Funds for health research

Laureates 2020

King Baudouin Foundation

Working together for a better society

Colophon

Title	Funds for health research – Laureates 2020
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Introduction

It is often said that your health matters more than anything else, and few people would disagree with that.

Nevertheless, we often do not realise how important it is to have a healthy mind and a healthy body until something goes wrong. Whether we have a medical condition ourselves or see a loved one suffering, we always want the same thing: the best possible care under the best possible conditions.

In this country, we are able to rely on a health care system that works well and has highly trained and dedicated staff. This is a privilege, but there is definitely still room for improvement. Care providers are under pressure to perform at their best despite only having minimal time and resources. Research can often be a struggle as well. Medical science is developing at a blistering pace, new perspectives are opening up all the time and new discoveries create possibilities for new treatment options. Anyone who wants to play a significant part in this process needs a lot of energy, motivation, determination and resilience. These highly motivated researchers do exist, and they deserve all the support we can offer them. The results of their work will help us and future generations will benefit as well.

To ensure that the quality of health care research stays as high as possible in Belgium, we need not only scientists but also people who are able to make a financial contribution. Fortunately, more and more people are willing to help. Many people are grateful for the excellent care that they or a loved one have received. They are hopeful that efforts will continue to be made to find the best approach to a condition in a way that takes the patient's own wishes and needs into account. They want to help talented young people to build careers in medical research and give established researchers a boost so that they can continue their work on a promising line of research. One way of doing this is by setting up or supporting a Fund for health research within the King Baudouin Foundation.

Thanks to the generosity of all these people, the Foundation is already managing over 100 Funds that are carrying out research in very diverse fields such as cancer, rare diseases, ageing, neurology, diabetes, cardiology, etc.

The Funds are managed in such a way that the donor's wishes are considered paramount and a tailored approach is developed. At the same time, the Foundation seeks to make the best possible use of the resources available and to create the greatest possible impact. This may lead to choosing specific niche areas of research, using new tools for philanthropic support, cooperating with other funding institutions, research centres, patient organisations, etc.

All Funds are administered by a Steering Committee that decides on the definition of the Fund's mission, the use of the financial resources, etc. When a call is launched, the Committee can rely on the expertise of an independent jury for selection of the laureate(s). In order to develop an overall, future-oriented vision on the best ways to deliver philanthropic support in the field of health research, the Foundation relies on the knowledge of the recognized experts of the 'Advisory Committee Research' and the 'Advisory Committee Cancer'.

In 2020, a total of 49 research projects in a huge variety of healthcare fields have received support, with funds totalling 6.6 million euros.

This brochure provides a brief summary of the laureates 2020 and their research work. Some of these projects are very close to our own experience, while others are carried out at a more abstract level. They are all, however, built on a firm belief in science and in the importance of a healthy future for everyone.

We hope you will enjoy reading about them.

Eva Van Braeckel

UGent
Ghent
Rare disease – Cystic fibrosis

Fund Alphonse & Jean Forton

in collaboration with the Belgian Cystic Fibrosis Association

Charcot-Leyden crystals and Galectin-10 as potential diagnostic and therapeutic target in cystic fibrosis-associated allergic bronchopulmonary aspergillosis (ABPA)

Grant € 223.820

Background: A lot of CF patients have damaged airways, which often harbor fungi (like Aspergillus) that grow there without causing damage. In some CF patients however, the immune system reacts to the fungi and causes an allergic reaction that can make CF much worse, because the mucus that is already difficult to cough up becomes even more sticky and rubbery, and starts to occlude small airways. This overreaction to fungi is called allergic bronchopulmonary aspergillosis (ABPA), and occurs in up to 10% of CF patients. The disease is hard to diagnose and difficult to treat, often requiring months of intake of steroids and antifungal drugs. In our local CF population, severe flare-ups of ABPA have been seen in CF patients even while on the CFTR modulating drugs ivacaftor or tezacaftor/ivacaftor, suggesting that also these new drugs do not prevent ABPA.

Project objectives: There is an urgent need to better diagnose and treat ABPA in CF patients. In the current project we will study how frequent ABPA can be found in CF patients, and how ABPA affects the quality of the mucus (viscosity and elasticity) and causes obstruction of the airways by formation of sticky, rubbery plugs (called allergic mucin), which we hope to detect by bronchoscopy and CT scanning. Our team has found that the "allergic mucin" contains a lot of needle shaped crystals, called Charcot-Leyden crystals (CLCs). Using newly developed methods, we will measure the presence of the CLCs and of the protein Galectin-10 (Gal-10), the building block of CLCs, and will see if the presence of these CLCs can be used to better diagnose ABPA in CF patients. Using newly developed antibodies to Gal-10 that can dissolve CLCs, we will also study if treating the needle-like crystals by dissolving them has an impact on mucus plugging and stickiness of mucus and sputum in CF patients with or without ABPA.
Research question: We hypothesise that the presence of ABPA makes CF much worse, and that by improving the diagnostics and treatment of this comorbidity, we can improve patients' outcome. We make use of highly innovative research on Charcot-Leyden crystals to better diagnose the disease, and hopefully will identify a new drug target, the CLC crystal.

Study design: At least 15 CF patients presenting with ABPA (CFwABPA) will be included over 3 years' time, as well as 15 CF patients with negative sputum cultures for Aspergillus and absence of signs of Aspergillus allergy (CFsABPA). At least 15 patients already well known to have Aspergillus allergy or previously diagnosed with ABPA will also be studied (CFpABPA). Sputum samples will be collected, as well as bronchoalveolar lavage (BAL) samples obtained by ultrafine bronchoscopy in a subgroup, and mucus plugging scores will be calculated on a specialized low dose CT scan. The stickiness of the sputum will be characterized in terms of viscosity and elasticity, using a specialized machine. The role of Gal-10 and CLCs in the disease process of ABPA, will be measured using very new anti-Gal-10 antibodies that can detect and dissolve CLCs in allergic mucin.

Cohort definition: People living with CF >12 years old and able to expectorate sputum and/or willing to undergo a bronchoscopy.

François Vermeulen

UZ Leuven
Leuven
Rare disease – Cystic fibrosis

Fund Alphonse & Jean Forton

in collaboration with the Belgian Cystic Fibrosis Association

Magnitude, mechanisms and clinical relevance of differences in the response to CFTR modulator in rectal organoids from patients with CF homozygous for the F508del mutation

Grant € 220.995

Background: Modulators are a new treatment class for patients with Cystic Fibrosis. These treatments are specific for the mutations of the CFTR gene. Four modulators are already approved, more are expected in the next years. For around 90% of patients, approved modulators are available or expected to reach the patients in the next few years. Ideally, each patient should be treated with the 'best possible' modulator combination. Therefore a 'precision medicine' approach is warranted, using tools to predict which modulator is most efficient for each patient. Organoids are a 3D cell model derived from rectal cells of each individual patient, that could possibly predict the effect of modulators in the individual patient.

Objective: The objective of the present project is first to measure, then to understand the reasons for, and finally establish the meaning of the differences in organoid response between the patients with the most frequent genotype (F508del/F508del).

Study design and cohort definition: First, we will measure the differences in organoid responses to modulators in 60 patients, using a validated test called 'FIS assay'. Secondly, we will explore why some patients have better responses than others, by comparing (1) the production and the function of the CFTR protein, (2) the production of other transcripts/proteins and (3) the gene sequence responsible for CF, between the 15 patients with the highest and the 15 patients with the lowest responses. Thirdly, we will assess whether the patients with a higher organoid response to a modulator treatment also had more improvement (in lung function, weight, sweat chloride concentration or need for antibiotics). For this, we will analyse the organoid response in 30 patients treated with modulators during clinical trials or with a 'medical need' program and compare it to the effect of the drug in the patient.
These results will further validate the rectal organoids as a tool for 'precision medicine' that can be used to optimize modulator treatment for the large groups of patients with a F508del/F508del mutation.

Marianne Carlon

KU Leuven
Leuven
Rare disease – Cystic fibrosis

Fund Alphonse & Jean Forton

in collaboration with the Belgian Cystic Fibrosis Association

A gene editing strategy for refractory CFTR mutations causing cystic fibrosis

Grant € 230.000

Background: A number of medicines known as potentiators and correctors are available for patients and can correct the defects of approximately 33 different cystic fibrosis (CF)-causing mutations, accounting for 90% of CF patients. However, 90% of disease-causing CFTR variants cannot be corrected by any available small molecule therapies. Therefore patients carrying these mutations are left without any specific treatment, causing chronic disease progression and eventually premature death.

Research question/hypothesis: Gene therapy efforts of the past aimed at overexpressing CFTR, leaving the defective mutant CFTR present in the particular patient. CRISPR-Cas technology today enables scientists to instead correct CFTR mutations and therefore cure patients from the defective gene. We hypothesize that gene editing thus offers advantages over gene addition by allowing to correct CFTR expression and function in cells, this by expressing CFTR at natural levels and by offering a long-term cure if stem/progenitor cells are gene corrected.

Project objectives: The overall aim is to develop such a CFTR targeting gene therapy with the potential to provide a permanent cure for CF, and this for patients with CFTR mutations non-responsive to current CFTR modulators. Specifically, we will develop and investigate the potential to functionally correct the following mutations, G85E, L227R, L927P and N1303K by CRISPR gene editing. Together, these mutations account for ~2780 of CF patients (~3.5%) worldwide.

Study design/cohort definition: We will develop CRISPR-Cas gene editors for the four CFTR mutations (G85E, L227R, L927P and N1303K) and assess their ability to restore CFTR expression and function. We will perform initial experiments in cell lines for easy validation. Next, we will test a gene editing correction in patient derived intestinal organoids harboring at least one copy of the mutated gene. Finally, we will assess a functional correction in CF airway epithelia as ultimately a gene therapy is envisioned to significantly improve and cure CF lung disease.

