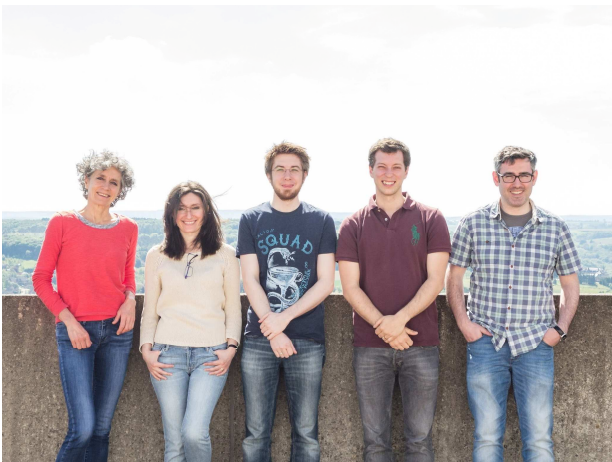


Press release

## Viruses hijack cancer genes to cause leukemia



Anne Van den Broeke and her team

Brussels, 23 May 2017 – A team of researchers led by **Anne Van den Broeke (Institut Jules Bordet - University of Brussels and GIGA-University of Liège)** has uncovered a novel mechanism by which viruses cause leukemia. These new findings, published on 23<sup>rd</sup> May in *Nature Communications*, could be key to the understanding of virus induced cancers and the development of targeted therapeutic strategies for a very aggressive type of leukemia.

### Studying a bovine virus to tackle human leukemia

Approximately 12% of human cancers worldwide are attributed to viral infection. Human T-cell leukaemia Virus-1 (HTLV-1), the first oncogenic retrovirus discovered in human, infects an estimated 20 million people worldwide and causes adult T cell leukemia (ATL), an aggressive leukemia with an extremely poor prognosis. The closely related Bovine Leukemia Virus (BLV) produces a very similar disease in cattle and sheep, with the latter providing a unique outbred animal model for cancer research.

It has been generally assumed that leukemia development is dependent on the production of cancer-promoting agents by the virus yet is independent of the location of the virus within the genome of the cancer cell. The research team was the first to discover that, contrary to the prevailing dogma, HTLV-1 and BLV do not integrate randomly in the host genome but rather in the vicinity of genes involved in cancer (“cancer drivers”). The most surprising observation was that these cancer drivers were systematically positioned upstream relative to the virus rather than downstream as would be expected mechanistically. The team further demonstrated the perturbation of the corresponding genes via interactions with viral “antisense” transcripts (viral factors synthesized in the opposite

orientation relative to the classical viral products), revealing a novel mechanism by which oncogenic viruses and antisense transcription contribute to cancer development.

Using novel next generation sequencing (NGS) methods, the researchers further showed that, in both humans and animals, these perturbations are present long before the leukemia becomes aggressive. The screen for finding the precise viral insertion spots in the sheep genome revealed a list of several hundreds of genes, a third of which have not been previously reported in cancer, thus providing a treasure trove of new candidate cancer driver genes for further investigations.

The study, carried out in collaboration with scientists of the Necker University hospital in Paris and the VIDO/Intervac research institute of the University of Saskatchewan in Canada, is the result of interdisciplinary research that combines oncology, viral pathogenesis and animal genomics.

### **New avenues for cancer research and clinical applications**

Having demonstrated the sequestration of host cancer drivers by the virus and the unexpected role of viral antisense transcripts in this process, the team now hopes that further research will be able to identify specific inhibitors as a basis for the future development of targeted therapies. Finally, the NGS method developed in this study can now be applied to monitor ATL patients, enabling better prediction of relapse and providing clinicians with a molecular tool to evaluate response to treatment.

### **Reference**

Nicolas Rosewick, Keith Durkin, Ambroise Marçais, Maria Artesi, Vincent Hahaut, Philip Griebel, Natasa Arsic, Véronique Avettand-Fenoel, Arsène Burny, Carole Charlier, Olivier Hermine, Michel Georges & Anne Van den Broeke (2017) Cis-perturbation of cancer drivers by the HTLV-1/BLV proviruses is an early determinant of leukemogenesis, *Nature Communications*, doi: 10.1038/NCOMMS15264

### **Senior investigators**

Dr Anne Van den Broeke (Institut Jules Bordet and GIGA) and Prof Michel Georges (GIGA).

Laboratory of Experimental Hematology, Institut Jules Bordet, Université Libre de Bruxelles (ULB), Boulevard de Waterloo 121, 1000 Brussels, Belgium.

Unit of Animal Genomics, GIGA-R, Université de Liège, Avenue de l'Hôpital 11, B34, 4000 Liège, Belgium.

### **Research funding**

This work was supported by the Fonds de la Recherche Scientifique (FRS), les Amis de l'Institut Bordet, Télévie, the International Brachet Stiftung (IBS) and the Fondation Lambeau Marteaux.

