

# ANNUAL REPORT

2017

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## INTRODUCTION

- 14 projects selected as a result of the 4<sup>th</sup> call for projects

A 4<sup>th</sup> call for projects was opened in January 2017 and led to the selection of 14 projects for an annual total budget of 3.5 million EUR. Funding was awarded for a 2-year period, commencing on 01 October 2017. The call was managed by FRS-FNRS within the framework of FRFS-WELBIO.

- 3 "Continuation Grants"

A "Continuation Grant" instrument was introduced during the 2017 call for projects. This instrument was defined to consolidate the most innovative projects and to enable researchers to pursue their fundamental research as a continuation of their first WELBIO project, as long as prospects for creating economic value could be identified.

- First returns on investment

In 2017, WELBIO received its first returns on investment thanks to a fruitful collaboration between the firm arGEN-X and the laboratory of Prof. P. Coulie (UCL - WELBIO 2011-2015) and Prof. S. Lucas. An agreement was signed between arGEN-X and AbbVie, which, in 2016 led to an initial payment of \$40,000,000 from AbbVie to arGEN-X, a part of which came back to WELBIO via UCL in 2017. As the collaboration continued successfully, AbbVie then made an additional payment ("milestone 1"). In total, WELBIO received a total of EUR 351,562 in 2017.

- New prospects for creating economic value

Pathways to creating economic value are emerging for several WELBIO projects. Three patent requests were therefore submitted in 2017. Furthermore, funding (WALInnov, BioWin) was obtained for projects stemming from 3 WELBIO projects, which will involve partnerships with Walloon companies. Finally, the first spin-off company creation project, was initiated, based directly on the results of a WELBIO project.

28 very high-level projects are currently being funded and supported by WELBIO. This is testament to the strength the life-sciences skills the researchers in our country's French-speaking universities have. Unfortunately, too many great quality projects proposed by extremely talented researchers could not be retained, due to insufficient funds. We can only repeat last year's message: the fragility of WELBIO's funding is still the major challenge that must be overcome. Fundamental research, in particular in our field, is a long-winded enterprise in which continuity and long-term stability is absolutely necessary. The creation of FRFS in 2013, was intended to guarantee WELBIO's sustainability. In practice, this objective has not yet been achieved. We are therefore

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forced to note that WELBIO's minimal funding is reappraised every year. WELBIO is currently waiting to find out the direction defined by its new responsible minister, in particular to know whether the means will be available to launch a 5<sup>th</sup> call for projects.

## SCIENTIFIC RESEARCH

### 1. A 4<sup>th</sup> call for projects

Since its creation, WELBIO has operated through calls for projects. These calls are launched every two years. Two contingents of projects are thus supported simultaneously. Due to WELBIO's integration into the Fonds de la Recherche Fondamentale Stratégique (FRFS [The Strategic Fundamental Research Fund]) the 2015 call schedule overran. The FRFS and WELBIO therefore agreed to align the 2017 call for projects with the 2015 call for projects schedule. The 4<sup>th</sup> CALL for projects was therefore launched in January 2017 with a view to projects starting on 1<sup>st</sup> October 2017. The 8 WELBIO projects initiated in 2013, which should initially have finished at the end of January 2017, benefited from an exceptional extension period of 8 months to ensure they would link-up with the call for projects 2017.

A reflection process on the strategy for this 4<sup>th</sup> call for projects was conducted in 2016 by a "call for projects" working group which was set up within WELBIO. This working group consists essentially of the academic members of WELBIO's board of directors. The board of directors for FRFS was informed of the working group's conclusions with a view to defining the rules and conditions of this new call, in which new rules and conditions had been introduced including elements that reflect WELBIO's specific strategic fundamental research mission better. Based on excellence in fundamental research, this feature can be summed up in two key concepts:

**The need to create industrial value:** this is reflected by evaluating the "attention paid to creating economic value". This point has been the subject of increasing attention over the course of this 4<sup>th</sup> call for projects:

- For the first time, 2 of the independent international Scientific Committee's members came from industry;
- A pre-selection phase was introduced for projects, which enabled the Scientific Committee to discuss the best projects in more depth to determine their final ranking and for it to be based not just on the scientific excellence of the project and the researcher, but also on a more in-depth analysis of the potential to create economic value. This analysis, coordinated by WELBIO, included a prior art search in the patent databases (conducted in collaboration with Picarré), an analysis of the potential to create industrial value (conducted in collaboration with BioWin) and a financial analysis.

**Long-term action:** our experience over the last few years has shown, where necessary, that the economic value of discoveries arising from fundamental research projects, is generally not realised in the 4 first years. It is therefore important for WELBIO to be able to support projects over a longer term, to allow the pathways for creating economic value that began during the initial project to come to fruition. A "Continuation Grant" instrument was therefore introduced this year. The WELBIO

researchers whose initial project came to an end in 2017, were able to propose a project as a continuation of their first WELBIO project. This new project had to include a "work package" intended to implement a plan to create economic value.

58 proposals were submitted in response to this 4th call for projects. Funding was granted to the 14 highest-ranking projects out of the 26 projects that were preselected.