Piet Cools

UGent
Ghent
Rare disease – Cystic fibrosis

Fund Alphonse & Jean Forton

in collaboration with the Belgian Cystic Fibrosis Association

Improving the phage selection protocol for the treatment of the cystic fibrosis patients with multidrug-resistant lung infections

Grant € 224.186

Background: The lungs of cystic fibrosis patients are often infected with bacteria resistant to all antibiotics. Phages are viruses that attack very specifically certain bacteria, but are completely harmless for humans. These phages are used by our research group to treat bacterial infections, if antibiotics are no further option. To choose the most effective phage from our collection against a bacterial pathogen, we culture this pathogen from a patient's sputum in the laboratory. We then choose the phage that kills this pathogen most effectively. However, there is an important difference between lung pathogens cultured in the laboratory (where bacteria are present as free-living single cells) and pathogens present in the lungs of patients. In the lungs, these pathogens are present in thick biofilms, structures formed by these pathogens as a way of protection. We don't know if phages that are able to kill cultured pathogens are also capable of killing these pathogens present in biofilms in the CF-lung.

Project objectives: We want to test a new approach where we select phages for therapy based on a test that mimics the situation in the CF-lung in the best possible way. Therefore, we will use sputum coughed-up from deep in the lungs. We will then test how well our different phages can kill the pathogens in this sputum, where pathogens are present in biofilm, just the way they are in the lung. Furthermore, we want to find markers that predict if certain bacterial pathogens will be resistant to certain phages. Lastly, we aim to investigate if we currently fail to detect some pathogens present in the lungs because they are in a dormant status in the biofilm and are currently missed by our routine techniques.

Research questions:
1. Can we improve our strategy of selecting the most effective phages for phage therapy by testing phages on sputum?
2. Do we currently fail to detect certain pathogens present in the lungs using our culture-based techniques, or: can be show that there are better diagnostics than current ones? 3. Can we find markers of resistance of pathogens towards the different phages.

Study design and cohort: We aim to recruit patients seen at the University Hospitals of Antwerp, Brussels, Ghent and Leuven, and the Saint-Vincentius Hospital Antwerp. We will test how effective our phages are directly on pathogens and compare this with testing phages directly on the sputum. We will look for markers of resistance in the pathogens and for better diagnostics using molecular and/or protein-based techniques.

Mieke Boon

UZ Leuven
Leuven
Rare disease – Cystic fibrosis

Fund Alphonse & Jean Forton

in collaboration with the Belgian Cystic Fibrosis Association

In depth characterisation of the site and nature of airway obstruction and associated vascular remodeling in cystic fibrosis

Grant € 200.000

Background: Cystic fibrosis is a life-threatening disease associated that mainly causes recurrent and chronic respiratory infections. Due to the presence of thick mucus, chronic infection arises. This infection induces inflammation and secondary destruction of the airways. Eventually, the airways get destroyed after complete obstruction by thick mucus in combination with bacteria and inflammatory cells. Irreversible and progressive destruction leads to respiratory failure, for which lung transplantation is necessary.

Project objectives: To get a detailed understanding of the mechanisms of airway obstruction in CF by characterizing the site and nature of airway obstruction in more detail.

Research question: How do airways in CF lungs get obstructed and what is the influence on the blood vessels?

Study design: Using explanted lungs, we will use several very detailed technologies to 1) visualize the exact site and degree of airway obstruction with a resolution of 0.01 mm, 2) investigate what types of cells and substances are important for airway obstruction, 3) evaluate the changes in the blood vessels around the obstructed airways.

Cohort definition: 10 CF lungs, collected at transplantation, will be compared to 10 unused donor lungs. Areas with obvious airway obstruction will be analyzed in more detail.

Peter Witters

KU Leuven
Leuven
Rare disease – Cystic fibrosis

Fund Alphonse & Jean Forton

in collaboration with the Belgian Cystic Fibrosis Association

Vascular & immune microenvironments in patients with CF-associated liver disease

Grant € 268.510

Background: Cystic fibrosis (CF) is the most frequent lethal genetic disorder within the Caucasian race, with a median survival rising to more than 35 years. CF is truly invalidating for patients and greatly affects their quality of life. Although lung disease is the most serious aspect of CF, CF-associated liver disease (CFLD) is also frequent (one third of patients). CLFD represents the first non-pulmonary, non-transplant-related cause of death in CF and no effective treatment exists at the moment.
Our group and work from other peers have highlighted blood vessel abnormalities in CFLD and showed that there is a vascular component in CFLD, with endothelial cells (ECs), lining the inner side of blood vessels, considered to be cardinal in the pathogenesis.

Project objectives: We aim at unravelling the mechanisms by which CFLD develops, find alternative non-invasive methods to investigate ECs in CFLD patients, and develop treatment opportunities.
Research question & hypothesis
Our unpublished findings indicate that CFTR is really important in ECs, and that a defect in its expression lead to vessel inflammation and molecular aberration with autophagy (the recycling machinery of the cell) being blocked. We believe that healing the vessels will lead to the alleviation of CFLD gravity/development.

Study design: The current research project aims to extend and confirm our findings. First we will perform a detailed characterization of CFLD liver by using state-of-the-art technique allowing to study organs at the single cell level. This will show us which cell type behaviors are affected in CFLD. We will then analyze small vesicles, secreted by ECs, in CF patients to monitor the health status of blood vessels and as an indicator of liver disease. Finally, using the same non-invasive approach, a specific ECs model will be used to investigate treatment response.
This research project holds great promise, will lead to a better insight in the development of liver disease in CF and might open new avenues for prevention and curing CFLD.

Thierry VandenDriessche & Marinee Chuah

VUB
Brussels
Rare genetic neuromuscular diseases

Funds Walter Pyleman, Cremers-Opdebeeck & Richard Depasse

POMPE-CURE: Development of an innovative gene therapy platform for Pompe disease

Grant € 200.000

Pompe disease (GSD II) is one of the most common and important hereditary muscle disorders that is caused by a genetic defect in acid a-glucosidase (GAA). GSD It is a potentially life-threatening autosomal recessive genetic muscle disorder that affects approximately one in 40,000 births. These diseases are characterized by a dysfunction of the skeletal muscles, diaphragm and heart. Typically, the afflicted patients gradually lose all muscle function and ultimately die from heart and lung failure. Though current treatment for GSD-II alleviates some of the symptoms, these treatments are not curative and are largely inadequate since the large majority of patients ultimately still die from their underlying genetic disorder. Current treatment of Pompe patients with recombinant(r) GAA protein is not curative and inadequate since the large majority of patients still suffer from significant morbidity and mortality and/or develop antibodies to rGAA that renders the therapy ineffective.

Hence, there is an urgent need to develop an efficacious and safe therapy that tackles the genetic cause of the disease by efficiently and safely introducing a functional copy of the therapeutic gene into the patients' cells. This proposal's overall vision is to develop the next-generation muscle-directed gene therapy to effectively treat patients suffering from life-threatening hereditary muscle disorders. To realize this vision, the *POMPE-CURE* proposal's overarching significant goals are: (i) to develop a unique and novel gene therapy technology specifically designed to increase the delivery and production of the therapeutic genes in the affected target tissues; (ii) to test the potential broad applicability and validate the efficacy and safety of this next-generation gene therapy platform in a preclinical animal model for Pompe disease, an essential step towards establishing a *bona fide* cure of this disease of high unmet medical need. This POMPE-CURE proposal is highly focused and may ultimately pave the way towards a phase I clinical trial in patients suffering from Pompe disease, which highlights its translational potential and medical relevance. The research outcomes will ultimately have a direct social and indirect economic impact on Pompe disease but has broad implications for patients and their families suffering from other rare muscle disorders.

Pierre Vanderhaeghen

VIB – KU Leuven – ULB
Leuven
Rare diseases

Fund Generet

in collaboration with the F.R.S.-FNRS

Modelling orphan neurodevelopmental diseases and treatments in human neurons in vivo

Prize € 1.000.000

Neurodevelopmental diseases such as intellectual disability and autism spectrum disorders remain difficult to treat because the underlying mechanisms are largely unknown. What's more, it is almost impossible to experimentally study these diseases in humans at the cellular level, given the relative inaccessibility of live human neuronal material.

In this project, Pierre Vanderhaeghen and his team will focus on several important orphan neurodevelopment diseases of genetic origin using an innovative model of human neuronal development in a living organism: following xenotransplantation in the mouse brain.

This is a highly interdisciplinary project, with potentially high impact for our basic knowledge of human brain function and translation to understand and treat orphan diseases. It will rely on the synergistic combination of human clinical genetics, pluripotent stem cell technologies, brain xenotransplantation, combined with neuronal cell biology, electrophysiology and in vivo multiphoton microscopy.

Specifically, the team will test the hypothesis that the rate of maturation that characterizes human neuron development in the cortex is abnormal in these diseases, thereby revealing a novel mechanism that may make the human brain uniquely sensitive to developmental defects. Moreover and importantly, this innovative model will be used as a tool to validate new potential therapeutic compounds identified by other partners.

Collectively, these experiments will allow for the first time to study in the impact of key genes linked to human disease on human neuronal development and function in a living organism, hopefully leading to novel insights on orphan diseases, and leading in the long run to efficient therapeutic development.

Peter Feys

UHasselt
Hasselt
Multiple sclerosis

Funds Claire Fauconnier & Guy Sallets

Walking-related fatigability in persons with MS: psychometric properties of cognitive and coordination fatigability assessment & proof-of-concept of a rehabilitation intervention

Grant € 49.622

People with MS experience worsening in performance for a while when doing a task, such as reduced walking speed while shopping or going for a hike. This is defined as fatigability which is a change in performance over time. Until now, it is unclear whether fatigability is due to motor aspects such as coordination problems and cognitive factors or even both. Preliminary data has shown that people with MS with walking fatigability showed a significant decrease in their movements of their legs when performing a 6' bipedal coordination task in sitting position. However, the reliability of this new measurement method has not yet been determined. Cognitive fatigability measured by clinical measures also needs further investigation of reliability. Knowing such information about measurement will allow us to identify the effect of different interventions for treating fatigability.

So far, no interventional research has included exclusively people with MS with walking-related fatigability. It is unknown if the reduction in walking speed can be reversed by rehabilitation. Dance therapy could be a first intervention addressing problems of fatigability. A pilot study has shown that dance therapy significantly improved the impact on fatigue but its effect on performance fatigability is still unknown. The proposed research will first examine the reliability of the bipedal coordination task, and of cognitive fatigability using clinical measures, and examine relations between measures. Then it will investigate the effect of an eightweek intervention on fatigability in MS by conducting a randomized controlled trial. People with MS (n=24) will be allocated to a dance or a control physiotherapy group. Measures will be collected at baseline and post-intervention. The results will enhance the understanding of the relationship of motor and cognitive fatigability and fatigue, and underlying factors of motor and cognitive dysfunction.

