INSTITUT JULES BORDET INSTITUUT

SCIENTIFIC REPORT 2022
For the years 2020, 2021 and 2022
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Institut Jules Bordet (IJB) has taken an important step in its history. As was announced last year, IJB is now completely installed in an extraordinary new infrastructure. The building, referred to as “New Bordet”, is perfectly integrated into the Université Libre de Bruxelles’ academic campus. This move to the campus offers all the potential to develop strong synergies between the comprehensive cancer center, which is public and OECI (Organization of European Cancer Institutes)-certified, the academic general hospital Erasme, and the University’s health related faculties, especially its academic labs. Like a jewel box, the campus constitutes a unique place where all the stakeholders can act to promote translational and clinical research, the basis for the most innovative care and teaching. Pursuing its development, IJB also nurtures all its previous initiatives to promote academic research, especially via the European Organization for the Research and Treatment of Cancer (EORTC), the Breast International Group (BIG), and the Oncodistinct Network. In this context, the role of the “Association Jules Bordet” remains vital, and we thank the association very warmly.

From a broader perspective, and besides its move, IJB is now part of a dynamic hospital group that is a major player in the Brussels area and beyond in Belgium. IJB is one of the pillars of the Hôpital Universitaire de Bruxelles (HUB). In fact, the HUB is a group of 3 major players in Brussels and beyond, including IJB, Hôpital Erasme and HUDERF/UKZKF (Hôpital Universitaire Des Enfants Reine Fabiola / Universitair KinderZiekenhuis Koningin Fabiola). The inclusion of IJB within the HUB gives the comprehensive cancer center a unique opportunity to grow and to benefit from the new synergies, the shared values and a strong culture and ambition for innovation. It aims to promote IJB’s position within the international scene and, more precisely, within the European networks of comprehensive cancer centers. With its 250 beds dedicated to cancer and its unique environment, it is clear that IJB is committed to delivering the best care and services for every patient and their relatives, as well as for any stakeholder seeking to align with others to fight cancer. This is encrypted in IJB’s DNA, and all its caregivers and dedicated research teams are here to overcome the challenges that cancer involves. As proven by its history, IJB intends to remain a pioneer in developing strategies that integrate the latest discoveries and technological advancements to fight cancer with the utmost efficiency. With this ambition in mind, we commit to ensuring that IJB will benefit from the unconditional support of HUB and its co-founders, the City of Brussels and the Université Libre de Bruxelles.
Research in Numbers

General data

Number of tumors recorded in Institut Jules Bordet’s cancer registry annually

- On average, **1750** patients are diagnosed or treated with a new tumor incident.
- and about **3500** are attended to at the Institute for a new tumor episode (including new relapse episodes).

Number of dicussions in multidisciplinary teams

- **5629** in 2018
- **6280** in 2019
- **6102** in 2020
- **6529** in 2021

Compliance with MDT meetings

As in many institutions, the general approach is to discuss each new case and its therapeutic management in a multidisciplinary team (MDT) meeting. Compliance has been assessed using random samples in two specific areas: new incident breast tumors and hematological malignancies. Compliance with MDT decisions was also investigated.

- **Breast tumors:**
  - From about 300 MDT discussions, we found that unexplained non-compliance with therapeutic decisions was very low for each therapeutic procedure (<1% for surgery, <1% for chemo-, immunotherapy and targeted agents, 5% for radiotherapy, and about 15% for hormonotherapy). Non presentation at an MDT meeting before initiating a treatment procedure was the highest for radiotherapy (20%) but remained under 10% for the other treatment types (sample of about 200 breast cancers).

- **Hematological malignancies:**
  - About 200 MDT discussions were selected (for new incident tumors and relapse episodes) and an unexplained non-compliance rate of 10% was documented. On a sample of about 250 administrations of systemic treatment, non-presentation at an MDT meeting before treatment initiation occurred in roughly 25% of the cases.

The reports written about the above compliance evaluations were used to formulate recommendations for the future.

Hospital cancer registry status (Incidence year 2020-2021)

- **812** Rare tumours (restricted registration)
- **2599** Common tumours (full registration)

- **2185** Common tumours (restricted registration)
- **917** Rare tumours (full registration)
Research projects

More than 100 research projects receive ethics committee approval each year.

On average, about 800 new patients are included each year in prospective studies.

Patients included in prospective trials 2020-2021

Research personnel

Institut Jules Bordet employs 1375 persons in total (1020 FTEs). Since research and care activities are closely integrated, every staff member is involved in research activities at various levels within the Institute. There are, however, 208 professionals (187 FTEs) specifically dedicated to research.
Finance & funding

Budget

€15.9 MM Annual research budget

9% Percentage of Institut Jules Bordet’s annual budget dedicated to research

Funding

Research funding comes both from non-commercial sources through donors, foundations, and academic partnerships, and from commercial sources through collaboration with industry.