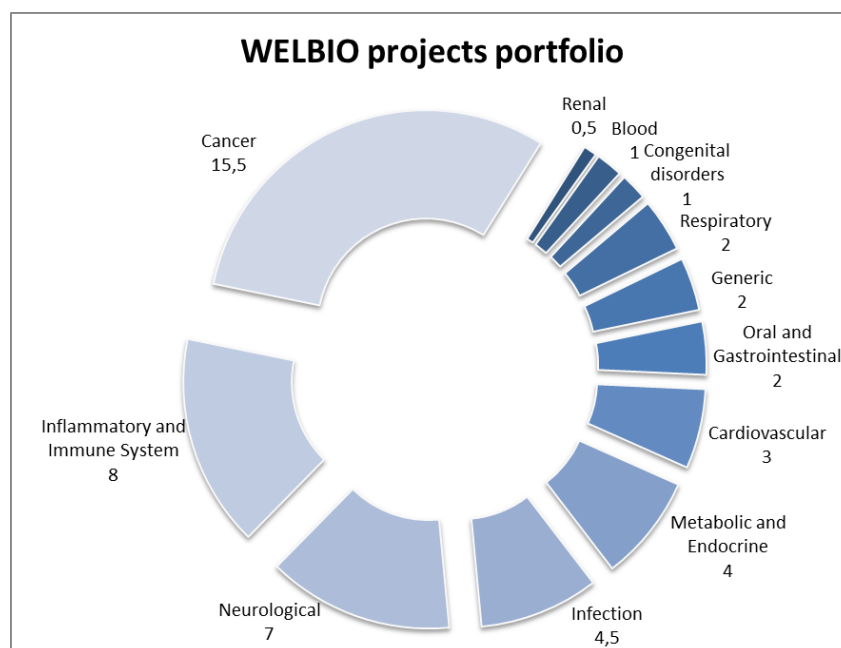
Furthermore, funding for the 14 projects selected in 2015 was renewed for a new 2-year period.

## THE PROJECT PORTFOLIO

By the end of 2017, the project portfolio included 28 FRFS-WELBIO PROJECTS.

WELBIO's annual budget is still too modest in comparison to the excellent potential for life-sciences research by our country's French-speaking universities. 14 projects were selected at the end of the last call for projects, but it is clear that several projects that were just "below the bar" also deserved to be supported.

Since its creation and up to today, WELBIO has funded 51 projects. The fields of research that are funded, are determined by the best proposals. No field of research is defined in advance but, on the whole, projects are oriented towards biomedical sciences, filling the funnel before the project pipeline of the BioWin competitiveness cluster. The graph below shows how the 51 WELBIO projects can be divided according to the HRCS (Health Research Classification System).



Classification of the 51 projects supported by WELBIO since its inception according to the HRCS  
(2 categories are attributed per project)

## Projects initiated in 2017:

### "Advanced grants" 2017-2019:

- **Jean-Luc Balligand:** EUR 508,299 / 2 years  
Université catholique de Louvain  
*Cardiac Aquaporin-1: a new regulator of myocardial remodeling*
- **Stefan Constantinescu:** EUR 684,250 / 2 years  
Université catholique de Louvain  
*Targeting mechanisms of pathogenic mutant calreticulin signaling via thrombopoietin receptor and JAK2 in myeloproliferative neoplasms*
- **Pierre Coulie:** EUR 625,600 / 2 years  
Université catholique de Louvain  
*Cytolytic CD8 T lymphocytes in severe forms of human autoimmune diseases, towards diagnostic markers and new therapeutic avenues*
- **François Fuks:** EUR 699,220 / 2 years  
Université libre de Bruxelles  
*Unravelling the Role of RNA Epigenetics in Health and Disease*
- **Anna Maria Marini:** EUR 570,400 / 2 years  
Université libre de Bruxelles  
*Rh factors and the control of membrane permeability to ammonium*
- **Pierre van der Bruggen:** EUR 699,775 / 2 years  
Université catholique de Louvain  
*At the crossroads of cancer and autoimmunity: novel therapeutic targets on exhausted human T cells*

### "Starting grants" 2017-2019:

- **Benjamin Beck:** EUR 399,485 / 2 years  
Université libre de Bruxelles  
*Characterization of the Molecular Core of Esophageal Cancer*
- **Pierre Close:** EUR 399,797 / 2 years  
Université de Liège  
*Translation reprogramming through wobble tRNA modification in cancer*
- **Abel Garcia-Pino:** EUR 399,992 / 2 years  
Université libre de Bruxelles  
*Cellular and molecular bases of the regulation of bacterial persistence by (p)ppGpp synthetases/hydrolases*
- **Thomas Marichal:** EUR 398,913 / 2 years  
Université de Liège  
*Epithelial cells as master regulators of mucosal homeostasis: unraveling the regulatory role of Rab guanine nucleotide exchange factor-1 (RABGEF1).*
- **Benoit Vanhollebeke:** EUR 399,998 / 2 years  
Université libre de Bruxelles  
*Deciphering the regulatory mechanisms of blood-brain barrier function*

## "Continuation grants" 2017-2019:

- **Marc Parmentier:** EUR 699,215 / 2 years  
Université libre de Bruxelles  
*Chemerin and its receptors in tumoral angiogenesis*
- **Fabrice Bureau:** EUR 399,97 / 2 years  
Université de Liège  
Lung regulatory macrophages: phenotype, function and therapeutic potential
- **Patrice D. Cani** – EUR 399,960 / 2 years  
Université catholique de Louvain  
*Targeting NAPE-PLD, novel bioactive lipids and specific gut microbes to improve cardiometabolic disorders associated with obesity*

## Projects renewed in 2017:

### "Advanced grants" 2015-2019:

- **Cédric Blanpain:** EUR 297,000 / year  
Université libre de Bruxelles  
*Mechanisms controlling tumor heterogeneity in squamous cell carcinoma*
- **Alain Chariot:** EUR 297,000 / year  
Université de Liège  
*Dissecting oncogenic pathways*
- **Jean-François Collet:** EUR 279,000 / year  
Université catholique de Louvain  
*Discovering the molecular mechanisms involved in the protection of the bacterial cell envelope from stress: a step towards the design of new antimicrobial drugs*
- **Alban de Kerchove d'Exaerde:** EUR 293,000 / year  
Université Libre de Bruxelles  
*Genetic Identification of the neural circuits involved in Attention deficit/ Hyperactivity disorders (ADHD)*
- **Yves Dufrêne:** EUR 258,000 / year  
Université catholique de Louvain  
*Staphylococcus aureus biofilms: understanding bacterial adhesion and developing new anti-adhesion strategies*
- **Decio L. Eizirik:** EUR 291,000 / year  
Université libre de Bruxelles  
*Beta cell splicing signature of diabetes*
- **Benoît Van den Eynde:** EUR 297,000 / year  
Université catholique de Louvain  
*Finding new immunotherapy targets in the tumor microenvironment by in vivo shRNA pool screening in autochthonous melanomas and by studying hypoxia-driven immunosuppression*
- **Pierre Vanderhaeghen:** EUR 297,000 / year  
Université libre de Bruxelles  
*Using human pluripotent stem cells to understand brain diseases and for the design of novel brain repair therapies*
- **Emile Van Schaftingen:** EUR 297,000 / year  
Université catholique de Louvain  
*Metabolic repair and metabolic diseases*
- **Miikka Vikkula:** EUR 297,000 / year  
Université catholique de Louvain