Emilie Lommers

ULiège
Liège
Multiple sclerosis

Funds Claire Fauconnier & Guy Sallets

Multimodal quantification of brain microstructure and cortical synaptic density in MS patients

Grant € 50.000

Multiple sclerosis (MS) is a common and most dreaded cause of handicap in young individuals. Indeed, its disabling aftermaths, its unpredictable course, the daily burden and side effects of its treatments warrant this collective fear.

Classically, MS is viewed as an inflammatory disease of the white matter, that expresses itself as 'plaques' of demyelination. Nevertheless, new evidence shows that MS is much more complex, with both focal and diffuse anomalies in both white and grey matters of the brain. In particular, it seems that beyond focal lesions of the cortex, there is a reduction of the density of synapses, the tiny structures responsible for information transmission from one neuron to the next.

Sadly, conventional MRI, on which MS diagnosis and follow up is primarily based, is blind to most pathological aspects of MS. Therefore, MS experts heavily rely on their clinical sense and personal experience to diagnose and treat MS, a situation which neither desirable nor optimal. In a perfect world, they should buttress their diagnostic and therapeutic decisions on robust, quantitative, reproducible biomarkers of disease activity.

This project precisely wants to establish a multimodal quantitative imaging protocol, combining advance PET and ultra-high field MRI (7Tesla), to reveal the various aspects of MS pathology in the brain.

We will combine quantitative measures of iron accumulation (a marker of inflammation but also neurodegeneration), myelination, fibre tract integrity and cortical density of synapses in patients suffering from MS and in a control population of healthy participants. Advanced statistics will allow us to reveal all the complexity of MS brain pathology, the focal lesions of white and grey matters but also the diffuse synaptic reduction and change in cortical microstructure that are thought to underpin the cognitive decline frequently observed in MS patients.

If this proof of principle is positive, we intend to carry on, establishing the added value of this imaging scheme in MS diagnosis in certain difficult situations, and in MS treatment, by helping MS experts estimate their patient's MS genuine activity. In the long term, we aim at building a predictive model of disease progression, based on these rich data. The current project only pursues the first objective, paving the way to improving MS patients' life through earlier diagnosis and individually optimized treatment.

Roman Praschberger

VIB – KU Leuven
Leuven
Lewy Bodies Dementia

Fund Bonmariage de Bouyalski

in collaboration with Stichting Alzheimer Onderzoek – Fondation Recherche Alzheimer

Unravelling cell-type specific vulnerability pathways in response to pathogenic tau and α-synuclein

Grant € 100.000

In this project we want to find new factors that can prevent brain cell loss in certain dementias. This is important, because this loss is what causes many symptoms and we currently have no drugs that can efficiently stop this. We know that in many neurodegenerative diseases certain proteins aberrantly precipitate within individual brain cells, which then causes damage. Yet while some brain cells seem to be highly vulnerable to these changes, others are not. We want to unravel the secrets of these protected cells, as this might give us the body's very own road-map as to how we can treat vulnerable cells – e.g. those cells that when lost cause memory impairment in Alzheimer's disease. We make use of a powerful model – the fruit fly, which we have genetically modified to express these precipitating proteins. Because their brains are much smaller than human brains, we can now assess their entire brains with all their >200 unique cell types at the same time. With modern microfluidics technology this allows us to 'read' the inner workings of >10 000 individual cells at the same time, which is how we then extract the differences between 'weak' and 'strong' cells.

The best outcome of this research in our fruit fly models would be to find new factors protecting against neuronal loss triggered by aberrant protein precipitation. Upon successful completion we will publish these findings, which will then allow other scientists to build on these results. Beyond this 2-year grant also we ourselves plan to assess the most promising hits in human disease model brain cells that are derived from stem cells.

Araks Martirosyan

VIB – KU Leuven
Leuven
Dementia

Fund A.B.

in collaboration with Stichting Alzheimer Onderzoek – Fondation Recherche Alzheimer

Confronting dementia in the front line: the role of astrocytes

Grant € 100.000

Dementia is an acquired loss of cognition, that is sufficiently severe to affect day-to-day functions, such as social interactions and employment. Currently, there are 47 million people living with dementia worldwide; by 2050, this number is expected to increase to 131 million. Dementia is characterized by neuronal loss. Interestingly, the pathological hallmarks (plaques and tangles) of the most common form of dementia, Alzheimer's Disease (AD), have also been observed in the brains of Parkinson's Disease (PD, Lewy body type) patients who develop dementia in 80% of cases. Besides neuronal loss, both PD and AD brains are characterized by reactive astrogliosis – a response of astrocytes (a major cell type in the brain that is involved in the promotion of neuronal survival and growth) to disease. Essentially two distinct phenotypes of reactive astrocytes are reported – so-called 'A1' and 'A2' states. Reactive 'A2' astrocytes show increased production of neurotrophic and synaptogenic factors and play a neuroprotective role. In contrast, 'A1' astrocytes upregulate neurotoxic factors, including components of the complement cascade (C1r, C1s, C3, and C4), and become directly toxic for neurons. A1 astrocytes have been observed in a number of neurodegenerative diseases, including in post-mortem tissue from AD and PD patients. Upregulation of a common panel of neurotoxic genes implies a similar A1 state across diseases. However, astrocytes are known to be heterogeneous and to respond differentially to disease, raising the question of whether all A1 astrocytes are the same? Do astrocytes in various affected brain regions become reactive by the same mechanisms or not? What are the signals they exchange with the surrounding cells? And finally, would it be possible to find common targets to suppress neurotoxic A1 reactivity in AD cortex and PD substantia nigra (the brain regions most susceptible to each disease) to prevent neuronal loss? In this project, I propose to systematically investigate the development of astrocyte reactivity in AD and PD, using 2 computational analysis of single cell sequencing data from human post-mortem samples, obtained at differing stages of disease progression and from targeted brain regions. I will apply advanced machine learning techniques and cutting-edge, large-scale in situ transcriptomics technologies to reveal molecular drivers of neurotoxic astrocyte reactivity and explore the consequences of astrocyte reactivity for local cells (with an emphasis on neuronal health), providing an unbiased view of how astrocyte reactivity contributes to the development of dementia. Crucially, my research will show whether clinically distinct AD and PD dementias are essentially the same disease (at the molecular level) that can be treated by common drugs, or whether they are molecularly different diseases requiring a targeted clinical approach.

Joni Gilissen

VUB
Brussels
Dementia

Fund Maurange

Navigating community dwelling persons living with dementia and family caregivers through stages of dementia: acceptability and adaptation of the personalized, scalable Care Ecosystem via stakeholder interviews and workshops

Springboard grant € 67.073

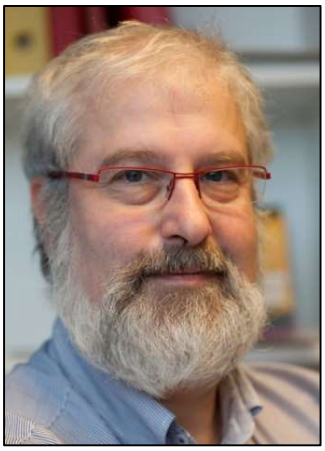
This project is aimed at adapting an existing and evidence-based US dementia care model to better fit the primary care model in Flanders, Belgium.

Dementia is one of the leading causes of disability among older people and its prevalence doubles every 20 years, with high costs associated. Because the needs of people living with dementia are chronic and cumulative, they require quite some extensive support from health and social care professionals, as well as from their family caregivers, along the way. It has been shown that primary care physicians play a pivotal role in being the first contact point and gatekeeper to more specialist dementia care for their patients. It is therefore important that these professionals are supported by specialists who can provide an extra layer of personalized support to these people and their caregivers and who can help them in navigating to care that suits their needs.

Internationally it has been acknowledged that care interventions are best if they are individualized and if they consider the person living with dementia as a whole, as well as include their family carers. Evidence is accumulating for the effectiveness, at least in the short term, of tailored psychosocial interventions to manage both their own and their families' health, care and social needs. Evidence-based interventions for carers have widely been shown to be able to reduce depressive and anxiety symptoms over years and to be cost-effective.

The Care Ecosystem is a model of dementia care designed to provide cost-efficient care for people living with dementia and their caregivers throughout their disease trajectory, from beginning to the end. The main focus is on improving/maintaining the quality of life of both the person with dementia, as well as his/her family caregiver(s) by focusing on needs that are apparent —and are shown to be considerably complex as the disease worsens. The main component of this model is the care team navigation that is led by Care Team Navigators (CTNs), who serve as the main point of contact for patients and caregivers in the Care Ecosystem and who guides them to specialist dementia care that can complement their primary care (e.g. social workers, pharmacists, and other healthcare professionals). Their work is guided by care protocols and they are supported and supervised by the primary care physician. This telephone and web-based intervention was shown to increase participants' quality of life, decrease emergency department admissions (which are most often associated with distress among people living with dementia), and decrease family depression and caregiver burden in the US.

We propose a qualitative study in both primary care physicians, support organizations in the field, experts and people living with dementia and their family caregivers. We will involve these different stakeholders to assess whether this Care Ecosystem would be acceptable to test and implement in Flanders, and which components should then be adapted and how. We hope this will serve as a first step in evaluating the longer-term effects of this model in our own healthcare system.



Pierre van der Bruggen

De Duve Institute – UCLouvain
Brussels
Biomedical sciences

Fund Maurange

How to promote sustained human anti-tumor CD8 T-cell responses?
A focus on transcription factors

Grant € 28.694

Immunotherapy has become a major focus of oncology research. A better understanding of interactions of the tumour with its microenvironment could lead to new therapies for patients whose cancer does not respond to current treatments. The overall objective of this project is to better understand the mechanisms that hinder the effectiveness of cancer immunotherapy. We are particularly interested in killer white blood cells, the CD8 T-cells. These T-cells become easily exhausted within a tumour. We will perform in-depth analyses of T-cells isolated from tumours collected from cancer patients, with the aim of identifying markers of T-cell exhaustion. The results of our research may help to improve future cancer treatments.