Total funding breakdown by type of partnership (2020-2021)

- 38% Direct Industry Partnership
- 62% Academic Partnership

Academic partnership funding breakdown by type of funder (2020-2021)

- 10% National Public Bodies
- 10% National Charities
- 41% International Research Organisations
- 35% Association Jules Bordet
- 3% International Charities

Publications

Scientific production in terms of publications is about 250-300 papers a year, with about 40 having an impact factor above 10:

- The sum of the impact factors for all the publications per year ranges between 1428 and 1816:

  Impact factor sum and distribution 2020-2021

- Number of publications

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<th>Year</th>
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<th>2019</th>
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  - 320 IF < 5
  - 79 10 ≤ IF < 30
  - 211 5 ≤ IF < 10
  - 45 IF > 30
Improve our understanding of tumor heterogeneity by means of a transversal research team from the IJB research laboratories working to discover new biomarkers and/or new treatment targets.

Focus on better ways to distinguish patients with poor versus good prognosis and patients who respond poorly or well to anticancer therapies: this is key to innovating cancer management. Investing in "omics" technologies, modern imaging techniques, and artificial intelligence can help us to avoid the under- or overtreatment of patients; in other words, our goal is to demonstrate the contribution of these tools to improved treatment personalization in the fields of surgery, radiotherapy, and drug therapy.

Contribute to the important domain of new anticancer drug development, with an emphasis on novel partnership models with the pharmaceutical industry that reinforce academic freedom as well as the efficient conduct of proof-of-concept clinical trials with innovative designs, particularly in the field of immune-therapeutics. Similarly contribute to the development of improved radiotherapy and surgical techniques as well as new radiotheranostic approaches.

Involve patients and citizens in research. Develop a portfolio of research initiatives centered on patient empowerment and wellbeing, not only during treatment, but also during the survivorship period and in the palliative context.

1 Dissecting Tumor Heterogeneity
2 Contributing to "Precision Oncology"
3 Fostering Innovation in Cancer Management
4 Developing New Approaches to Patient Empowerment and Well-being
Strategic Vision

The oncology landscape has changed rapidly during the last 15 to 20 years, and it is characterized by a revolution in molecular diagnostics and imaging, the adoption of less mutilating surgeries, the spread of more accurate high-tech radiotherapy techniques, and the exponential growth of innovative anticancer drug treatments as well as supportive therapies.

A personalized, holistic approach focusing on the different medical and non-medical aspects of patient care has become our goal.

While IJB has undoubtedly contributed to this progress at national and international levels in its more than 80 years of existence, it no longer stands alone in the landscape of “modern oncology” in Belgium and belongs to a growing list of accredited cancer institutes across Europe.

In recent years, special effort has been made to identify the particular strengths of IJB in developing research projects to accompany patients’ cancer paths and to address their most critical needs. Research at IJB was maintained during the COVID-19 pandemic despite the very stressful circumstances: this is the time to express our gratitude to our highly motivated research teams.

To prioritize research projects, special attention is paid to the likelihood of their bringing concrete changes to clinical practice, their need for strong academic input, and their multidisciplinary nature. As a result, the IJB research agenda for 2020-2022 encompasses 4 pillars, very similar to the ones selected for the years 2016-2019.

Now that New Bordet has been built on the campus of the Université Libre de Bruxelles alongside other research laboratories and the academic general hospital Erasme, new research opportunities are being explored to involve the best researchers of both worlds and to help IJB continue to play a leadership role in cancer management innovation.

IJB's research pillars are expected to be refined in 2023-2024.
Research Pillars
PILLAR I • Dissecting Tumor Heterogeneity

The IJB laboratories were created by a previous generation of visionary clinicians active in 3 main domains – medical oncology, hematology and surgery (H. Tagnon, JC. Heuson, P. Stryckmans, F. Lejeune) – but also in pathology and molecular biology (A. Claude, Nobel Prize Laureate). Their ambition was to contribute to a better understanding of cancer at the cellular and molecular levels, as this knowledge would form the basis for improved patient treatment.

Today’s researchers can count on the unprecedented development of new technologies to explore in greater depth the interactions between cancer cells and their microenvironment, as well as the potential mechanisms underlying resistance to anticancer therapies.

With the use of genomic, transcriptomic, epigenetic, and immunological tools, researchers are dissecting tumors and their environment, hoping to better understand tumor heterogeneity and to identify new clinically relevant biomarkers and/or new treatment targets.