## Development of diagnostic tools for lymphedema

### "Starting grants" 2015-2019:

- **Christophe Desmet:** EUR 150,000 / year  
Université de Liège  
*Study of the regulation of hematopoiesis and T cell fate through translational control*
- **Isabelle Migeotte:** EUR 150,000 / year  
Université libre de Bruxelles  
*Role of mechanical forces and cytoskeletal rearrangements in epithelial-mesenchymal transition and cell migration at mouse embryo gastrulation*
- **Kristel Van Steen:** EUR 150,000 / year  
Université de Liège
- **DESTINCT: DEtecting STatistical IInteractions in Complex Traits Valérie Wittamer:** EUR 150,000 / year  
Université libre de Bruxelles  
*Ontogeny of microglia, the resident macrophages of the central nervous system*

### Projects terminated in 2017:

### "Advanced grants" 2013-2017:

- **Michel Georges**  
Université de Liège  
*Integrating genetics and functional genomics to identify causative genes and variants controlling inherited predisposition to inflammatory bowel disease*
- **André Goffinet**  
Université catholique de Louvain  
Mechanisms of brain wiring
- **Marc Parmentier**  
Université libre de Bruxelles  
*Role of leucocyte chemotactic factors in tumor progression*

### "Starting grants" 2013-2017:

- **Fabrice Bureau**  
Université de Liège  
*Ontogeny and molecular differentiation pathways of lung interstitial macrophages*
- **Patrice D. Cani**  
Université catholique de Louvain  
*Study of the interactions existing between the gut microbiota and the host : impact on the onset of obesity and type 2 diabetes.*
- **Stanislas Goriely**  
Université libre de Bruxelles  
*Transcriptional control of memory CD8 T cell differentiation*
- **Cédric Govaerts**  
Université libre de Bruxelles  
*Structural characterisation of CFTR using nanobodies*
- **Charles Pilette**  
Université catholique de Louvain  
*Impaired mucosal immunity in severe asthma*

## 2. WELBIO RESEARCHERS

WELBIO researchers are all either F.R.S.-FNRS researchers or researchers appointed at a university of the French Community of Belgium. At the end of 2017, 12 of the 28 WELBIO researchers had an F.R.S.-FNRS mandate (as a qualified researcher, senior research fellow or director of research), while the others were funded directly by their University.

The excellence of the results obtained by the WELBIO researchers is highlighted year on year, by the number of **PRESTIGIOUS SCIENTIFIC AWARDS** they receive.

In 2017:

- Patrice Cani, WELBIO investigator at UCL, Cédric Govaerts, WELBIO investigator (2013-2017) at ULB and Laurent Nguyen, WELBIO investigator (2011-2015) at ULiège, were appointed/promoted to FNRS Research Fellows;
- Jean-François Collet, WELBIO investigator at UCL and Alban de Kerchove d'Exaerde, WELBIO investigator at ULB, were appointed/promoted to FNRS Directors of Research;
- Cédric Blanpain, WELBIO investigator at ULB, was awarded the first "Cancer Research Award" by the Fondation contre le Cancer [Belgian Foundation against Cancer] in the "Fundamental Research" category.
- Patrice Cani, WELBIO investigator at UCL, FNRS Research Fellow, held the Francqui Chair 2017 at the Université de Liège's Faculty of Veterinary Medicine. He also received the "Belgian Endocrine Society Lecture Award" 2017.
- Jean-François Collet, WELBIO investigator at UCL, FNRS Research Fellow, was elected as a member of the Belgian Royal Academy;
- Stefan Constantinescu, WELBIO investigator at UCL, is laureate for the Fundamental Medical Sciences Prize (a five-yearly prize for medical science - a Government awarded prize - Belgian Royal Academy of Medicine). He also received a "Special Recognition Award" from the A\*Star Experimental Therapeutic Centre (Singapore) and was appointed Vice-President of the Federation of European Academies of Medicine;
- Emile Van Schaftingen, WELBIO investigator at UCL, was promoted to the rank of baron.
- Pierre Vanderhaeghen, WELBIO investigator at ULB, obtained a UCB scientific prize from the Fondation Médicale Reine Elisabeth for Neurosciences.

## 3. RESEARCH TEAMS

Between February 1st 2011 and 31 December 2017 **452** PEOPLE worked on WELBIO projects alongside the principal investigators.

The majority of them (~70 %) consisted of scientists supported in their work by laboratory technicians.

Around 40% of the staff were subsidised by WELBIO, the others were supported by FNRS, FRIA, Télévie, ERC and the Fondation contre le Cancer.

At the end of 2017, 123 people were working on the 28 ongoing WELBIO projects. 18 scientists and 8 laboratory technicians benefit from a contract that is directly linked to a WELBIO project, which is equivalent to a total of 22.6 FTE.

Recruitment is still underway for the projects initiated at the end of 2017.

## 4. SCIENTIFIC PUBLICATIONS

**53 PUBLICATIONS** were published in 2017. 24 articles were published in prestigious journals (with an impact factor of above 10) such as *Nature*, *Science*, *Cell*, *Nature Cell Biology*, *Nature Nanotechnology*, *Gut*, *Immunity* or *Neuron*.