Nicolas Capelli

De Duve Institute – UCLouvain
Brussels
Biomedical sciences

Fund Maurange

Modulation of RSK kinase activity and target specificity by cellular and pathogens' proteins

Grant € 45.000

Our laboratory discovered that 3 unrelated pathogens, including viruses and bacteria, evolved in a convergent fashion to hijack a family of cellular enzymes (protein kinases named RSK). Proteins encoded by these pathogens use the very same mechanism to redirect these RSK kinases to non-canonical substrates, thereby evading the innate immune response or increasing their replication ability.

The aim of this work is twofold:

1. Identifying additional pathogens that evolved a similar mechanism to hijack RSK kinases.
2. To test whether human proteins play a similar role, i.e. to regulate the substrate specificity of these kinases in the cell.

This basic research can lead to a better understanding of the cellular functions of RSK kinases and of their regulation, which may impact human development.

It is also aimed at identifying common mechanisms that are used by pathogens to escape immune defenses with the hope to learn how to counteract these pathogenic mechanisms.

Fund Doctor J.P. Naets

The Fund Doctor J.P. Naets supports interdisciplinary medical research at the ULB (IRIBHM, Institut de Recherche Interdisciplinaire en Biologie Humaine et Moléculaire) and small promising teams, with a priority for projects focusing on thyroid research.

In 2020, 5 projects were supported for a total amount of € 338.000.

Carine Maenhaut & Olivier Hancisse

Molecular characterization of papillary thyroid carcinoma: study of the role of ADAR on microRNA biogenesis and sequence

Understanding the genetic changes that underlie carcinogenesis and tumour progression requires to define cancers molecular phenotype. We study thyroid tumours, the most frequent endocrine tumours. They comprise a spectrum of well-defined morphological phenotypes with variable rates of growth, differentiation and biological aggressiveness. While genomic alterations are abundantly studied in cancers, few studies are devoted to post-transcriptional modifications of RNA which might affect their sequence, among which RNA edition. So, the aim of this project is to study the role of ADAR, enzyme responsible for RNA editing, on microRNA biogenesis and sequence.

Vincent Detours

Genome-wide intra-tumour heterogeneity and somatic evolution of anaplastic thyroid cancer at the single-cell resolution

Thyroid cancer (TC) will become the fourth most diagnosed cancer by 2030, mostly due to earlier diagnosis of papillary thyroid carcinomas (PTC) 90%. However, anaplastic thyroid cancers (ATC),although representing only 1-2% of all TC, almost invariably kill patients within the first year after diagnosis. Somatic coding mutations, especially in known cancer genes, have been well characterised in single-sample ATC studies. However, the whole-genome landscape, including complex structural rearrangements seen in TC, as well as the extent of intra-tumour heterogeneity and the underlying evolution of ATC, a critical clinical challenge in cancer treatment, remain unknown. Here, we propose the first multi-region bulk and single-cell whole-genome sequencing characterisation of PTC and ATC, to study the genome-wide somatic mutation landscape, the intra-tumour genetic heterogeneity, especially at the cell-ploidy level, and evolution of TC to its most advanced stage.

Alain Boom & Renaud Beauwens

Importance of Anoctamin 1 in endocrine glands with emphasis on thyrocyte and beta-cells : analogies and differences

We have previously demonstrated the expression of the calcium activated chloride channelanoctamine-1 (Ano1) in the thyroid and in the beta-cells of the endocrine pancreas. In beta-cell of the pancreas, the activity of Ano1 appears critical to maintain the membrane potential as long as glucose is elevated. Increasing glucose concentration increases ATP, induces release Ca++ from an acidic NAADP sensitive Ca++ stores. In the thyroid, the calcium-activated chloride channel Ano1might also appear to induce the release of NAADP and the activation of Ano1 in relation to iodide fluxes in the intrafollicular space allowing iodide to be oxidized and incorporated into thyroglobulin for the production of thyroid hormones. The main goal of the present proposal is to uncover the mechanism of activation of Ano1 in the thyroid, in particular we plan to examine whether the factors involved beta-cell activation of Ano1 are also playing some role within the thyroid.

Xavier De Deken & Karima Merakchi

Thyroid function and inflammation in a new animal model overexpressing the interleukin-4 in the thyroid

Autoimmune thyroid diseases (AITD) are the most common organ-specific autoimmune diseases. Patients with Hashimoto's thyroiditis, the third most frequent autoimmune disease in the United States, develop hypothyroidism, while patients with Graves' disease develop hyperthyroidism caused by TSH receptor activating autoantibodies. The role played by IL-4 in the development of AITD remains controversial. A new transgenic mouse line (Thyr-IL-4) expressing IL-4 in the thyroid was generated. Gene expression profiling reveals thyroid overexpression of several genes involved in inflammation. The aim of our project is to better characterize the phenotype of Thyr-IL-4 mice in the development of AITD using immunization protocols after crossing with different permissive mouse strains for AITD.

Pierre Roger

Preclinical efficacy assessment of CDK4/6 inhibitory drugs in aggressive thyroid cancers and evaluation of phosphorylated CDK4 as sensitivity biomarker

The CDK4/6 inhibitory drugs including palbociclib (Ibrance) are now standard of care for the treatment of advanced breast cancers. CDK4, the primary target of these drugs, is a central enzyme in cell cycle regulation, the process by which a cell duplicates its genetic material and shares it equally between two daughter cells. This process is altered in most cancers, leading to uncontrolled cell multiplication. Our research team identified a modification of CDK4, its activating phosphorylation on T172, as the most relevant biomarker predicting sensitivity to these new drugs. We use this diagnostic tool and other derived tools to assess the extent to which advanced cancers of the thyroid gland including anaplastic carcinomas, currently without effective treatment, could respond to CDK4 inhibitory drugs, and evaluate new drug combinations involving these inhibitor

C. Maenhaut

O. Hancisse

V. Detours

A. Boom

R. Beauwens

X. De Deken

K. Merakchi

P. Roger

Xavier De Deken

ULB
Brussels
Thyroid diseases

Fund Yvonne Smits

Role of hydrogen peroxide in thyroid tumorigenesis using a novel transgenic mouse model overexpressing the H2O2-generating complex DUOX2/DUOXA2

Grant € 80.000

Background: Thyroid carcinoma is the most common endocrine malignancy and about 1% of the population is affected. Beside irradiation, the causes of thyroid cancers remain elusive. Oxidative stress was associated with the development of several cancers, including thyroid.

Project objectives: The goal of our study is to evaluate the implication of the oxidant molecule hydrogen peroxide (H2O2) necessary for the thyroid hormone synthesis in the development of thyroid tumors using a novel transgenic mouse model overexpressing the H2O2 generator DUOX2 specifically in the thyroid.

Research question/hypothesis: The pathological consequences of H2O2 overproduction will be evaluated at cellular and molecular levels and by tracking the emergence of thyroid nodules, papilla, hyperplasia or tumoral lesions.

Study design: Our transgenic animals will be treated to induce a chronic oxidative stress following a long term overproduction of H2O2 in the thyroid. This doxycycline inducible system presents the advantages to control the period of H2O2 generation and the possibility to revert the phenotype by stopping the treatment. To favour oxidative stress-induced diseases, the animals will be treated with anti-thyroid drugs or cross with other existing mouse models of thyroid cancers.

Jolanda van Hengel

UGent
Ghent
Cardiology – basic research

Belgian Heart Fund

in collaboration with the Belgian Society of Cardiology

Generation and characterization of three novel induced pluripotent stem cell-derived cardiomyocyte lines as a model to study the pathophysiological mechanisms of arrhythmogenic cardiomyopathy

Grant € 20.000

Arrhythmogenic cardiomyopathy (ACM) is a genetically inherited disease characterized by progressive cardiomyocyte loss and fibro-fatty replacement of the ventricular myocardium. ACM is mostly caused by mutations in genes encoding proteins of the intercalated disc, with *PKP2, DSG2*, and *DSP*, encoding for plakophilin-2, desmoglein-2, and desmoplakin, respectively, being most frequently mutated.

Arrhythmogenic cardiomyopathy classically manifests as ventricular arrhythmias and loss of heart muscle cells, which is often the first clinical manifestation of the disease, and are an indication for cardiac transplantation. The heterogeneous landscape of ACM pathogenesis complicates the search for effective therapeutic options. To this day, the molecular mechanisms underlying this disease remain poorly understood and characterized, even for patients with an identified mutation. Our ultimate aim is to gain a better understanding of the molecular mechanisms, by further exploring the microRNA dysregulation, as previously observed in ACM models and patients.

As a first part of the project, we are generating three human induced pluripotent stem cell (hiPSC) lines, which will be derived from ACM patient urine samples. These hiPSC lines will harbor a mutation in *DSG2*, *DSP* and *CTNNA3* (the latter encoding for αT-catenin). An isogenic control line carrying the corrected gene will be generated for each hiPSC line using CRISPR/Cas9. After differentiation, the resulting induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) will be characterized on electrophysiological, molecular and ultrastructural level. We will focus on morphology and function and analyse the effect of stress on iPS-CMs by mechanical means.

In order to study the pathogenic mechanisms of ACM, RNA sequencing will be performed to profile gene expression in the different ACM and control cardiomyocytes in basal and stressed conditions. We hypothesize that different genetic mutations can lead to a specific miRNA expression pattern, resulting in altered modulation of signaling pathways. Comparing differentially expressed genes and miRNA levels between different ACM lines and their respective control lines will allow us to further refine the genotype-phenotype correlation within the broad ACM spectrum. This may enable more tailored miRNA-based strategies than currently available for the diagnosis and treatment of ACM patients.

Henri Gruwez

UZ Leuven
Leuven
Cardiology – clinical research

Belgian Heart Fund

in collaboration with the Belgian Society of Cardiology

SURGICAL-AF 2 study: the clinical impact of remote heart rhythm monitoring by photoplethysmography-based smartphone technology in the rehabilitation after cardiac surgery. A randomized, open-label, multicenter, pragmatic clinical trial.