At IJB, this preclinical and translational research is most developed in the areas of breast cancer, melanoma, gastrointestinal tumors, and hematological malignancies.

A tumor mass not only contains a heterogeneous population of cancer cells but also various noncancerous cells, including adipocytes, fibroblasts, immune and inflammatory cells, neuroendocrine cells, pericytes, vascular and lymphatic endothelial cells, secreted factors and extracellular matrix proteins, collectively known as the tumor microenvironment (TME). Within the TME, cancer cells interact and have crosstalk with noncancerous cells, which can drive different mechanisms such as tumorigenesis, angiogenesis, and metastasis. The TME can also shape therapeutic responses and resistance, justifying the recent impetus to target components of the TME, which is best exemplified by the clinical success of immune checkpoint inhibitors. Many research projects at IJB focus on the TME in solid tumors and share the common goal of understanding how its variation affects malignant growth and dissemination as well as patient response to treatment and clinical outcomes. The ultimate goal of such research is to identify and characterize the mechanisms that promote tumorigenesis and metastases as a basis for discovering exploitable targets for improved patient care and survival.
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In view of the relocation of the Bordet Institute to the Anderlecht Campus, all research laboratories have been organized into a single entity, the Bordet Cancer Research Laboratories (BCRL) (see figure 1).

The objective of this unification is excellence and professionalization of research at the institute, by promoting research potential and scientific creativity through collaboration both internally and with the laboratories of the Faculty of Medicine. Moreover, the BCRL aims to provide adequate protection of IJB and its researchers, focusing on the lack of redundancy, as well as maintaining and increasing a competitive position in research (national and international landscape). Finally, another main objective is efficiency, such as cost control and mutualisation of platforms.

Since March 2021, the management of the BCRL was entrusted to Christos Sotiriou, appointed as director, to Françoise Rothé, appointed as deputy director, and to a Scientific Board comprising all the heads of laboratories and the coordinators of the research platforms.

The BCRL Scientific Board meets regularly, attending monthly meetings, and discusses strategic scientific recommendations to improve research and lab activities. Together with its director, the BCRL Scientific Board is responsible for setting a dynamic and realistic philosophy/strategy for excellence and quality, ensuring integration and collaboration of all groups within the IJB community (including clinical units). The BCRL aims at developing a state-of-the-art infrastructure (core facilities, bioinformatics support...), increasing its visibility (communication...) and ensuring liaison with the U-CRC (figure 2). The director of BCRL implements a regular review of the BCRL to ensure its optimal management.

Today, the BCRL comprises nine laboratories, including six faculty laboratories (LOCE - Clinical and Experimental Oncology Laboratory, GI - Gastrointestinal Laboratory, BCTL - Breast Cancer Translational Research Laboratory, Onco Vir - Onco-Virology Laboratory, LTCC - Clinical Cell Therapy Laboratory, MIU - Molecular Immunology Laboratory, LCIO - Lung Cancer and Immuno-Oncology Laboratory, LCE - Cancer Epigenetics Laboratory, MRI – Physics & Radiophysics Laboratory). The LCIO, LCE and MRI RadioPhysics & Physics are the latest additions to the BCRL.

The majority of the BCRL labs are part of the U-CRC, which assemble several labs and research units on the Erasmus Campus (see figure 2).
**Equipments/Facilities**

- Single cell analysis (10X Genomics Chromium platform)
- Spatial transcriptomics (10X Genomics Visium and Nanostring GeoMX platforms)
- NGS facility
- Epigenomics profiling platform
- Flow cytometry
- Multispectral IF imaging platform
- Confocal microscopy
- In vivo imaging facility (microPET, SPECT, MRI)
- Incucyte life-cell analysis platform
- 3D culture facility
- Mouse facility
- Bioinformatics facility
Breast Cancer Translational Research Laboratory (BCTL)

Our goal is to better understand breast cancer biology with a focus on disease dissemination and progression. We aim to assess whether tumor heterogeneity and its microenvironment impact response to therapy and clinical outcome.

Team and infrastructure

The laboratory is headed by Christos Sotiriou together with Françoise Rothé. The team includes 2 medical senior scientists, 3 postdoctoral scientists, 7 PhD students, 3 laboratory technicians, 2 research fellows, and 1 administrative assistant.

The laboratory is fully equipped with molecular and cellular biology equipment, including droplet digital PCR, single cell analysis, and spatial transcriptomics platforms. The laboratory has access to the ULB’s sequencing core facility with a NovaSeq sequencer for high-throughput, next-generation sequencing (NGS) analyses. The laboratory has expertise in state-of-the-art bioinformatic analyses of several types of omics data, including single cell and spatial transcriptomic data.