Some of the most notable publications:

- How stem cells lead to the healing of skin injuries (C. Blanpain)  
  
Aragona, M., Dekoninck, S., Rulands, S., Lenglez, S., Mascré, G., Simons, B. D. & Blanpain, C. *Defining stem cell dynamics and migration during wound healing in mouse skin epidermis*. **Nat. Commun. 8, (2017)**
- Cellular therapy to develop a new treatment for asthma (F. Bureau)  
  
Sabatel, C., Radermecker, C., Fievez, L., Paulissen, G., Chakarov, S., Fernandes, C., Olivier, S., Toussaint, M., Pirotin, D., Xiao, X., Quatresooz, P., Sirard, J.-C., Cataldo, D., Gillet, L., Bouabe, H., Desmet, C.J., Ginhoux, F., Marichal, T. & Bureau, F. *Exposure to Bacterial CpG DNA Protects from Airway Allergic Inflammation by Expanding Regulatory Lung Interstitial Macrophages*. **Immunity 46: 457-473 (2017)**.
- How rhinovirus exacerbates asthma in individuals (F. Bureau and Th. Marichal)  
  
Toussaint, M., Jackson, D. J., Swieboda, D., Guedán, A., Tsourouktsoglou, T. D., Ching, Y. M., Radermecker, C., Makrinioti, H., Aniscenko, J., Edwards, M. R., Solari, R., Farnir, F., Papayannopoulos, V., Bureau, F., Marichal, T. & Johnston, S. L. *Host DNA released by NETosis promotes rhinovirus-induced type-2 allergic asthma exacerbation*. **Nat. Med. 23, 681–691 (2017)**.
- The dialogue between innate hepatic immunity and bioactive lipids is involved in the development of diseases associated with obesity (P. Cani)

Duparc, T., Plovier, H., Marrachelli, V. G., Van Hul, M., Essaghir, A., Ståhlman, M., Matamoros, S., Geurts, L., Pardo-Tendero, M. M., Druart, C., Delzenne, N. M., Demoulin, J. B., Van Der Merwe, S. W., Van Pelt, J., Bäckhed, F., Monleon, D., Everard, A. & Cani, P. D. Hepatocyte *MyD88* affects bile acids, gut microbiota and metabolome contributing to regulate glucose and lipid metabolism. **Gut** **66**, 620–632 (2017).

- New discovery to combat antibiotic-resistant bacteria (JF. Collet)

Asmar, A. T., Ferreira, J. L., Cohen, E. J., Cho, S. H., Beeby, M., Hughes, K. T. & Collet, J. F. *Communication across the bacterial cell envelope depends on the size of the periplasm*. **PLoS Biol.** **15**, (2017).

- Discovery of a new peptide to combat staphylococcus aureus (Y. Dufrêne)

Feuillie, C., Formosa-Dague, C., Hays, L. M. C., Vervaeck, O., Derclaye, S., Brennan, M. P., Foster, T. J., Geoghegan, J. A. & Dufrêne, Y. F. *Molecular interactions and inhibition of the staphylococcal biofilm-forming protein SdrC*. **Proc. Natl. Acad. Sci.** **114**, 3738–3743 (2017).

- A molecule to regenerate insulin-producing cells in diabetics (D. Eizirik)

Ben-Othman, N., Vieira, A., Courtney, M., Record, F., Gjernes, E., Avolio, F., Hadzic, B., Druelle, N., Napolitano, T., Navarro-Sanz, S., Silvano, S., Al-Hasani, K., Pfeifer, A., Lacas-Gervais, S., Leuckx, G., Marroquí, L., Thévenet, J., Madsen, O. D., Eizirik, D. L., Heimberg, H., Kerr-Conte, J., Pattou, F., Mansouri, A. & Collombat, P. *Long-Term GABA Administration Induces Alpha Cell-Mediated Beta-like Cell Neogenesis*. **Cell** **168**, 73–85.e11 (2017).

- Inflammatory Bowel Diseases: researchers identify the genetic culprits (M. Georges)

Huang, H., Fang, M., Jostins, L., Umićević Mirkov, M., Boucher, G., Anderson, C. A., Andersen, V., Cleynen, I., Cortes, A., Crins, F., D'Amato, M., Deffontaine, V., Dmitrieva, J., Docampo, E., Elansary, M., Farh, K. K. H., Franke, A., Gori, A. S., Goyette, P., Halfvarson, J., Haritunians, T., Knight, J., Lawrance, I. C., Lees, C. W., Louis, E., Mariman, R., Meuwissen, T., Mni, M., Momozawa, Y., Parkes, M., Spain, S. L., Théâtre, E., Trynka, G., Satsangi, J., Van Sommeren, S., Vermeire, S., Xavier, R. J., Weersma, R. K., Duerr, R. H., Mathew, C. G., Rioux, J. D., McGovern, D. P. B., Cho, J. H., Georges, M., Daly, M. J. & Barrett, J. C. *Fine-mapping inflammatory bowel disease loci to single-variant resolution*. **Nature** **547**, 173–178 (2017).

- The identification of biomarkers for sensitivity to new anti-CDK4 medicines in breast cancer (P. Roger)

Raspé, E., Coulonval, K., Pita, J. M., Paternot, S., Rothé, F., Twyffels, L., Brohée, S., Craciun, L., Larsimont, D., Kruys, V., Sandras, F., Salmon, I., Van Laere, S., Piccart, M., Ignatiadis, M., Sotiriou, C. & Roger, P. P. *CDK4 phosphorylation status and a linked gene expression profile predict sensitivity to palbociclib*. **EMBO Mol. Med.** **9**, 1052–1066 (2017).

- Human neurons implanted into a mouse brain are more susceptible to Alzheimer's disease (P. Vanderhaeghen)

Espuny-Camacho, I., Arranz, A. M., Fiers, M., Snellinx, A., Ando, K., Munck, S., Bonnefont, J., Lambot, L., Corthout, N., Omodho, L., Vanden Eynden, E., Radaelli, E., Tesseur, I., Wray, S., Ebner, A., Hardy, J., Leroy, K., Brion, J. P., Vanderhaeghen, P. & De Strooper, B. *Hallmarks of Alzheimer's Disease in Stem-Cell-Derived Human Neurons Transplanted into Mouse Brain*. **Neuron** **93**, 1066–1081.e8 (2017).