## International collaborations

Hôpital universitaire Necker, Paris, France – Dr Olivier Hermine and Dr Ambroise Marçais

VIDO/Intervac, University of Saskatchewan, Saskatoon, Canada – Dr Philip Griebel

## Enclosed

- Photograph of the research team headed by Anne Van den Broeke
- Scientific diagram explaining the new model of viral carcinogenesis (see attached PDF for image and caption)

## For more information:

Dr Anne Van den Broeke: [anne.vandenbroeke@bordet.be](mailto:anne.vandenbroeke@bordet.be)

Prof Michel Georges: [michel.georges@ulg.ac.be](mailto:michel.georges@ulg.ac.be)

## Press contacts

---

### Institut Jules Bordet

Ariane van de Werve

Tel: +32 2 541 31 39

GSM : +32.48617 33 26

E-mail : [ariane.vandewerve@bordet.be](mailto:ariane.vandewerve@bordet.be)

[www.bordet.be](http://www.bordet.be)

### University of Liège

Didier Moreau

Tel +32 4 366 52 17

GSM : +32 494 572 530

E-mail : [dmoreau@ulg.ac.be](mailto:dmoreau@ulg.ac.be)

## About the Jules Bordet Institute

---

An integrated multidisciplinary centre, unique in Belgium, the Jules Bordet Institute is an autonomous hospital devoted exclusively to cancer.

For more than 75 years, the Jules Bordet Institute has been providing its patients with diagnostic and therapeutic strategies at the forefront of progress to prevent, detect and actively combat cancer. The Institute pursues three missions: care, research and teaching. Its international reputation attracts the world's leading cancer experts. Its spirit of innovation has enabled it to participate in the development and discovery of major new methods of diagnosis and treatment with the aim of bringing the findings to the patient as rapidly as possible.

In May 2013, the Jules Bordet Institute received official accreditation and designation from the OECI (Organisation of European Cancer Institutes) as a "Comprehensive Cancer Centre", a quality label reserved for multidisciplinary cancer care institutions whose activities include research and teaching. This is a first for Belgium.

The Jules Bordet Institute is a member of the Iris and Université Libre de Bruxelles hospital networks. With its 160 beds dedicated exclusively to cancer patients, every year the Institute treats more than 6,000 in-patients, 12,000 out-patients and provides 75,000 consultations. To effectively meet future demographic and scientific developments, the Institute is planning to build a new Institut Bordet on the ULB university campus in Anderlecht, next to the Erasmus Hospital. Inauguration is planned for 2018.

Rue Héger-Bordetstraat 1, B-1000 Bruxelles/Brussel

T + 32 (0)2 541 31 11, F + 32 (0)2 541 35 06, BELFIUS: BE72 0910 0972 7816, [www.bordet.be](http://www.bordet.be)

Institut Jules Bordet, Association Hospitalière de Bruxelles régie par la loi du 8 juillet 1976  
Jules Bordet Instituut, Ziekenhuisvereniging van Brussel onderworpen aan de wet van 8 juli 1976



- Jules Bordet Institute website: [www.bordet.be](http://www.bordet.be)
- To consult the Jules Bordet Institute presentation brochure, go to: <http://www.bordet.be/fr/presentation/brochure/index.html>
- To view the Jules Bordet Institute presentation video, go to: <http://www.bordet.be/fr/presentation/organigr/textes/bordet.htm>

### About the GIGA Research Institute of the University of Liège

---

Established in 2007 at the University of Liège, the GIGA Research institute fosters interdisciplinary research in the biomedical sciences with an aim towards ground-breaking medical innovations. The institute is comprised of >500 members (PIs, senior scientists, postdocs, PhD students, technicians) with expertise in medical genomics, in silico medicine, neuroscience, cancer, infection-inflammation-immunity and cardiovascular sciences.

### About the ULB Cancer Research Center, U-CRC

---

The "ULB-Cancer Research Center" (U-CRC), headed by Prof. Francois Fuks, brings together researchers from the Faculty of Medicine of the ULB, the Erasmus Hospital and the Bordet Institute.

Focused on the patient, the fundamental and translational research is carried out in close contact with clinical research.

The U-CRC, which is a centre of reference both nationally and internationally for cancer research, is dedicated to increasing cooperation between teams, sharing technological platforms and promoting interdisciplinary research.

The U-CRC website: <http://ucrc.ulb.be>

### About the Friends of the Bordet Institute

---

The Friends of the Jules Bordet Institute is a non-profit-making organisation with the sole aim of supporting and financing research at the Jules Bordet Institute, a cancer centre that is a reference in Belgium and abroad. As the largest private donor to the Bordet Institute, "The Friends" have donated almost 12 million euros in the past five years.

Considerable progress has been made in the field of oncology in recent years. Our understanding of the biological origin of cancer is growing all the time. Whereas 10 years ago we spoke of the microscopic analysis of tumours, today we speak of genetic profile, of sequencing, etc. Dozens of new molecules and markers have been developed, permitting the advent of personalised treatment. This progress has to a large extent been made possible through the extraordinary technological progress of recent years. But these new techniques that now enable us to probe the infinitesimally small are increasingly expensive.

For more than 40 years, the help of the "Friends" has enabled the Jules Bordet Institute to pursue its research using the most advanced technologies, thereby providing patients with the most innovative screening and treatment techniques. Techniques that generate life and hope.

By helping and supporting "The Friends of the Bordet Institute" you are participating in the many research programmes that they support and that all pursue a single aim: victory for life.

To find out more about the association The Friends of the Jules Bordet Institute, go to the website [www.amis-bordet.be](http://www.amis-bordet.be)

To find out more about the "101 tables pour la vie", go to the website [www.101tables.com](http://www.101tables.com)