Grant € 20.000

Atrial fibrillation (AF) is a cardiac arrythmia in which the atria of the heart (front chambers of the heart) lose their ability to contract in synchrony with the heart. This results in an irregular heartbeat. AF is the most common cardiac arrythmia and is important because it is associated with negative outcomes such as heart failure, stroke and mortality.

Up to 60% of patient who underwent cardiac surgery develop AF. Post-operative atrial fibrillation is known as POAF. Often this arrythmia occurs in episodes which start and cease spontaneously. These episodes can remain undetected as they are often asymptomatic. In hospital the heart rhythm is monitored for arrythmias. But to date there is no rhythm surveillance at home after discharge.

Rhythm surveillance after discharge from cardiac surgery will enable early POAF detection which leads to three major benefits. At first, patient with POAF can be treated with blood thinners to reduce stroke risk. Secondly, early detection of AF enables early rhythm control which is associated with superior outcomes. Thirdly, patients often develop POAF as a result of an underlying substrate. After cardiac surgery the underlying substrate is often a post-operative adverse event. By monitoring for POAF we will simultaneously be monitoring for post-operative adverse events enabling earlier detection and treatment of post-operative adverse events.

In the SURGICAL-AF 2 trial we will monitor the heart rhythm after discharge in patients who underwent cardiac bypass surgery or surgery of the heart valves. Monitoring will be performed using a smartphone application. The patient can analyze his or her heart rhythm simply by placing a finger on the smartphone camera. An automatic algorithm will provide feedback to the patient. When an abnormal rhythm is detected an early follow up visit shall be organized. This surveillance strategy provides a reliable, patient centred and cost-effective post-operative rhythm monitoring for POAF.

The SURGICAL-AF 2 study will evaluate if post-operative rhythm monitoring is better than the classical follow-up. It investigates the incidence of POAF and the effect of POAF surveillance on therapy changes, readmissions and healthcare related quality of life. It the SURGICAL-AF 2 trial is successful, the study will also investigate a potential effect on long term stroke occurrence and mortality.

An Van Berendoncks

UZ Antwerpen
Antwerp
Sports cardiology

Belgian Heart Fund

in collaboration with the Belgian Society of Cardiology

Supervised home-based combined endurance resistance exercise training programme in asymptomatic adult patients with congenital heart disease. A prospective randomised-controlled trial to evaluate effectiveness, safety and quality of life.

Grant € 15.000

Background: Exercise training is an important treatment strategy in order to increase peak oxygen uptake in adult patients with congenital heart disease (ACHD). Nevertheless, only a minority of ACHD patients receives formal exercise advice or training. Participation to a structured Cardiac Rehabilitation program often needs to overcome logistical challenges in this young population as it requires considerable input of time and resources. Home-based rehabilitation can be an opportunity in this patient population.

Objective: In this research project, the effect of a home-based supervised combined endurance resistance training program on exercise capacity will be investigated in the young, asymptomatic population of ACHD. Secondary, changes in prognostic ventilatory parameters, muscle strength, quality of life, daily activity and safety of the home-based program will be assessed.

Methods: 50 ACHD patients will be randomized 1/1 to an intervention group, receiving tailored home-based bike training and strength training, or a control group receiving the standard general exercise advise. In the intervention group, attention will be paid to assess exercise adherence and training compliance by means of an online application which serves as a bridge between patient and physiotherapist.

Outcome: In both groups, physical function tests (Cardiopulmonary exercise test and 1RM muscle strength tests) will be performed to define VO2peak, ventilatory markers of exercise and maximal muscle strength at baseline and after 16 weeks. Quality of life will be reported in both groups using utility scores and changes in daily physical activity will be measured by an activity tracker. Safety of the home-based rehabilitation will be assessed by documenting adverse events, hospitalization and all-cause mortality.

Discussion: We hypothesize that the implementation of strength training will significantly impact quality of life. Shifting the intervention to the patients home, we are convinced to reach more ACHD patients with the beneficial effects of exercise training.

Gilles De Keulenaer

UAntwerpen
Antwerp
Cardio-oncology

Belgian Heart Fund

in collaboration with the Belgian Society of Cardiology

Cardiovascular disease and cancer are linked through the NRG1/ERBB3 signaling system

Grant € 15.000

Most research in cardio-oncology is devoted to the study of cardiotoxic effects of chemotherapeutics or radiotherapy. These studies are important to allow optimal cancer treatment without cardiac side effects. However, there is also another aspect that associates cardiology and oncology. Recently, it has become evident that from a basic pathophysiological perspective cardiovascular disease (CVD) and cancer are mechanistically connected. Overlap in pathophysiology between CVD and cancer would explain why cancer is accelerated by CVD (and in particular by heart failure) as recently shown in epidemiological human studies and recapitulated in mice with intestinal cancer. The underlying mechanisms of the cancer-inducing effects of heart failure are currently unknown and clinically relevant. Therefore, it is necessary that physiological processes at the crossroads of both diseases are meticulously tested.

In this project, we hypothesize that endothelial secretion of neuregulin-1 (NRG1), which is known to be increased in diverse forms of CVD including heart failure, accelerates intestinal and breast cancer. NRG1 is an endothelium-derived growth factor known to mitigate heart failure with diverse etiologies. Clinical trials with NRG1 are ongoing, and small molecule mimics are under development in our laboratory. However, NRG1 binds to different ERBB receptor tyrosine kinases, of which some are oncogenes expressed by cancer cells. ERBB4 receptors are mostly linked to protection of the CV system, whereas ERBB2/ERBB3 receptors expressed by intestinal and breast cancer cells are linked to rapid cancer progression and increased invasiveness.

In this project, using clinically relevant transgenic mouse models with spontaneous development of intestinal or breast cancer (and known to express various ERBB receptors), we want to analyze whether induction of heart failure accelerates cancer progression through endothelium-derived NRG1, and whether NRG1induced activation of ERBB2 and ERBB3 indeed participates. This project will (i) enhance our fundamental understanding of the mechanistic links between CVD and cancer (ii) unfold the risk for cancer when NRG1 or other (specific and non-specific) ERBB agonists are used pharmacologically.

Bernard Cosyns

UZ Brussel
Brussels
Cardio-oncology

Funds for research in cardio-oncology

Funds Pierre Masure, Alphonse & Marie Walckiers, De Winter-Vermant, Julien Rongvaux, Monique Scheldewaert, Yvette Gembauve, Joanna Damman, Bernard Demeyer, Georgette Paulus, Christiane De Block and Elise Vandendorpe

Development, implementation and evaluation of Group Care consultations within a new follow-up program for patients with pre-existing cardiac disease or cardiovascular complications developed after oncological treatment

Grant € 163.645

Heart disease is worldwide the leading cause of death for men and women and is closely followed by cancer. Improvements in cancer treatment have led to a growing number of patients surviving cancer. Unfortunately, often new heart diseases develop as a side effect of the treatment. Therefore, long-term follow-up within the cardio-oncology clinic is essential in the treatment of the cardiovascular side effects and prevention of future heart conditions. Moreover, in these patients multiple risk factors such as diabetes, overweight or smoking are often present. The follow-up should therefore also focus on reducing these risk factors.

Traditionally, a patient meets yearly with a doctor or a nurse on a one-to-one basis. But limited time impedes the focus on education and coaching. Ideally, the long-term follow-up should be accessible for all patients and developed according to the latest evidence in the field with the focus on achieving or maintaining optimal health, well-being, and quality of life.

Group clinics deliver care to small groups of patients with the same condition at the same time rather than each patient meeting a doctor or a nurse on a one-to-one basis. The group meets at regular intervals to talk about a relevant topic such as exercising or healthy eating habits. This way, they also learn from and can help each other. Each group care session is facilitated by a the same two nurses who will guide the group for the coming years.

In this project, we want to determine the relevant topics and the teaching materials used in these sessions. First, by asking advice to experts such as doctors, nurses and physiotherapists, and also invite general practitioners and cancer survivors themselves. Next, we want to find out whether or not group clinics works better and are a better use of resources than one-to-one appointments. We also want to find out what patients and health professionals think about group clinics. Finally, we want to find whether the quality of life and health habits improved after one year of group clinics.

Delfien Bogaert

UGent
Ghent / Utrecht
Paediatric cancer

Fund Prinses Máxima Centrum Belgium

Clinical fellowship in pediatric hematology-oncology

Fellowship € 244.000

In Belgium, more than 400 children or adolescents are diagnosed with cancer each year. One out of four dies from the disease and two out of three survivors suffer from long-term effects of treatment later in life.

The improvement of their survival and the achievement of an optimal quality of life after treatment not only requires to invest in pediatric cancer research but also in the training of pediatricians.

Selected pediatricians in Belgium will have the privilege to follow a top training and to build an international network.

Delfien Bogaerts is the first pediatrician who benefits from the two years fellowship in Belgium and at the Princess Máxima Center in Utrecht, granted by the Fund Prinses Máxima Centrum Belgium.

“The clinical fellowship in pediatric hematology-oncology offered by the Fund Princess Máxima Centrum Belgium will allow me to learn from leading experts in the field and achieve a high standard of clinical competence. The Princess Máxima Center in Utrecht is the national children’s cancer center in the Netherlands, which will give me a large exposure to pediatric malignancies encompassing all aspects of patient care”.

“For my training year in Belgium, I prefer Ghent University Hospital. Ghent University Hospital is one of the largest centers for pediatric hematology, oncology and stem cell transplantation in Belgium, with a longstanding experience and a large patient population.”

In October 2020, Delfien Bogaerts started her clinical training in pediatric haemato-oncology at the Ghent University Hospital. As from October 2021, she will pursue her training for one year at the Princes Máxima Centre in Utrecht. At the end of the two years fellowship, she will obtain the Belgian professional title of ‘paediatric haemato-oncologist’ and hopes to pursue a career as physician-researcher.

Aurore Liénard & Isabelle Merckaert

Jules Bordet Institute
Brussels
Cancer

Funds Thierry Maricq & Véronique Detournay

Selection made in cooperation with the Friends of the Bordet Institute

Children facing parental cancer: a new randomized controlled study assessing the efficacy of a personalized intervention remote psychological intervention to support parenting

Grant € 45.000

Children of cancer patients may suffer from emotional, behavioural or somatic difficulties. Parents have many questions about the impact of the disease on their children and how to support them. Hence, a preventive and psycho-educational intervention for children confronted with family cancer was created.

