambient temperature

EVANO Gwilherm - ULB

Catalytic deoxygenative functionalisation reactions for the synthesis of alkanes, alkenes and arenes

GEERTS Yves - ULB

A fresh look on the polymorphism of active pharmaceutical ingredients

MONBALIU Jean-Christophe - ULiège

Intelligent flow systems for advanced chemical manufacturing

RIGNANESE Gian-Marco - UCLouvain

Towards a materials informatics active-learning platform to design new electrocatalysts



CHAPTER



Societal and economic impact

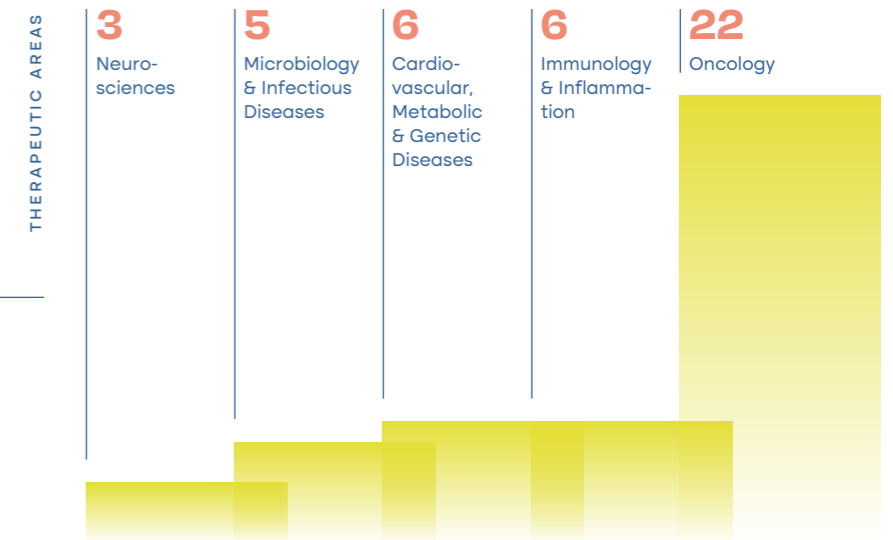
Fundamental research thrives on hypotheses and its outcomes are inherently unpredictable, often stemming from numerous trials, errors, and revised scientific hypotheses. This is why the WEL Research Institute prioritises regular meetings with its Investigators, in close collaboration with the universities of the Wallonia-Brussels federation and their Knowledge Transfer Offices (KTOs). The aim is to identify and protect unexpected results that could lead to innovation, and to develop strategies for transferring intellectual property to industry for the ultimate benefit of society.

Intellectual Property

A total of 42 patent applications has been filed by 2023, including 1 application within the year, of which 31 patent families were still active. Half of these are in the field of oncology, an area historically strongly represented in our WELBIO department.

Oncology
~50%

HALF OF THE PATENTS ARE IN THE FIELD OF ONCOLOGY.



Bridge Fund

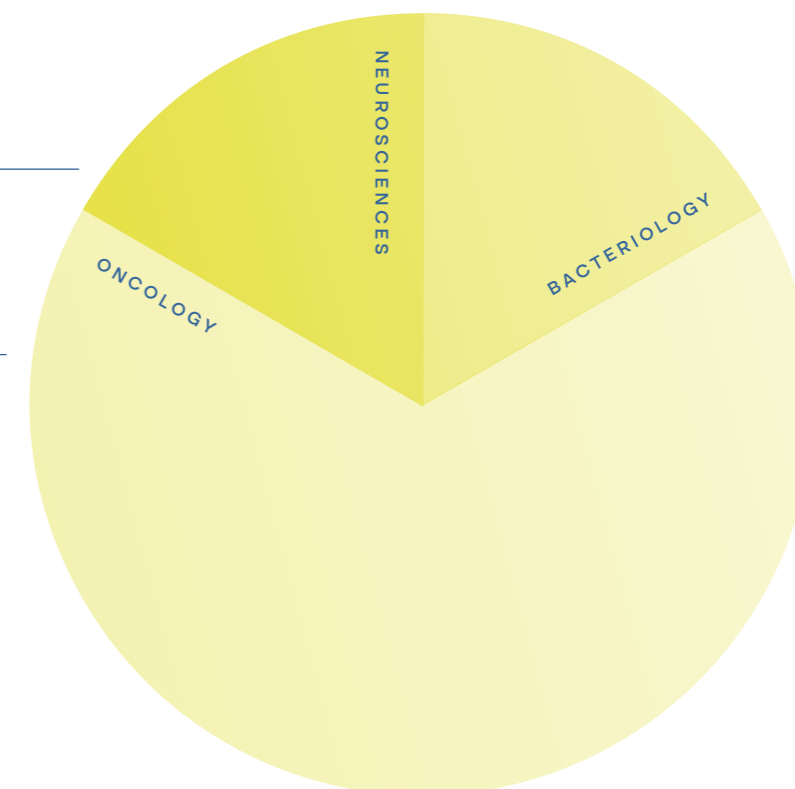
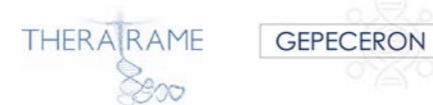
The Bridge Fund, managed by the Governing Board of the WEL Research Institute, supports the development of intellectual property from the Institute's programmes with the aim of facilitating key advances in industrial development and technology transfer.