- Identification of a mechanism responsible for the failure of immunotherapy in some patients (B. Van den Eynde)

Zhu, J., Powis De Tenbossche, C. G., Cané, S., Colau, D., Van Baren, N., Lurquin, C., Schmitt-Verhulst, A. M., Liljeström, P., Uyttenhove, C. & Van Den Eynde, B. J. *Resistance to cancer immunotherapy mediated by apoptosis of tumor-infiltrating lymphocytes*. **Nat. Commun.** **8**, (2017).

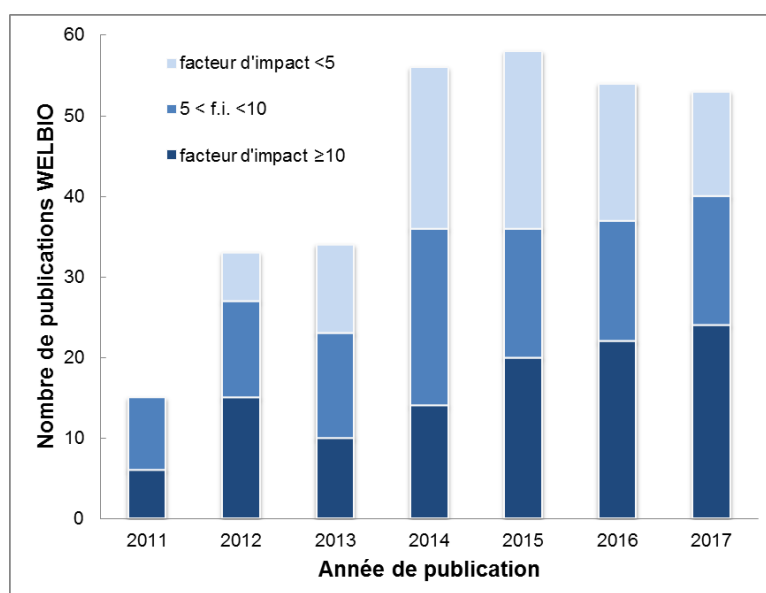
- A new metabolic repair enzyme to hydrolyse a damaged form of glutathione (E. Van Schaftingen)

Peracchi, A., Veiga-da-Cunha, M., Kuhara, T., Ellens, K. W., Paczia, N., Stroobant, V., Seliga, A. K., Marlaire, S., Jaisson, S., Bommer, G. T., Sun, J., Huebner, K., Linster, C. L., Cooper, A. J. L. & Van Schaftingen, E. *Nit1 is a metabolite repair enzyme that hydrolyzes deaminated glutathione*. **Proc. Natl. Acad. Sci.** **114**, E3233–E3242 (2017).

Welbio researchers also published a series of articles "reviews" or "perspectives" in renowned journals:

- Aragona, M. & Blanpain, C. *Transgenic stem cells replace skin*. **Nature** **551**, 306–307 (2017).
- Cani, P. D. *Gut microbiota - at the intersection of everything?* **Nat. Rev. Gastroenterol. Hepatol.** **14**, 321–322 (2017).

- Cani, P. D. Gut cell metabolism shapes the microbiome. **Science** **357**, 548–549 (2017).
- Ezraty, B., Gennaris, A., Barras, F. & Collet, J.-F. Oxidative stress, protein damage and repair in bacteria. **Nat. Rev. Microbiol.** **15**, 385–396 (2017).
- Leroy, E. & Constantinescu, S. N. Rethinking JAK2 inhibition: Towards novel strategies of more specific and versatile janus kinase inhibition. **Leukemia** **31**, 1023–1038 (2017).
- Geoghegan, J. A., Foster, T. J., Speziale, P. & Dufrêne, Y. F. Live-Cell Nanoscopy in Antiadhesion Therapy. **Trends Microbiol.** **25**, 512–514 (2017).
- Garg, A. D., Coulie, P. G., Van den Eynde, B. J. & Agostinis, P. Integrating Next-Generation Dendritic Cell Vaccines into the Current Cancer Immunotherapy Landscape. **Trends Immunol.** **38**, 577–593 (2017).



## 5. WELBIO RESEARCHERS IN THE PRESS

Following their prestigious publications, WELBIO researchers are often featured in articles or reports in the Belgian or overseas press. These few examples illustrate the various fields in which our researchers are obtaining major results.

- Cédric Blanpain (ULB): "How stem cells help healing" / Le Soir - 07/03/2017
- Fabrice Bureau (ULiège): "Bacteria for curing asthma" / RTBF – 28/03/2017

- Fabrice Bureau (ULiège): "ULg researchers discover how exposure to germs protects against asthma" / La Libre – 21/03/2017
- Yves Dufrière (UCL): "A team from UCL identifies a molecule to combat staphylococcus aureus" / Le Vif – 23/03/2017
- Patrice Cani (UCL): "Discovery: Curing obesity and type 2 diabetes with an intestinal bacterium" / Sciences et Avenir – 23/03/2017
- Jean-François Collet (UCL): "UCL researchers discover a new way to fight antibiotic-resistant bacteria" / La Libre – 19/12/2017
- Jean-François Collet (UCL): "UCL innovates in the fight against bacteria" / Le Soir – 19/12/2017
- Michel Georges (ULiège): "A predisposition to Crohn's disease: working towards identifying the genes responsible" / Le Vif – 28/6/2017
- Pierre Vanderhaeghen (ULB): "ULB makes an important step forward in Alzheimer's disease research" / La Libre – 24/02/2017
- Benoît Van den Eynde (UCL): "Cancer: UCL research will boost immunotherapy" / Le Soir - 10/11/2017

## ADDING VALUE

WELBIO has a strategic fundamental research mission in the field of life sciences. One of its characteristics is the need to create industrial value from scientific discoveries. To this end, WELBIO invests in individualised support for its researchers in order to establish a strategy to increase the economic value of the results integrated in the research and, in close collaboration with members of the company-university interfaces of the host universities, it supports the development of and the creation of economic value from inventions

It is important to realise that WELBIO funds fundamental research projects for which the result is, by definition, uncertain, and for which several years are needed between the start of the project and the realisation of any value-creation activities. The research funded by WELBIO is innovative but high-risk. Only a fraction of the projects will ever succeed in creating concrete industrial value. Creating value for WELBIO's fundamental research projects must therefore be approached from multiple angles: protection of intellectual property, targeted or applied research projects stemming from WELBIO, collaboration with industry or new major sources of funding such as the European Research Council (ERC).