Aims

- To map tumor and stroma cell architecture and assess cell-to-cell interactions at an unparalleled level
- To portray the immune landscape including immune cell composition and geographic localization (TLS, TCR and BCR repertoires)
- To assess how tumoral, stroma and immune cell composition and organization impact disease progression, response to therapy and clinical outcome

Main projects

- Mapping tumor and immune cell architecture using spatial transcriptomics and single cell sequencing to gain novel insights into treatment resistance in all breast cancer molecular subtypes
- Collecting tissue prospectively from patients with triple negative breast cancer (TNBC) and HER2-positive disease undergoing neoadjuvant treatment: this activity is ongoing with the integration of single cell RNAseq and immune phenotyping in order to explore the impact of heterogeneity on treatment response
- Mapping TNBC heterogeneity by leveraging spatial transcriptomics and artificial intelligence: moving towards optimized patient care
- Decoding metastatic breast cancer by integrating multiomics data and artificial intelligence in the context of the AURORA study
- Analyzing the impact of intra tumor heterogeneity on low genomic risk breast cancer recurrence in the MINDACT study

Recent achievements

- Reported the largest genomic and transcriptomic profiles of paired primary and metastatic breast tumors in AURORA, the Breast International Group (BIG) molecular screening initiative
- Identified copy number aberrations associated with response to neoadjuvant anti-HER2 therapy: results from the NeoALTTO Phase III clinical trial
- Mapped the genomic alterations and the immune landscape that characterize each of the TNBC molecular subtypes, opening new avenues to develop novel targeted therapeutic approaches for patients with TNBC
- Identified molecular alterations associated with the metastatic progression of invasive lobular cancer and potential mechanisms of endocrine resistance, offering new paths for drug development in this setting
- Unraveled the metastatic dissemination of luminal breast cancer via daughter-to-daughter and parallel metastasis dissemination
- Provided insights into invasive lobular carcinoma (ILC) progression through phylogenetic analysis to develop novel paths for optimized ILC care

SELECTED PUBLICATIONS


more at bctl.bordet.be/
**Gastrointestinal Cancer Laboratory (GI)**

“Our goal is to identify prognostic and predictive biomarkers for gastrointestinal cancers, and to translate our findings into applications for clinical practice. We also aim to elucidate the mechanisms underlying the immuno-resistance of colorectal cancers and to develop more effective, immunomodulatory therapeutic strategies.”

**Team and infrastructure**

The laboratory is headed by Alain Hendlisz and Francesco Sclafani, and its team includes 2 PhD students (an MD and a biologist), 2 MDs, 1 MD research fellow, 1 laboratory technician, and 1 medical student. The laboratory has access to techniques needed to analyze circulating biomarkers such as droplet digital (dd)PCR and multiplex ELISA immunoassays, and it manages a large biobank of prospectively collected plasma samples and other biological materials. Thanks to collaborations with a number of institutional, national, and international research teams, it has access to other research platforms, including genomics; single-cell and spatial transcriptomics; patient-derived xenografts and organoids; immunophenotyping and functional immunological assays; and gut microbiome analysis.

**Aims**

- To characterize the prognostic and predictive value of circulating biomarkers such as tumor DNA and cytokines in patients with early- and advanced-stage gastrointestinal cancer patients, and to translate these into practical tools for management decisions in clinical practice
- To analyze the role of the tumor microenvironment in mediating resistance to immunotherapy in mismatch repair proficient (MMR)/microsatellite stable (MSS) colorectal cancer, and to evaluate the potential of immunomodulation strategies (including radiotherapy and tumor-microenvironment-targeting drugs) to revert this
- To elucidate mechanisms of response and resistance to multi-kinase inhibitors such as regorafenib using in vitro models, organoids and patient-derived xenografts
- To explore the prognostic/predictive value and biological correlates of early metabolic response to treatment in early- and advanced-stage colorectal cancer

**Main projects**

- Performing circulating biomarker analyses on plasma samples from patients enrolled in Chronos & Kairos (a prospective, sample collection study of patients with gastrointestinal cancer) and COPERNIC (a study of ctDNA-driven early switch in chemo-refractory colorectal cancer)
- Conducting correlative biomarker analyses using biological samples from patients enrolled in “REGINA: a phase II trial of neoadjuvant regorafenib in combination with nivolumab and short-course radiotherapy in intermediate-risk, stage II-III rectal cancer”
- Analyzing the impact of neoadjuvant treatment on the immune cell repertoire and immune biomarkers in the tumor and microenvironment of rectal cancer
- Studying the changes in gene expression profiles after neoadjuvant chemotherapy and their impact on the outcome of patients with early-stage colon cancer enrolled in the PEPITA trial