In 2023, the Governing Board approved the funding of one Bridge Fund application, for a budget of €150,000, in the field of oncology. The aim of this Bridge Fund was to develop a cell-based functional assay to be used as a secondary screen in a drug discovery programme in collaboration with a new spin-off company being established in parallel.

By the end of 2023, a total of 7 Bridge Funds amounting to €913,610 had been awarded. These funds have supported patent applications, confirmed industry interest in new technologies, and helped develop functional screening tests for spin-offs. In addition, in 2023, the Governing Board also increased the maximum Bridge Fund allocation from €150,000 to €500,000 in order to enhance the opportunities for valorisation.

In 2023, Santero Therapeutics secured €8M in Series A funding to combat antimicrobial resistance, supporting development of novel antibiotics.

Progress



Spin-offs

In 2023, Santero Therapeutics announced an €8 million Series A funding round to develop novel antibiotics to combat antimicrobial resistance. This funding will support the further development of its innovative inhibitors for the treatment of multi-drug resistant infections. The spin-off, established in 2021, builds on more than a decade of fundamental research into bacterial metabolism carried out at the ULB labs of Abel Garcia-Pino and Cédric Govaerts.

Also in 2023, NeGIO Therapeutics was launched to undertake a drug discovery programme to develop a new oncology treatment.

The Brussels South Charleroi Biopark welcomed another new company, Cancer State Therapeutics, founded by Cédric Blanpain of the ULB. This venture aims to discover and develop first-in-class small-molecule therapeutics for unmet needs in oncology, and represents a significant step forward for Blanpain following the closure of Chromacure – a previous spin-off of the ULB and the WEL Research Institute, created in 2018.

By the end of 2023, six spin-offs had been created from research programmes in the WELBIO department. All are based in the Walloon region at locations including the Brussels South Charleroi BioPark, Mont-Saint-Guibert, and Liège. Together, these spin-offs have raised a total of €84 million in pre-seed and seed funding and have created 32 jobs.

Impact for patients

In 2023, AbbVie advanced ABBV-151 (ARGX-115) into Phase 2 clinical trials in solid tumours. This antibody, designed to block GARP and boost the immune response against tumours, builds on research by Pierre Coulie and Sophie Lucas at UCLouvain. Their findings revealed how GARP helps tumours evade immune detection. This antibody has been co-developed with Argenx through the preclinical phases of validation and is currently being investigated as ABBV-151 (livmoniplimab) in patients.



A Bridge Fund awarded to Pierre Coulie and Sophie Lucas in 2014 consolidated the intellectual property related to the anti-GARP antibody which is now investigated as ABBV-151 in Phase 2 clinical trials in solid tumours.

Communication

17 March 2023

The WEL Research Institute and the LIEU network hosted a webinar on intellectual property in life sciences, covering patentability criteria and the importance of strategic IP management and patent database searches for researchers, with insights from Benoît Van Driessche, LIEU Intellectual Property Advisor.

19 October 2023

Vinciane Gaussin, Managing Director, spoke at a panel during the 20th anniversary of the LIEU network, highlighting the collaboration between the WEL Research Institute and the Knowledge Transfer Offices (KTOs) of Wallonia-Brussels universities to translate scientific knowledge into socio-economic benefits.

25 October 2024

The WEL Research Institute and the support provided by the Walloon region to strategic research have been honoured at the "Soirée Fondamentale !" organised by the FNRS. Our Chairman, Philippe Denoël, discussed the Institute's crucial role in bridging the gap between fundamental research, innovation, and socio-economic impact.

CHAPTER

Management report

This report covers the 13th financial year, from 1 January 2023 to 31 December 2023.

Since 2022, the WEL Research Institute is composed of two departments: WELBIO (life sciences for health impacts) and WEL-T (engineering, chemistry and physics for an impact on sustainable transition). WELBIO and WEL-T correspond to the strategic axes defined by the Walloon Government within the Fonds de la Recherche Fondamentale Stratégique (FRFS), one of the associated funds of the F.R.S.-FNRS.

The WEL Research Institute and the FRFS complement each other in carrying out the mission entrusted to them by the Walloon region. The FRFS is in charge of the selection process and financial management of the 'Investigator programmes' that make up the WELBIO and WEL-T departments. The WEL Research Institute defines the overall strategy for the calls and drives the translation of the scientific discoveries resulting from the 'Investigator programmes' into societal and economic impact.

This is reflected in the financial flow as follows:

- Subsidies from the Walloon Region for strategic research within WELBIO and WEL-T are paid to the FRFS.

- The WEL Research Institute receives an annual grant (= 'WELRI amount') equal to 10% of the total subsidies from the Walloon Region, after deduction of the sums earmarked for the financing of the operating costs of the FRFS/F.R.S.-FNRS.