Since 2016, a “BenEval” tool has been tested to evaluate the benefits related to this intervention. The results indicate that benefits cover many aspects and appear to vary depending on the medical and family context. It also highlighted the need to further adapt the assessment tool to best fit the clinical situation and the feasibility of its implementation. In 2020, an adaptation of the ‘BenEval’ was developed and pre-tested.

The objective of this study is to implement a flexible version of this assessment and to systematize it in order to improve the quality of the interventions in this field of investigation.

Birgit Geoerger

Gustave Roussy
Villejuif, France
Paediatric cancer

Fund KickCancer

Selection made in cooperation with Innovative Therapies for Children with Cancer

European Proof-of-Concept Therapeutic Stratification Trial on Molecular Anomalies in Relapsed or Refractory Tumors in children (AcSé-ESMART)

Grant € 277.000

E-SMART is an ongoing international clinical study with an adaptative design for early-phase study of novel drugs in children and adolescents.

Adaptative design means the study allows for the testing of several drugs simultaneously and that it can be amended to include new drugs without going through the administrative burden of opening a new trial.

The tested novel drugs are drugs which are currently in development for the adults and which show promises for paediatric cancers.

This clinical trial is aimed at patients with a cancer that is either refractory or in relapse who have undergone a prior deep molecular analysis (whole exome sequencing and RNA sequencing) through a specific national program (such as iNFORM in Belgium). This prior test allows to identify whether and which targeted therapy is relevant for the patient.

In short, the study will allow all children with whatever type of cancer (solid tumours, leukaemia's or lymphomas), to access novel targeted therapies rapidly.

The study first opened in France in 2016 with 7 therapeutic arms evaluating 5 new agents (as single agent or in combination). The first phase of the study was a great success in terms of recruitment with 118 patients included in the study until May 2019.

The study expanded to 5 countries with new national sponsors in the Netherlands, the UK, Spain and soon in Italy and Denmark. The study is designed to be amended subsequently with new treatment arms in future for up to a maximum of 9 years. It is coordinated through the ITCC network (Innovative Therapies for Children with Cancer).

The financial support will allow to define:

- if the highest dose of a single drug or a combination of drugs used in adults is safe for children and adolescents with cancer that is either in relapse or refractory to standard therapy.
- if the pharmacodynamic profile of the drug is equivalent to that seen in adults.

Every new drug will be tested with an intent to file, i.e., the plan to submit a registration application for the paediatric indication of the agent. This will ensure that drugs are registered for use in children and used on label.

Belgian Society for Pediatric Hematology and Oncology & the Belgian Cancer Registry

Christophe Chantrain (CHC Clinique de l'Espérance), Laurence Dedeken (HUDERF), Maëlle de Ville de Goyet (UCLouvain), Caroline Piette (CHU Liège), Anne Uyttebroeck (UZ Leuven), Els Vandecruys (UZ Gent), An Van Damme (CUSL), Nancy Van Damme (Belgian Cancer Registry), Jutte Van der Werff ten Bosch (UZ Brussel) & Joris Verlooy (UZ Antwerpen)

BSPHO & the Belgian Cancer Registry
Belgium
Paediatric cancer

Fund KickCancer

Improving quality of survival after childhood cancer by monitoring late effects

Grant € 173.750

Currently, Belgian patients aged 0-19 years at their cancer diagnosis have a 5-year survival rate of 87%. However, these survivors continue to have an increased mortality and morbidity compared to the general population. Their treatment can cause serious side effects that can greatly affect the patients' survival and quality of life in the long term. Up to 90% of survivors will develop one or more late effects, including late mortality, subsequent malignancies, cardiotoxicity and reproductive complications. Many survivors treated in the past are not aware of their risk at developing late effects and have no summary of their treatment nor individually adapted follow-up plan. Long-term follow-up is not implemented nor funded in the national cancer program.

Based on the Belgian Cancer Registry database (complete since 2004) there were 4867 new cancer diagnoses made in the Belgian paediatric haematology-oncology centres for the incidence years 2004-2016 in children and adolescents aged 0-19 years. All the patients of this cohort, completed with the newly diagnosed patients (2017-2022) and alive at the end of treatment, will be registered in the database using a dataset in which all details about the cancer, cancer treatment, relapse, secondary malignancies and the occurrence of acute and late toxicities can be specified. Radiotherapy plans will be uploaded in a DICOM database. Every 5 years after diagnosis a follow-up registration is added.

This project will make it possible to:

- Collect the necessary data to gain knowledge about the late effects after childhood cancer treatment in these patients to be able to contribute to future research concerning late effects after childhood cancer on a national or international (European) level.
- Provide the patients involved in this project with a detailed treatment summary and a care plan for follow-up adapted to their treatment.
- Write a letter to the Ministry of Health to advocate implementing and funding long-term follow-up in the national cancer program based on the results of a selected cohort (20042013, age 0-14 years).
- Organize an 'awareness day' and a symposium to share knowledge and raise awareness about possible late effects with patients and parents.

An Van Damme

Cliniques Universitaires Saint-Luc – UCLouvain
Brussels
Paediatric cancer

Funds for research in paediatric hematology-oncology

Funds Simon Bauvin, Robert Brancart, Christian Lispet, Rosa Meynen, Denise Raes, Alberte Delferière and Dr & Mrs Charles Tournay-Dubuisson

Selection made in cooperation with the BSPHO

LOGGIC Core: Bioclinical Data Bank for Low Grade Glioma In Children

Grant € 125.000

Low grade glioma (LGG) is a group of brain tumours that are classically determined to be biologically benign. They are associated with a high 10-year overall survival of 94%. However, due to tumour localisation in important brain structures, the natural behaviour of these tumours is not always benign. Since these tumours are often not amenable to surgical resection, more than one in three patients needs drug treatment for non-resectable, clinically symptomatic and/or radiologically progressive disease. Some of these patients will need multiple rounds of treatment throughout childhood and adolescence. At diagnosis, it is currently not possible to identify these patients and adapt treatment accordingly. Therefore, the international LGG consortium of the society of paediatric oncology (SIOP) Europe has decided to develop a comprehensive concept for diagnosing, treatment and monitoring of patients with LGG over their entire disease history (LOGGIC program).

The LOGGIC Trial has been the subject of a previous grant by the King Baudouin Foundation and is aimed to define the optimal first-line non-surgical treatment for newly diagnosed LGG patients.

The LOGGIC Core is a molecular biomarker study that will define the underlying molecular alterations in LGGs. The aim is to prospectively determine novel biomarkers for treatment response prediction and risk stratification, and is the subject of the current grant application.

It is now recognized that activating alterations within the mitogen-activated protein kinase (MAPK) pathway are the underlying cause of all pilocytic astrocytomas, a sub-group of LGG. Furthermore, analysis of DNA methylation profiles shows that paediatric LGG is a biologically as well as histologically heterogeneous family of tumours, in which distinct molecular subgroups can be identified. Initial evidence suggests that distinct molecular alterations are significantly associated with clinical outcome independent from extent of surgical resection, age, anatomic location, and histological diagnosis.

Participation to the LOGGIC Core study is a condition for a patient for participation in the LOGGIC treatment Trial.

Heidi Segers

UZ Leuven
Leuven
Paediatric cancer

Funds for research in paediatric hematology-oncology

Funds Simon Bauvin, Robert Brancart, Christian Lispet, Rosa Meynen, Denise Raes, Alberte Delferière and Dr & Mrs Charles Tournay-Dubuisson

Selection made in cooperation with the BSPHO

Childhood Renal Tumors: UMBRELLA SIOP-RTSG 2016 & SIOP RANDOMET 2017

Grant € 150.000

Kidney or renal tumours are rare cancers in childhood (~6-7% of all cancers in children; 20 new patients per year in Belgium). Most renal tumours in children (~90%) are Wilms' tumours (also called nephroblastoma). A few tumours (~10%) will be a different type of kidney tumour. The precise treatment depends on the type of tumour and how far the tumour has spread to other organs. In the last decades, the chances of cure for children with WT have greatly improved, with a survival rate of ~90%. Nevertheless, for some children the treatment will remain not efficient enough. Moreover, survivors have currently been exposed to treatments with a significant risk of long-term side effects.

Experts from a number of countries throughout Europe and beyond, who have experience in the treatment of kidney tumours in children and adolescents (International Paediatric Oncology Society - Renal Tumour Study Group, SIOP-RTSG), have developed an international clinical research study UMBRELLA SIOP-RTSG 2016. This study for all children with a renal tumour will collect clinical information and biology samples (tumour tissue, blood and urine) for scientific research to identify new prognostic markers that may help to find new and better treatment approaches. This will improve patient selection for either more or less intensive therapy depending on their risk of relapse and survival.

Patients with a metastatic renal tumour can also take part in the international clinical research study SIOP RANDOMET 2017. This study will compare two different types of chemotherapy (standard regimen VAD (vincristine, actinomycin D, doxorubicin) versus new regimen VCE (vincristine, carboplatin, etoposide)) prior to the operation on the kidney tumour (preoperative chemotherapy) in order to analyse which chemotherapy regimen is the best in terms of efficacy (probability of cure) and toxicity (side effects on the short and long term).

Heidi Segers & Veerle Mondelaers

UZ Leuven – UZ Gent
Leuven – Ghent
Paediatric cancer

Funds for research in paediatric hematology-oncology

Funds Simon Bauvin, Robert Brancart, Christian Lispet, Rosa Meynen, Denise Raes & Alberte Delferière

Selection made in cooperation with the BSPHO

ALLTogether: acute lymphoblastic leukemia maintenance therapy and thiopurine enhanced maintenance therapy

Grant € 65.000

Acute lymphoblastic leukemia (ALL) is the most common cancer in children with more than 70-80 new patients per year in Belgium (25% of all paediatric cancers). In the last decades the chances of cure for children with ALL have greatly improved, with a survival rate of more than 85-90%. Nevertheless, for some children the treatment will remain not efficient enough. While other children (40-50%) risk overtreatment resulting in unnecessary, sometimes serious side effects. With the ALLTogether consortium, in which a uniform European treatment protocol is developed, we aim for a less harmful, but equally effective therapy for the low risk patients and an intensification of treatment for the patients with the highest risk of relapse.