**Recent achievements**

- Conducted the very first study looking at the dynamics of circulating tumor DNA in the neoadjuvant setting of colon cancer
- Analyzed the value of circulating tumor DNA dynamics as an indicator of the natural pace of tumor progression in advanced, chemo-refractory colorectal cancer
- Built a unique platform for correlative biomarker analyses and co-clinical trials around the REGINA study, to elucidate the determinants of the innate immuno-resistance of dMMR/MSS colorectal cancer and to develop effective immuno-modulatory therapeutic strategies in this setting

**SELECTED PUBLICATIONS**

[6] [7] [8]
Clinical and Experimental Oncology Laboratory (LOCE)

“For many years, through collaboration between 4 research units, we have developed basic and translational research focused on breast, head and neck, lung, and colorectal cancers as well as melanoma, and have been evaluating new therapeutic strategies in combination with radiotherapy.”

Team and Infrastructure
The LOCE is headed by Ahmad Awada (Director), Fabrice Journe (Lab manager) and Ghanem Ghanem (Past Director). The core team includes 6 post-doctoral scientists, 7 PhD students, 6 technicians, 1 data manager, and 1 administrative assistant. The LOCE is a multidisciplinary research laboratory recognized by the ULB’s Faculty of Medicine and comprises 4 research units: the Translational Research Unit (Dr. Nadège Kindt), collaborating with the Medical Oncology Department (Prof. Ahmad Awada); the Radiotherapy Research Unit (Dr. Mohammad Krayem), working with the Radiotherapy Department (Prof. Dirk van Gestel); the Melanoma Research Unit (Dr. Ahmad Najem), associated with the Cutaneous Tumor Network; and the Radiopharmaceuticals Research Unit (Dr. Zena Wimana), linked to the Nuclear Medicine Department (Prof. Patrick Flamen). The LOCE has developed 3 technological platforms, namely cell culture (cell banking and 3D culture), animal (PDX and humanized mice models), and PIRaTh (Preclinical Imaging & Radiation Therapy).

Aims
- The Radiotherapy Research Unit aims to develop new radiation therapy modalities in preclinical and translational oncology research; to improve the understanding of radiobiology (mechanisms of tumor radio-resistance and new radiation sensitizers) through 3D cell culture and animal models (using small-animal irradiator specifically dedicated to research and meeting the current needs of radiobiology and modern radiotherapy); and to evaluate various radioimmunotherapy and radiosensitizer combinations. In addition, the Unit examines modifications in the tumor microenvironment after radiotherapy and its consequences for the risk of metastatic spread.
- The Translational Research Unit strives to find new molecular targets and new drug combinations based on improved understanding of the synergy between cytotoxic agents, targeted drugs, and immunotherapies. Its objective is to support clinical trials (such as BrainStrom — see page 48) based on recent innovations in biology and treatment, and to accelerate the development of combinations of anti-cancer drugs for solid tumors in situations where no standard treatment is effective.
- The Melanoma Research Unit focuses on identifying new therapeutic targets/combination strategies; understanding the mechanisms regulating phenotypic plasticity and how the tumor microenvironment is involved; and investigating metabolic reprogramming and oxidative stress to exploit its vulnerabilities.
- The RadioPharmaceuticals Research Unit strives to improve our understanding of the radiobiology of radiotheranostics by exploring fundamental and applied aspects of radiobiology. It also aims to develop innovative radiotheranostics by generating new radiotracers for diagnosis or treatment.

Main projects
- Developing a new hypoxia-activated prodrug to improve the response to a combination of immunotherapy and radiotherapy in lung cancer
- Studying the combination of chemoradiotherapy with p53 reactivation in head and neck squamous cell carcinoma
- Investigating the immune landscape of the rectal tumor microenvironment after preoperative treatment with radiotherapy and/or chemotherapy in locally advanced rectal cancer
- Developing new therapeutic strategies for brain metastases from breast cancer
- Exploring the role of the tumor microenvironment in the development of brain metastasis from breast cancer and melanoma
Institut Jules Bordet Scientific Report 2022 | RESEARCH PILLARS – Dissecting Tumor Heterogeneity

- Studying novel microenvironmental factors favoring phenotype switching in melanoma
- Developing new therapeutic combination strategies in melanoma, targeting prohibitins, glutaminase, and oxidative stress in resistant melanoma
- Targeting mitochondria in melanoma
- Discovering new PET imaging biomarkers for immune checkpoints inhibitors
- Understanding the radiobiology of radionuclide therapy with 177Lu-dotate