For the 2023 financial year, the agreement signed by the FNRS and the WEL Research Institute on 4 November 2022 is applicable to the management of the funding allocated to the WEL Research Institute as follows:

- The total 'WELRI Amount' for 2023 is €2,287,500.
- The WEL Research Institute has submitted to the FNRS a claim for €650,000 to cover its operating costs for the period from 01.01.2023 to 31.12.2023. The amount of this claim was estimated on the basis of the provisional balance sheet drawn up on 30 September 2023 and presented to the WELRI Board of Directors on 23 November 2023.
- The 'WELRI BALANCE', corresponding to the difference between the 'WELRI Amount'

and the statement of claim, is €1,637,500. This balance, which will remain in the FNRS account, will be distributed in proportion to the initial allocation as follows:

- FRFS-WELBIO: €1,097,125 (67% of the balance)

- FRFS-WEL-T: €540,375 (33% of the balance)

The WEL Research Institute has published its annual accounts with the National Bank of Belgium since the 2017 financial year. Although the WEL Research Institute can be considered a

micro not-for-profit organisation, 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 €4,197.86 and consist of computer equipment.

Financial fixed assets amount to €7,497.00 and concern the guarantee for the rented offices in Wavre.

Receivables due within one year amounted to €29,900.00 and consisted of a 20% working capital advance on the Bridge Fund BF-2023-01 research agreement.

Cash investments amounted to € 2,629,722.68 in the form of two reserves to distribute the remaining liquidity of the WEL Research Institute.

These liquid cash sums have been allocated as follows:

Operating costs (2024):

€ 603,600.00

Bridge fund:

€ 2,026,122.68

A BPAID account was created to cover various small expenses and the remaining balance is €194.31. Adjustment accounts amounted to €6,901.65 and related to charges that were to be carried forward.

Total assets amounted to:

€ 2,678,413.50

Liabilities

The balance at 31 December 2022, under the heading of "other allocated funds", amounted to €2,482,545.35.

The result for the fiscal year was a profit of €60,576.94.

The balance at 31 December 2023, for other allocated funds, amounted to €2,543,122.29.

Supplier debts amount to €92,690.84.

The estimated tax liability for 2023 is €395.21.

Provisions for holiday pay amount to €41,663.60.

Other debts amount to €129.93 and relate to an administrator's current account of €129.93.

Total liabilities amounted to:

€ 2,678,413.50

Result

The grant for 2023 operating costs amounted to €650,000.00. Miscellaneous services and assets amounted to €115,626.55 and primarily consisted of operating costs, rent and fees.

Salaries and social contributions amounted to €333,520.46.

The estimated tax liability amounted to €395.21.

Net bank interest, after withholding tax, amounted to €5,782.49.

Financial charges amounted to €37.93.

The result for the fiscal year is a profit of:

€ 60,576.94

CHAPTER

Administrative and financial resources

GOVERNANCE

The Board of Directors of the non-profit organisation (asbl) WEL Research Institute is made up of representatives from industry, academia, and Ministers of the Walloon Region

Board of Directors

President: Jean Stéphane

(until 21 June 2023);

Philippe Denoël

(since 21 June 2023)

Vice-President: Pierre Lekeux

Representatives of the 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 sectors

Jean Stéphane, Member of the board of several biotech companies (until 21 June 2023)

Philippe Denoël, Head of External Vaccines R&D at GSK (since 21 June 2023)

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

Secretary General of the Fund for
Scientific Research
(F.R.S.-FNRS)

Véronique Halloin, Secretary General

Representatives from the
universities in the French
Community:

Jean-Christophe Renaud, Vice-Rector
Research, UCLouvain
Marius Gilbert, Vice-Rector, Research
and Development, ULB
Ruddy Wattiez, Vice-Rector Research,
UMons

Representative of the Walloon
Public Service

Jean-François Heuse, Inspector General

The WEL Research Institute team



VINCIANE
GAUSSIN

MANAGING
DIRECTOR

Vinciane Gaussin has more than 20 years of experience in life sciences in academic, biotech and non-profit organisations. She was the Managing Director of the WEL Research Institute from 2010 to 2015 and resumed this position in March 2021, after several years at a biotech company in California. Vinciane has a degree in bioengineering, obtained her PhD in 1996 (Belgium) and did her post-doctoral work at the Baylor College of Medicine (USA).



LAURENCE
BORGS

WELBIO
BUSINESS
DEVELOPMENT
MANAGER

Laurence Borgs is a neurobiologist, obtained a PhD in Biomedical and Pharmaceutical Sciences in 2009 and completed a post-doctoral fellowship in partnership with UCB Pharma. Combining scientific expertise and commercial leadership in various biotech life science companies, Laurence joined the WEL Research Institute in August 2022 as Business Development Manager for the WELBIO department.



PERRINE CALVEZ

WEL-T BUSINESS
DEVELOPMENT
MANAGER

Perrine Calvez is a chemical engineer. She obtained a PhD in materials chemistry in 2009, which led her to the global steel industry, where she held various positions: research and development, process engineer, marketing and environmental manager. In 2023, Perrine obtained an Executive Master's in Management from the Solvay Business School. Perrine joined the WEL Research Institute in October 2023 as Business Development Manager for the WEL-T department.

Contact

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