The current ALL treatment exists of an intensive multi-drug chemotherapy phase (6-9 months) followed by a maintenance therapy phase until 2 years from obtained remission (<5% blasts in bone-marrow). Maintenance therapy exists at least of oral daily 6-mercaptopurine (6MP) and weekly methotrexate (MTX). This 6MP/MTX maintenance therapy plays a key role for the cure of patients with ALL. However, maintenance therapy is one of the most challenging treatment phases, as physicians need to regularly adjust therapy to obtain the target degree of myelosuppression (since routine measurements of 6MP/MTX metabolites are rarely available), and patients need to be adherent to the therapy during a very long treatment phase, where there are no signs of leukemia, and where the maintenance therapy itself may be burdensome (e.g. fatigue, nausea, poor appetite, hypoglycemia, infections). Several studies that monitored maintenance therapy have indicated that poor or fluctuating adherence to maintenance therapy increases the risk of relapse. In this maintenance study we will evaluate the association of 6MP/MTX metabolites with the risk of relapse, survival and toxicity.

In a subgroup of patients with a high risk of relapse, we will intensify maintenance therapy by adding low dose of 6-thioguanine (6-TG) (“TEAM (Thiopurine Enhanced ALL Maintenance) study”). This TEAM sub-study hypothesizes that the risk of relapse can be reduced without an excess of unacceptable toxicities by adding very low dose oral 6TG to the 6MP/MTX maintenance therapy.

Kim De Veirman

VUB
Brussels
Hematologic cancer

Funds Catharina Weekers, Raymond Wuyts, Gezusters Loosveldt & Patrick Bouillon

Nanobody-based individualized AXL targeting to reverse immune suppression and overcome therapy resistance in Acute Myeloid Leukemia

Grant € 70.000

In blood cancers, including acute myeloid leukemia (AML), a protein, termed AXL, has been identified as a regulator of cancer cell growth and/or resistance to medication. For the majority of elderly AML patients, cancer comes back after several months to years. Current available drugs that target the AXL protein are unspecific and cause severe adverse effects in cancer patients. With this project, we aim to develop a novel method to visualize and specifically target AXL-positive cancer cells in AML patients. Therefore, we will use nanobodies (Nbs), a type of antibodies derived from camels, which are very small, easy to produce and are ideal building blocks to generate new compounds.

The project has 3 specific aims: (1) Develop Nbs to noninvasively image AXL-positive tumor cells. (2) Develop Nbs to specifically block the function of the AXL protein and investigate effects on cancer growth. (3) Investigate the function of AXL in immune cells, which are cells that help the body fight infections and cancer cells. Based on this information we aim to propose new therapeutic strategies to combine 2 or 3 drugs or develop Nbs that target 2 different proteins.

The proposed project will improve our understanding of the role of AXL in cancer and might lead to the development of new, personalized treatments for AML patients.

Rein Verbeke

UGent
Ghent
Hematologic cancer

Funds Catharina Weekers, Raymond Wuyts, Gezusters Loosveldt & Patrick Bouillon

Expanding the immune army: combatting multiple myeloma using a rational combination of Galsome nanovaccines and immune checkpoint inhibition

Grant € 79.864

The discovery of novel drugs and improved techniques for autologous stem cell transplantation have doubled the 5-year survival of patients suffering from multiple myeloma. Nonetheless, most patients ultimately relapse, making multiple myeloma an incurable disease. Consequently, there is an unmet need for novel treatment strategies that ensure long-term effects. In this project, we will rationally combine the complementary expertise of three research groups to develop a therapy based on harnessing the patient's own immune system in the battle against this disease. More specifically, we plan to develop a combination strategy, designed to spark, boost and sustain immunity against multiple myeloma.

To spark an immune response, a therapeutic vaccination platform is used, called Galsomes. These are nano-sized particles that act as vaccines. They package two essential compounds to spark an immune response, specifically directed against the cancer: a source of antigen (an antigen encoding mRNA) and an immunostimulant (α-Galactosylceramide). Based on the mode of action of Galsomes, it is very likely that they could have a strong therapy benefit in multiple myeloma. Therefore, a first part of this project will consist of modifying and optimizing Galsomes as an immunotherapy against multiple myeloma in a suitable mouse model.

Importantly, merely sparking an immune response will probably not be sufficient to completely remove all cancer cells. It is known that tumor cells try to tone down strong immune responses by putting brakes on the activated immune cells (so-called checkpoint molecules). Therefore, a valid strategy to boost and sustain the sparked immune responses, is to remove these brakes by administering checkpoint inhibitors. Several of these checkpoint inhibitors are already used in the clinic, but with varying success in case of multiple myeloma. Therefore, the second part of this project is designed to map which checkpoint molecules are present as well as when and where they occur after Galsome vaccination. This is done by non-invasive imaging and will provide crucial information to develop an evidence based combination therapy for Galsomes and checkpoint inhibitors. By evaluating this in detail and also looking at which specific cells of the immune system are present and blocked by these brakes, we can design this combination therapy accordingly and ensure localized and timely inhibition of these checkpoints. The ability of the resulting combination therapy to control multiple myeloma progression in mice, will be studied in the last part of this project.

Geert Carmeliet

KU Leuven
Leuven
Cancer

Funds D.V., Jozef Van Ammel & Nicolas Dehu

Selection made in cooperation with the Foundation against Cancer

Metabolic vulnerability of breast tumor cells during bone metastasis formation

Grant € 85.000

Breast tumor-derived bone metastases cause severe morbidity and remain a therapeutic challenge as current therapies do not cure. Tumor cells often spread to bone before the primary tumor is treated but they escape detection. Insight in the early bone metastatic stages is therefore necessary. We postulate that the metabolic profile of tumor cells regulates their proliferation in bone. More specifically, bone-specific nutrient availability and metabolic cross-talk with osteoblasts will allow tumor cells with a compatible metabolic profile to grow in bone.

To this end, we will use transcriptomics and metabolomics in preclinical models of bone metastases combined with metabolomics on in vitro co-cultures of tumor cells and osteoblasts. Using integrative bioinformatics, we will select interesting metabolic pathways and confirm their contribution to bone metastasis formation by genetic approaches and by a clinical retrospective study. Our project has the potential to lead to novel diagnostic or druggable targets.

Frédéric Amant

UZ Leuven
Leuven
Cancer

Fund Frans Janssen

in collaboration with the KWF Dutch Cancer Society

Cancer & pregnancy: follow up of children born from mothers that were treated for cancer during pregnancy

Grant € 150.000

Postpartum breast cancer is breast cancer that is diagnosed in the first 2 years after giving birth. This type of breast cancer has a prognosis and twice the risk of metastasis compared with breast cancers diagnosed during or outside the context of pregnancy. Since the risk of breast cancer increases with age and more and more women postpone their desire to have children until later in life, it is expected that the number of women with post-partum breast cancer will further increase in the coming years.

There is evidence that the poorer prognosis is due to molecular changes that take place during the involution process. This is the process whereby the breast, after delivery (if not breast-fed) or after the cessation of breastfeeding returns to its pre-pregnancy state. However, little is known about this.

The aim of this study is to find out whether postpartum breast cancer, which is diagnosed during the

involution process, has a poorer prognosis and different molecular and immunological properties than breast cancers diagnosed during or outside the context of a pregnancy. It will also be investigated whether the characteristics of breast cancer diagnosed during the breastfeeding period are comparable to those of breast cancers diagnosed during pregnancy.

Hans Wildiers & Christine Desmedt

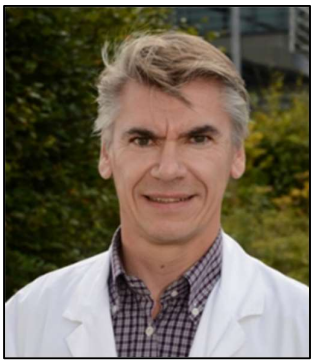
UZ Leuven
Leuven
Breast cancer

Fund Brigitte Huijts-Heidug

Further professionalization and expansion of the biobanking platform of the UZ Leuven Multidisciplinary Breast Centre

Grant € 25.000

Each year, about 700 new patients are diagnosed with breast cancer in UZ Leuven. This project supports the further establishment of a unique breast cancer blood bank (initiated in 2003), containing blood samples collected at different time points from breast cancer patients treated at the Multidisciplinary Breast Center in UZ Leuven. The samples are used for scientific research, in order to gain better insights in the disease itself as well as in the response of the body to different breast cancer treatments. In cancer cells, some specific proteins are dysregulated, causing unlimited growth of tumours. Because the affected pathways can strongly differ between patients, a specific therapy may give good results in one case, while completely failing in another case. Treatment decisions are based on biomarkers which can be measured in the tumour itself or in the blood. In some cases, however, accurate selection of the most appropriate therapy still remains challenging for oncologists. There is a high need for additional and reliable (blood) biomarkers that could help identifying patients who will benefit from a given treatment, and on the other hand patients who are at high risk of developing serious adverse effects as a result of the treatment. Besides guiding treatment choices, blood biomarkers can also be useful to monitor the disease course. In addition, genetic factors that may play a role in breast tumour development and treatment can also be studied in DNA isolated from the blood. Finally, breast cancer biomarker research could also reveal new therapeutic targets for the development of new drugs.



Jean-Luc Van Laethem & Ivan Borbath

Hôpital Erasme, ULB & Cliniques St-Luc, UCL
Brussels
Pancreatic cancer

Fund A.B.

Randomized multicenter phase II comparative study aimed at evaluating the impact of stereotaxic radiotherapy in addition to neoadjuvant chemotherapy in localized and potentially resectable pancreatic cancer

Grant € 100.000

Surgical resection is the only potentially curative treatment for patients with pancreatic cancer with the aim of curative R0 resection (R0 meaning no cancer cells seen microscopically at the primary tumor site) and related improvement of survival. As a standard , surgery is usually followed by adjuvant therapy that improves survival but neoadjuvant therapy (NAT) is a rapidly emerging concept that needs to be explored and validated in terms of therapeutic options, in both resectable and borderline resectable pancreatic tumours.