Recent Achievements

- Established a humanized mouse model as a valuable pre-clinical model for cancer radio-immunotherapy research and targeted/immuno-therapy combinations
- Established a breast cancer brain- and leptomeningeal metastasis mouse model
- Showed that brain metastases display higher infiltration of pro-tumoral macrophages than primary associated tumors
- Discovered that dasatinib, a c-Kit inhibitor, stimulates its proper mechanism of resistance through a CRTC3/MITF/Bcl-2 pathway, which may explain its modest clinical efficacy in patients with melanoma
- Used MNK1/2 inhibitors to repress phospho-eIF4E, a strategy to inhibit melanoma plasticity and improve response to anti-PD-1 immunotherapy
- Showed that bufalin, a bufadienolide isolated from toad venoms, has a high antiproliferative activity on melanoma cells
- Discovered that melanoma cells can switch between a melanocytic and a mesenchymal-like state, but an intermediate state exists that is driven by a distinct and stable “mixed” gene regulatory network rather than being a symbiotic heterogeneous mix of cells
- Integrated metabolomic and proteomic findings that revealed metabolic pathways and key proteins as potential new targets to reverse drug resistance
- Developed a predictive kinome signature that helps to identify patients with innate resistance to MAPK double inhibition

SELECTED Publications
Molecular Immunology Laboratory (MIU)

In 2013, the MIU laboratory identified tertiary lymphoid structures (TLS) in breast cancer as sites where immune cells organize into mini-lymph nodes in tumors. We associated their presence with increased tumor infiltrating lymphocytes (TIL) and positive clinical outcomes. Over the past 10 years, our efforts have focused on identifying compositional balances, including phenotypic and functional differences, in immune cells resident in active vs inactive TLS. We hypothesize that functionally active TLS create a local microenvironment rich in the cellular and molecular elements necessary for generating effective anti-tumor immunity.

Team and infrastructure
The team includes 1 laboratory head, Karen Willard-Gallo, 2 post-doctoral scientists, 3 PhD students (2 MDs pursuing a PhD), 2 technicians, 1 tissue analyst, 1 cytometrist, and 2 trainees (per semester).

The MIU laboratory has expertise in all classical approaches for immunophenotyping, flow cytometry, functional immunological assays, DNA, RNA and protein analysis, immunohistochemistry, immunofluorescent image analysis (including confocal microscopy), and chromogenic and multiplex immunohistochemistry. The laboratory is equipped with specialized equipment, including 2 flow cytometers for analysis and sorting, a Vectra®Polaris™ imaging system, a Leica Bond RX™ autostainer and a Roche Ventana™ autostainer. In addition, a post-doc and a research associate from an immuno-oncology company work part-time in our laboratory on collaborative projects to identify new biomarkers and targets for the immunotherapy of cancer.

Aims
- To identify and validate immune mechanisms associated with TLS functionality and the generation of active anti-tumor immunity in human cancer
- To investigate the dynamics and balance between effector and regulatory TIL subpopulations in cancer-associated TLS
- To analyze active immune responses to neo-adjuvant treatment in breast cancer
- To identify new biomarkers that reflect changes associated with active immune responses (and active TLS) in cancer patients, including those linked with immunotherapy toxicity

Main projects
Ongoing projects:
- Running a prospective collection of fresh tumor tissues and blood samples from breast and ovarian cancer patients (currently >1800 samples dating from 2012); same-day analysis of TIL in fresh samples together with cryopreservation of PBMCs, TIL, tumor supernatant and plasma for future analyses; characterizing TIL and TLS in fixed and embedded tissues and maintaining a dedicated patient database with clinico-pathological parameters
- Analyzing key T and B TIL subpopulations in TLS, including a recent large RNA sequencing experiment (N=160) with micro-dissected TLS and whole tumor sections from patients whose tumors contain 1) TIL but no TLS; 2) only inactive TLS; or 3) a preponderance of active TLS
- Examining pre- and post-neoadjuvant paired biopsies/surgical specimens for TIL immunophenotypes, functional characteristics, and their association with treatment response
- Monitoring blood and tissue of patients treated with immune checkpoint inhibitors in an effort to identify biomarkers that predict severe immune reactions
- Correlating host immune responses with disease severity in COVID-19 infected cancer patients, non-cancer patients, and healthcare workers
- Collaborating in the RESCUE project (VUB-UCL-Bordet/ULB) that aims to identify biomarkers of response versus resistance to novel cancer immunotherapies in patients whose tumors are refractory to PD-1 and CTLA-4 immune checkpoint blockade.