### 1. INVENTION DISCLOSURES AND PATENT APPLICATIONS

End of 2017, **21** DISCLOSURES of inventions were submitted within the context of 15 research projects. PATENT APPLICATIONS were submitted for **8** INVENTIONS of which **6** are still ongoing. They cover a variety of fields: diagnosis and treatment of cancer (in particular by immunotherapy), the treatment of asthma by cellular therapy, treatment of neurodevelopmental disorders.

### 2. COLLABORATION AND LICENSING OPTION AGREEMENT

The collaboration between the company arGEN-X and the laboratories of Pierre Coulie, a WELBIO researcher at UCL and Sophie Lucas (UCL), is progressing very well. An agreement was signed in 2016 between arGEN-X and AbbVie, a global biopharmaceutical company, leading to a payment of \$40,000,000 from AbbVie to arGEN-X. This agreement pertains to the clinical development of the therapeutic antibody ARGX-115 which is directed against the GARP protein (target identified during P. Coulie's 2011-2015 WELBIO project. This antibody blocks the immunosuppressive activity of Treg lymphocytes and thus activates the immune system's capacity to eliminate cancer cells. In 2017, a first preclinical milestone was reached, which led to the payment of \$10,000,000 from AbbVie to arGEN-X .

In accordance with the terms of the collaboration and exclusive licensing option agreement signed with the company arGEN-X, a fraction of these amounts came back, via UCL, to WELBIO in 2017. WELBIO therefore made its **1<sup>st</sup>** RETURNS ON



**INVESTMENT** ( EUR 351,562 received in 2017) demonstrating the pertinence of its operational model.

### 3. INVESTMENTS LINKED TO MONITORING VALUE CREATION (BRIDGE FUND)

The Bridge Fund is intended for WELBIO investigators and aims to ensure the transition between the fundamental research and the development of a results package that makes it possible to support a patent application, to apply for more applied research funding or to conclude a collaboration and licensing agreement, even to envisage the creation of a spin-off.

1 "Bridge Fund" **FUNDING** was granted in 2017:

- Cédric Blanpain (ULB) - 18 months, EUR 149,844 budget

Prof. Blanpain and his team discovered a "universal" marker for solid tumour cells, which can be used to detect circulating tumour cells (CTC) of different cancers, whatever their origin and their degree of differentiation. The basis for the project is to validate the clinical interest of this marker for detecting circulating tumour cells, and from a diagnostic point of view, to monitor the response to therapies and early detection of tumour recurrence. The results will be used to evaluate the "value" of the method and to define the strategy for creating economic value.

### 4. DGO6 - WALInnov

The WALInnov programme developed by the Public Service for Wallonia Research (DGO6) aims to encourage targeted research within universities and to reinforce the excellence of the best research teams. With this programme, Wallonia's ambition is to support research projects with a high scientific and technological potential that focus on the needs of one or more businesses. When supporting a scientific innovation with a clearly-identified economic impact (in the long term), WALInnov is the instrument of choice to take over from WELBIO once it has embarked on a clear path for creating economic value.

In 2017, in response to the programme "WALInnov Exercice 2017 2nd call" and on the strength of the results obtained with his "Bridge Fund" project ("CDx solutions for the new CDK4 inhibitory drugs"), Pierre Roger (ULB, WELBIO 2011-2015) successfully submitted a research project entitled "CICLIBTEST - Diagnostics companions to CDK4-inhibitors adapted to different cancers". This project will begin in 2018 and will be conducted in collaboration with Jean-Pascal Machiels (UCL) and in partnership with the company OncoDNA (Gosselies).

François Fuks, WELBIO researcher at ULB, also successfully submitted a project ("An innovative approach for the epigenetic study of RNA in cancer") in response to the same programme « WALInnov Exercice 2017 2nd call". The theme of this project is

linked to François Fuks' WELBIO project, which started at the end of 2017. This project will be conducted in collaboration with Alain Chariot (WELBIO Researcher at ULiège) and in partnership with the Diagenode company (Seraing).

Please also note that the IMMUCAN project ("Identification of new targets involved in mechanisms of resistance to immunotherapy of cancer") started in 2017. This project, which was submitted within the context of the WALInnov 2016 programme involves a collaboration between several WELBIO researchers at UCL (Pierre Coulie, Pierre van der Bruggen and Benoît Van den Eynde), researchers at ULB and at ULiège, in partnership with the company iTeos Therapeutics (Gosselies).

## 5. BLOWIN

Innovation in the fields of biotechnologies and health is a strategic issue for Wallonia, which has launched several initiatives (organisations and funding, specific to biotechnologies or with a more general focus) in support of this innovation. WELBIO and BioWin are two of these initiatives. WELBIO which focuses on excellence in fundamental research, operates at the start of a chain in which BioWin, which focuses on applied research, is an actor situated further towards the end.

Several WELBIO researchers are or have been involved in BioWin projects, demonstrating their involvement in increasing the industrial value of their work.

In 2017, for the first time, BioWin approved a project that capitalised directly on a WELBIO project. This project called iCone (Human cortical neurons from stem cells), is based on the results of the first WELBIO project conducted by Pierre Vanderhaeghen a WELBIO researcher at ULB and one of the key opinion leaders in the field of stem cells and neurons. This project aims to create an industrial activity based on technologies for producing human cortical cells from induced pluripotent stem cells. It is due to start in 2018 and will be conducted within the framework of a public-private consortium consisting of 2 academic groups and companies based in Wallonia, including 2 SMEs that specialise in the production of cellular therapies.