In this setting, preoperative FFX (mFolfirinox) seems to be feasible and can be prolonged by radiation therapy (chemoRT or SBRT) with promising benefit for patients in terms of R0 resection and prolonged survival. However, the exact and best therapeutic sequence is not yet known and the additional role of adding radiation therapy to chemotherapy requires validation in randomized trials.

We recently reported feasibility and preliminary efficacy data of the whole therapeutic sequence combining preoperative FFX x 6 cycles (G-Nab-P in some cases) prolonged by 5 days SBRT (35 Gy + 8 Gy boost). We propose now to evaluate the impact and efficacy of adding SBRT to preoperative neoadjuvant mFFX or Gem-NabP in patients with borderline or high risk resectable pancreatic adenocarcinoma. We hypothesize that this full sequence strategy of pre-operative treatment is safe and feasible and will improve both the R0 resection rate and prognosis (DFS as primary end point) of pancreatic adenocarcinoma, especially by targeting the tumoral vascular encasement.

Katrien Benhalima

UZ Leuven
Leuven
Diabetes

Diabetes Liga Research Fund

in collaboration with the Diabetes Liga

Closed-loop insulin delivery in pregnant women with type 1 diabetes: a randomized controlled trial: the CRISTAL study

Grant € 170.000

Pregnant women with type 1 diabetes (T1DM) are at increased risk of complications such as overweight babies, pregnancy poisoning, premature birth, caesarean sections, congenital malformations and stillbirth. Even with the increasing use of glucose sensors that can measure sugar levels continuously and insulin pumps, pregnant women with T1DM continue to have, on average, high sugar levels during pregnancy. With the CRISTAL study, we want to investigate whether the use of an artificial pancreas (an insulin pump that delivers insulin automatically based on the sugar values measured by the glucose sensor), can provide better control of the sugar levels in pregnancy and as such contribute to fewer pregnancy complications. We want therefore to evaluate the safety, efficacy, feasibility and cost-effectiveness of an artificial pancreas (780G Medtronic system) compared to routine treatment in pregnancy (regular insulin pump or insulin injections). We plan to include 92 participants by 10 large hospitals (UZ Leuven, UZA, UZ Gent and UZ Brussel, Imelda Bonheiden, OLV-Aalst-Asse, AZ St Jan Brugge, AZ Groeninge Kortrijk, AZ St Nikolaas and AZ Delta Roeselare). Half of all participants will be assigned to the artificial pancreas intervention and the other half will continue with their current treatment. Participants can be included in the study up to 12 weeks of pregnancy. Follow-up is planned until delivery.

Julie Jacob

UZ Leuven
Leuven
Diabetes

Diabetes Liga Research Fund

in collaboration with the Diabetes Liga

E-CLAIR: Efficiency and Cost-effectiveness of Artificial Intelligence based Diabetic Retinopathy Screening in Flanders

Grant € 80.000

Diabetes patients are at increased risk of losing sight due to the development of diabetic retinopathy (DR). DR is a vascular disease of the retina which is due to high blood sugar levels. Screening for DR is very important since most patients do not experience any symptoms until advanced stages of the disease. If recognized early, the vision-threatening side-effects of DR can often be prevented with appropriate management. However, detecting DR is time consuming and currently requires in Flanders an appointment with an eye specialist.

In countries such as the UK, and US, large scale DR screening networks have been established to mitigate this problem. Trained graders, instead of eye specialists, do here the routine eye checks to obtain an early detection of DR. Offering a solution to too long waiting times and high cost of eye specialists.

In the E-CLAIR project we want to go one step further then current state-of-the-art DR screening networks by applying AI for the routine eye checks. Multiple DR screening pathways, tailored for the Flemish region, will be created and evaluated in ophthalmology departments in Flemish hospitals for their efficiency and cost-effectiveness. We believe that the usage of AI and human graders in Flemish eye hospitals has the potential to significantly enhance the eye care received by diabetic patients while reducing health-care costs.

Fund for scientific research in rheumatology

The Fund for scientific research in rheumatology supports clinical and multicentre programs, either in academic or non-academic Belgian institutions. The Fund especially focuses on projects that are open to collaborations with other interested centres and which cannot easily be supported through other existing national or international programs. Translational or basic research can also be supported in a preparative phase for more established funding opportunities.

In 2020, 7 projects were supported for a total amount of € 130.830

Eric Gracey

UGent – VIB

Cataloguing the cellular and transcriptional heterogeneity of mechanical-damage associated tendon disorders

Tendon-related diseases range from those of overuse (tendinopathy) to those of autoimmune origin(inflammatory arthritis). Collectively, such diseases place a large burden on society and are difficult to treat as the underlying biology is poorly understood. In this project, we will catalogue the complete cellular landscape of the healthy and diseased Achilles tendon using advanced cellular and molecular techniques. This will open the door for research into disease-modifying therapeutics.

Ellen De Langhe

KU Leuven

Systemic sclerosis and occupational silica or solvent exposure: investigating epidemiology, gene-environment interactions and objective markers of exposure to improve occupational epidemiology, risk assessment and prevention

Systemic sclerosis can develop in genetically predisposed individuals upon exposure to environmental triggers. We will investigate the association between occupational exposure to silica or solvents and systemic sclerosis. We will determine genetic backgrounds to evaluate the relation between exposure, genetics and disease characteristics. We will evaluate objective markers of exposure. This would allow for true preventive strategies and lead to better understanding of disease processes.

Ruth Wittoek

UGent

Structural sonography in healthy children and adolescents

Musculoskeletal ultrasound (US) is widely used in adult rheumatology. Although well accepted and harmless, use of US in daily pediatric rheumatology practice is not yet generalized. In order to differentiate normal from pathological findings, normative data are mandatory but currently lacking. Moreover, measures may vary in children according to age. In this project, structural US will be performed in 500 healthy children from all age groups allowing to collect data of healthy growing joints.

Veerle Somers & Pieter Ruytinx

UHasselt

Elucidating the role of double homeobox protein 4 (DUX4) in the pathology of inflammatory arthritis

Antibodies against double homeobox protein 4 (DUX4) were recently identified in a subset of patients with axial spondyloarthritis. DUX4 is silenced in most adult cells and tissues. We foundDUX4 expression in synovial tissue obtained from patients with inflammatory arthritis. In this study, we aim to get more insight in the role of DUX4 in the pathology of inflammatory arthritis.

Delphine Bertrand

KU Leuven

How can we optimize the treatment with rituximab for patients with Rheumatoid Arthritis in daily clinical practice?

Rituximab is an effective drug, however it is expensive and might be accompanied with an increased risk of infections. With this project we would like to study patients' perceptions and experiences regarding tapering and on-flare retreatment with rituximab based on interviews. By means of a randomised controlled trial, we plan to study if patients can be equally well controlled when gradually lowering the dose of rituximab and if systematic retreatment is superior to on-flare retreatment.

Manouk de Hooge

UZ Gent

Comparing axial radiographic damage and mobility of the spine in psoriatic arthritis (PsA) with newly diagnosed spondyloarthritis (SpA)

Also to compare limitations in spinal movement (BASMI)of newly diagnosed PsA patients to newly diagnosed SpA patients, to investigate the difference in radiographic damage in PsA patients with and without axial involvement, and to investigate whether PsA patients evolve over time to (non-) radiographic axSpA.

Olivier Malaise

CHU Liège

Multimodal study of glucocorticoid-induced osteoporosis and myopathy: evaluation of bone and muscle toxicity by MRI, serum analysis and architecture measurement after different doses of glucocorticoid therapy initiation

We study both glucocorticoid-induced osteoporosis and myopathy by multimodal approach's, withfirst the most recent and accurate evaluation techniques (MRI for muscle and HR-pQCT for bone),but also daily clinics techniques (muscle force evaluation, DEXA-scan) and biological biomarkers. Comparisons with the demographic data and glucocorticoids dose will determinate which patients are the most at risk for bone loss and muscle atrophy and should be the target for preventive actions.

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E. De Langhe

R. Wittoek

V. Somers

P. Ruytinx

D. Bertrand

M. De Hooge

O. Malaise

Anne Dams

Genk
Insurance medicine

Fund Benevermedex

Return to work after Hernia Repair, a survey to understand the motivation of the prescription behavior of general practitioners and surgeons

Prize € 3.500

Surgical repairs of inguinal hernia are performed frequently, in Belgium approximately 25 000 a year and half of these patients are at their working ages. Duration of convalescence after inguinal hernia repair is therefore of major socioeconomic interest. Laparoscopic hernia repair was developed in the early nineties. One of the motivations for the additional cost of this operation was that the duration of hospitalisation would shorten, making a quicker return to work (RTW) possible.

We are now three decades on, and I wanted to investigate if we reached this goals. I sent a questionnaire to general practitioners in Limburg (province in Belgium) and to abdominal surgeons in Flanders to ask them about their convalescence recommendations. The same questions were asked in relation to sports and car driving. I compared these answers with the guidelines of the HAS (Haute Autorité de Santé – France) and RSC (Royal College of Surgeons of England). The result of my study was that in 2020 we still prescribed too much sick leave, and, even more important, that we prescribed it for the wrong reasons. 90% of the general practitioners and even 80% of the surgeons prescribe it to prevent recurrences. However, the available literature does not support the idea that early resumption of work-related activities would lead to the recurrence of an inguinal hernia. The duration of convalescence after groin hernia repair is affected by preoperative recommendations and expectations, but may also be affected by socio-cultural factors and surgical 'traditions'. I believe that this survey can help us from excluding these myths in policies of RTW and help us in prescribing national guidelines. In this way it can contribute to more socioeconomic wellbeing of the patients.

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Youri Taes	Diabetes Liga Research Fund
Ben Van Camp	Funds Catharina Weekers, Raymond Wuyts, Gezusters Loosveldt & Patrick Bouillon
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Working together for a better society

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The Foundation is an actor for change and innovation in Belgium and Europe, serving the public interest and increasing social cohesion. It seeks to maximise its impact by improving skills in organisations and for individuals. It also stimulates effective philanthropy by individuals and corporations.

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The King Baudouin Foundation was set up in 1976, on the occasion of the 25th anniversary of King Baudouin's reign.

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