Recent achievements
- Demonstrated that functional Th1-oriented Tfh TIL are mature in patients and reside in tumor-associated TLS
- Established that Tfh TIL are regulated by functional Tfr TIL, govern TIL-B and CD8+ TIL activation, help generate immunological memory and active effector responses in tumors, and are linked with a good clinical prognosis
- Identified CXCL13 as a key chemokine for TIL recruitment and TLS formation with further characterization of this chemokine as a durable biomarker for active immune responses and TLS in cancer
- Recognized and characterized TLS in breast cancer

SELECTED PUBLICATIONS
[14] [15] [16] [17] [18]
Lung Cancer & Immuno-Oncology Laboratory (LCIO)

“The goal of our research is to understand how lung tumors grow and progress to a lethal disease, with a focus on immuno-metabolic perturbations and the function of tumor-associated neutrophils. Understanding the poorly-characterized role of these cells in cancer and how they communicate with other cells of the tumor environment may lead to better comprehension of this devastating disease and to new perspectives for treatment.”

Team and infrastructure

Since recruiting the principal investigator (PI), Etienne Meylan, to the ULB in September 2021 from the Swiss Federal Institute of Technology (EPFL), in Lausanne, Switzerland, the Laboratory has been strategically located on two ULB sites, the new IJB and the Gosselies campus, to enable basic, preclinical and translational research. It comprises the PI and 3 staff members (1 technician, 1 PhD student, and 1 postdoc) and is equipped with standard molecular and cell biology techniques and approaches. The PI has over 15 years of experience in genetically-engineered mouse models of lung cancer.

Aims

- To establish a translational research pipeline at IJB to investigate neutrophil biology in human lung tumors
- To interrogate how a tumor impacts tumor-associated neutrophil phenotypes
- To dissect the mechanisms of neutrophil actions for tumor growth and for response to therapy

Main projects

- Performing a molecular characterization of the effects and impact of short-chain fatty acids and fibers on tumor-associated neutrophils in lung adenocarcinoma (supported by an FNRS MISU grant)
- Comparing the biology of tumor-associated neutrophils between the two main histological types of lung cancer: adenocarcinoma and squamous cell carcinoma (supported by Télévie)

Recent achievements

- Identified a tumor-supportive role for tumor-associated neutrophils in primary lung cancer
- Defined a methodology to deplete neutrophils specifically and efficiently in mouse models
- Used mouse genetics to demonstrate the contribution of 2 glucose transporters expressed by tumor cells for lung cancer growth
- Identified altered glucose metabolism of tumor-associated neutrophils, which contributes to their tumor supportive capacity

SELECTED PUBLICATIONS

[19] [20] [21]
Onco-Virology Laboratory

*Our goal is to improve how to identify asymptomatic HTLV-1 carriers at high risk of progression to aggressive adult T-cell leukemia (ATL), to develop molecular tools to advance treatment decision making for ATL, and to identify novel treatment targets. We aim to track tumor evolution in viral cancers by developing novel cutting-edge NGS technologies.*

THE Team

The team is headed by Anne Van den Broeck, a DVM-PhD and comprises 2 post-doctoral scientists, 1 post-doctoral researcher with expertise in bioinformatics, 2 PhD students, and 1 microfluidics engineer. The team is supported by technicians dedicated to animal experiments (USASK, Canada) and has access to the GIGA Institute’s genomic platform (University of Liège).

Aims

- To study clonal heterogeneity and tumor evolution through longitudinal exploration of clonal landscapes and virus-host interactions in Human T-cell leukemia virus (HTLV-1) induced Adult T-cell leukemia (ATL) and its corresponding animal model (BLV, bovine leukemia virus, cattle and sheep), from early premalignant stages to full-blown tumors.
- To transform basic laboratory research findings into novel tools to improve the clinical management of HTLV-1 asymptomatic carriers of HTLV-1, patients with aggressive ATL, and patients affected by human papillomavirus (HPV)-associated oropharyngeal cancers.

Projects

- Applying cutting-edge NGS technologies to explore tumor heterogeneity, track rare premalignant ancestor clones, and uncover drivers of tumor evolution and oncogenic switch. To achieve these goals, develop novel dual-tracking targeted single-cell NGS tools and custom high-throughput microfluidics.
- Analyzing clonality and single-cell NGS of HTLV-1 asymptomatic carriers to identify patients at high risk of progression to aggressive ATL (Tokyo cohort, JSPFAD, Japan).
- Applying long-read NGS technologies to assess HPV genomic integration as a biomarker of aggressiveness, prognosis, and therapeutic response in patients with HPV-positive head and neck squamous cell carcinoma (HNSCC).