## 6. NEW MAJOR FUNDING

In 2017, Guido Bommer (UCL) obtained an **ERC CONSOLIDATOR GRANT** to fund his project "Novel Metabolic Pathways in Cancer" which aims to study the function of a new metabolic pathway in the development of cancer. The results previously obtained thanks to WELBIO funding of the project conducted by Emile Van Schaffingen, on which Guido Bommer collaborated closely, were crucial in obtaining funding of 2 million EUR over 5 years.

**EOS**, *Excellence of Science*, is a new programme that facilitates collaboration between research groups from Belgium's two linguistic communities on common

fundamental research projects, in all of the scientific disciplines. This programme will span four years. It is funded by F.R.S.-FNRS, for the Fédération Wallonie-Bruxelles [Wallonia-Brussels Federation], and by the FWO for the Flemish community.

38 projects were selected in 2017. 9 WELBIO researchers or former WELBIO researchers are participating in 5 of these projects.

- Pierre Vanderhaeghen (ULB) and Laurent Nguyen (ULiège, WELBIO 2011-2015) will collaborate on the project "Temporal and spatial control of synaptic patterning: from basic mechanisms to human-specific innovations and diseases";
- Jean-François Collet (UCL) and Yves Dufrêne (UCL) will collaborate on the project "Protein flow in the bacterial cell envelope: sorting, folding, targeting and quality control";
- Benoît Van den Eynde (UCL) and Pierre Coulie (UCL) will collaborate on the project "Refining cancer cell death and danger signals for the improvement of immunotherapy";
- Patrice Cani (UCL) and Michel Georges (ULiège, WELBIO 2013-2017) will collaborate on the project "Quantitative profiling in applied gut microbiome research";
- Fabrice Bureau (ULiège) will participate in the project "Understanding Heterogeneity of Eosinophils in Airway Disease".

## 7. SPIN-OFFS

In 2017, the first spin-off company creation project, was initiated, based directly on the results of a WELBIO project. This project should finish at the start of 2018. It will be described in more detail in the next annual report.

Furthermore, two WELBIO researchers' projects to create spin-offs are progressing. These spin-offs are based on research carried out prior to WELBIO funding the researchers concerned. The first, A-Mansia, is dedicated to therapies based on gut microbiota (treatment for obesity). It stems from work by Patrice Cani (UCL) and his colleagues at the Université de Wageningen. The second, BetaBild, is devoted to imaging pancreatic beta-cells (treatment of diabetes). It stems from work by Decio Eizirik (ULB). Please note that this work dates back to 2006 and was the subject of one of the first BioWin projects.

## ADMINISTRATIVE AND FINANCIAL RESOURCES

### GOVERNANCE OF WELBIO (ASBL)

WELBIO ASBL's Board of Directors is made up of representatives from academia, industry and government. In accordance with Article 33 of the WELBIO ASBL articles of association, administrators do not receive any payment for their services, except for reimbursement of all incurred costs.

During the financial year 2017, the Council was composed as follows:

Representatives of the Walloon Government:

- Philippe Busquin, Minister of State, representative of the Minister-President
- Pierre Leonard, Deputy Head of Cabinet, representative of the Minister of the Economy
- Vincent Yzerbyt, Professor, UCL, representative of the Minister responsible for research and new technology

Representatives of the field of economics and industry with an interest in life sciences:

- Jean-Pierre Delwart, President of Eurogentec SA
- Frédéric de Sauvage, Vice-President of Genentech
- Jean Stéphane, administrator for several companies in the biotechnology sector, Chairperson for WELBIO's Board of Directors
- Jean-Christophe Tellier, CEO, UCB

Academic experts with international recognition in the field of life sciences

- Jacques Dumont, Professor, Université libre de Bruxelles, Vice-Chairperson for WELBIO's Board of Directors
- Louis Hue, Professor, Université catholique de Louvain
- Pierre Lekeux, Professor, Université de Liège

Representatives of universities of the French Community

- Rudi Cloots, Vice-Rector for Research, ULg
- Jean-Christophe Renaud, Pro-Rector for Research, UCL
- Serge Schiffmann, Vice-Rector for Research and Regional Development, ULB

Representative of the Fonds de la Recherche Scientifique [Scientific Research Fund] (F.R.S.-FNRS)

- Véronique Halloin, General Secretary

Representative of the Public Service for Wallonia - General Operational Director for the Economy, Employment & Research (DGO6)

- Isabelle Quoilin, Managing Director

Following two resignations and two replacements, the composition of the Board of Directors will be reviewed at a General Assembly which will convene in 2018. WELBIO would like to thank Philippe Busquin, Jean-Pierre Delwart, Jacques Dumont and Pierre Léonard for their contribution to WELBIO in their roles as directors. WELBIO would

particularly like to express its deep gratitude to Mr Dumont for his leading role in the creation of the Institute.

## GENERAL MANAGER

Mr Pierre Van Renterghem has been General Manager of WELBIO since October 2015.

He has held a variety of roles in industry, academia and institutions After obtaining his PhD in sciences at the Université libre de Bruxelles (ULB) and fulfilling a post-doctorate role at the KU Leuven / VIB, Pierre Van Renterghem joined Bristol-Myers Squibb as a Data Management Scientist. His education in molecular biology and his professional experience of data management led him to develop national DNA databases at the Institut National de Criminalistique et de Criminologie (INCC) [National Institute of Forensics and Criminology]. He ran the INCC's Biology section before joining Europol as the Senior Specialist in charge of forensic intelligence and international exchanges of DNA data. His role later evolved to define strategies for information management and to coordinate the development of Europol information processing systems. In parallel with his primary activities in forensics and international police cooperation, Pierre Van Renterghem also fulfilled a range of teaching duties at universities and for professionals.

## FONDS DE LA RECHERCHE FONDAMENTALE STRATEGIQUE [THE STRATEGIC FUNDAMENTAL RESEARCH FUND]

In 2013, WELBIO modified its administrative structure. Following the decrees bringing assent to the cooperation agreement of 4 December 2012 between the French Community and the Walloon region, concerning the funding of strategic fundamental research within the framework of crossover policies, WELBIO was integrated as a delegated mission of Wallonia into the Fonds de la Recherche Fondamentale Stratégique (FRFS) to serve as a strategic axis for Life Sciences. The FRFS is a fund associated of the FNRS, tasked by the Walloon Government to organise the administrative and financial management of calls for projects for the strategic axes of research in Wallonia.

WELBIO ASBL was created as a Platform for leadership and commercialisation of FRFS-WELBIO for the strategic axis of Life Sciences.

## FINANCIAL RESOURCES

When WELBIO was founded on 12 December 2008 by the Walloon Government, it was awarded an initial budget of 15 million euros. In December 2012, the Walloon Government and the Walloon-Brussels Federation decided to award WELBIO a minimum annual budget of 6 million euros. Since 2014, the WELBIO subsidy has been paid to the FRFS. An amount corresponding to 10% of this subsidy (reduced by 4% to

cover the administrative operation of the FRFS and the Scientific Committee) must then be paid to WELBIO ASBL.

Within the context of the current budget, this subsidy is not paid automatically or in its entirety year on year. However, the setting up of a transversal management for the Fonds de la Recherche Fondamentale Stratégique [The Strategic Fundamental Research Fund], which was decided by the Walloon Government in its meeting of 12 May 2016, made it possible to release the resources so WELBIO could pursue its activities and launch the 2017 call for projects.

## THE MANAGEMENT REPORT FOR WELBIO ASBL

### PREAMBLE

This concerns the eighth financial year, which covers the period from 1 January 2017 to 31 December 2017.

For the financial years 2010 to 2016, the subsidies received were recorded as liabilities on the balance sheet against the permanent cash receipts. That was justified for the following reasons:

- In 2010, the total budget was EUR 30 million of which funding and payments to researchers had to be spread over several financial years.
- Between the financial years 2010 to 2014, the difference between the dates when funding was received and the dates when instalments of money were paid for research programmes can easily be distinguished.

Since 2015, the financing of research programmes has been outsourced to FRS-FNRS within the framework of the FRFS (Fonds de la Recherche Fondamentale Stratégique). The non-profit organisation WELBIO ASBL as a Platform for development and value creation (PAVA), receives an annual subsidy that is equal to 10% of the total funding for the WELBIO strategic axis, after deduction of the amounts intended to fund FRS-FNRS. As such, the non-profit organisation receives an annual subsidy of EUR 576,000 (9.6% of EUR 6,000,000) to cover operating costs; the balance is allocated to investments linked to monitoring the creation of economic value (Bridge Fund).

However, because the annual subsidy is intended to cover the current activities of WELBIO ASBL, the decision was made in 2017 to record the annual subsidy as an operating subsidy and to enter it against the income statement. Consequently, the classification of the non-profit organisation has changed due to the criteria related to size. The non-profit organisation has gone from a "small" non-profit organisation to a "large" non-profit organisation, and the annual accounts must be filed with the National Bank using the abbreviated form for the first time.

## Assets

The tangible fixed assets amount to EUR 1,011.46 and relate to IT equipment.

The financial fixed assets amount to EUR 3,450.00 and relate to the security deposit for the rented offices in Wavre.

The amounts receivable within one year amount to EUR 577,230.60 and are made up of one NSSO instalment for the sum of EUR 1,230.60 and the 2017 subsidy to be received for the sum of EUR 576,000.00.

Short-term cash investments amount to EUR 1,560,846.05 and consist of two reserves to allocate WELBIO's remaining liquid assets.

On 31 December 2017, the amount of cash available in WELBIO's various bank accounts amounted to:

Green account:	EUR 990,810.64
Flexibonus:	EUR 323,686.93
Current account:	EUR 246,348.48
	-----
	EUR 1,560,846.05

These liquid assets are allocated as follows:

Operating costs (2018):	EUR 233,600.00
Bridge fund:	EUR 1,327,246.05
	-----
	EUR 1,560,846.05

The adjustment accounts amount to EUR 1,261.44 and relate to deferred charges.

**Total assets amount to EUR 2,143,799.55.**

## Liabilities

To improve the performance of the balance sheet, we compensated the past as at 31/12/2016 in the following way:

Permanent cash receipts:	EUR 25,363,116.00
Loss carried forward:	– EUR 23,536,673.60
Balance:	EUR 1,826,442.40

This balance as at 31/12/2016 currently appears in the section "other allocated funds"

The result for this financial year is a profit of EUR 212,037.27.

The balance of the other allocated funds as at 31/12/2017 amounts to EUR 2,038,479.67.

Trade payables amount to EUR 1,581.39.

Provisions for costs and debt obligations amount to EUR 79,905.09.

Estimated tax due for 2016 amounts to EUR 90.21.  
Estimated tax due for 2017 amounts to EUR 204.58.

Outstanding wage withholding tax amounts to EUR 3,710.45.  
Provisions for holiday pay amount to EUR 19,828.16.

**Total liabilities amount to EUR 2,143,799.55.**

## *Result*

The debt obligations for three Bridge Fund agreements that commenced in 2016 were paid and/or provided for, with a total sum of EUR 145,514.61. A new agreement commenced in 2017, for a sum of EUR 29,969.00.

Miscellaneous services and goods amount to EUR 42,834.33 and mainly consist of operating costs and professional fees.

Wages and social security contributions amount to EUR 144,922.86.

Depreciation amounts to EUR 755.59.

Estimated tax due amounts to EUR 218.99.

Net bank interest after deducting withholding tax amounts to EUR 722.10.

Financial expenses amount to EUR 469.45.

**The result for this financial year is a profit of EUR 212,037.27.**



## CONTACT

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