Recent achievements

- Demonstrated that NGS clonality enables the identification of HTLV-1 carriers at high risk of progression to aggressive ATL; risk stratification tool with increased sensitivity, specificity, and precision versus previous biomarkers (Japanese cohort).
- Developed a novel long-read Oxford Nanopore NGS method to identify clonally expanded precursor/malignant cells and to sequence the entire viral genome at the tumor-specific genomic integration site.
- Discovered clonal and sub-clonal mutational signatures in patients with ATL and the significance of these signatures in defining an unfavorable indolent subtype.
- Developed novel cutting-edge single-cell NGS approaches (a dual-tracking scRNA-seq tool and a high-throughput droplet microfluidic approach) for tumor heterogeneity and precursor tracing.

SELECTED PUBLICATIONS

[22] [23] [24] [25]
Clinical Cell Therapy Laboratory (LTCC)

“...Our goal is to understand the clonal heterogeneity and the interaction of leukemic cells with their immune and stromal microenvironments. With a particular focus on chronic lymphocytic leukemia, acute myeloid leukemia, and multiple myeloma, we hope to identify new prognostic markers and to discover innovative treatment targets...”

Team and infrastructure

The laboratory is headed by Laurence Lagneaux and comprises 1 medical senior scientist (MD, PhD), 3 senior scientists (PhD), 1 scientific collaborator (MS), 6 PhD students, and 1 technician. It has access to cellular culture and molecular biology facilities (including real-time PCR, fluorometer), multiplex ELISA system (Bioplex 200), flow cytometry (MACSQuant®), Nanotrack analyzer, and ultracentrifuge for extracellular vesicle analysis.

Aims

- To decipher the immune landscape of hematological malignancies:
  - Chronic lymphocytic leukemia (CLL) crosstalk with immune microenvironment via extracellular vesicles
  - Acute myeloid leukemia (AML) and more specifically the molecular profile and function of T-infiltrating lymphocytes with the risk of relapse of AML after standard treatment and allogeneic transplantation
  - Multiple myeloma (MM) mesenchymal stromal cell interaction with immune cells of the microenvironment
  - Identification of immune evasion mechanisms based on sialoglycan interactions with the immunoregulatory Siglec receptors expressed by immune cells

- To understand the clonal heterogeneity and the origin of leukemic cells
  - CLL is considered to be a monoclonal disease but multiple leukemic clones coexist in patients
  - Study their immunoglobulin structure to highlight the stimulating antigens of the disease

- To investigate mechanisms by which mesenchymal stromal cells (MSC) mediate immunosuppressive effects and to discover novel immune targets for the development of immunotherapeutic strategies

Main projects

- Dissecting the crosstalk between malignant cells and their microenvironment (e.g., MSC, immune cells) and investigating their different ways of communication (e.g., via extracellular vesicles, via microRNA)
- Studying the immunosuppressive microenvironment in MM: role of bone marrow–mesenchymal cell (BM-MSC) glycosylation
- Exploring the feasibility of extracellular vesicles to deliver siRNA and drugs for therapeutic targeting, starting with pancreatic cancer
- Deciphering the clonal heterogeneity of CLL using next generation sequencing of immunoglobulin sequences
- Predicting epitope and modelling of antibody-antigen structure to discover CLL stimulating antigens
- Confirming in a large AML patient cohort the preliminary observation of a correlation between the transcriptomic and methylation profiles of CD3+ T cells isolated from patients and their risk of relapse with standard therapy
- Understanding how differentially expressed miRNAs in AML mediate the communication between leukemia cells and TIL

Recent achievements

- Demonstrated the existence of multiple leukemic clones within the same CLL patient
- Showed evidence of the existence of harmful crosstalk between cancer cells and MSC in CLL and MM
- Demonstrated the impact of MSC extracellular vesicles on survival, gene expression, and chemoresistance of CLL cells
- Identified genomic aberrations involved in Richter transformation via whole genome sequencing
- Established microRNA profiling of CLL extracellular vesicles by small RNA sequencing
- Identified first circulating microRNA signatures in bone marrow and plasma of AML
- Showed the correlation between CD3+ T cell dysimmunity and AML relapse risk
- Highlighted the contribution of endothelial progenitors in the osteogenic potential of MSC via extracellular vesicle liberation

SELECTED PUBLICATIONS

[26] [27] [28] [29] [30]
Cancer Epigenetics Laboratory (LCE)

Our goal is to understand how epigenetic modifications contribute to the progression of tumors and their resistance to therapy, and to utilize epigenetic alterations to improve the diagnosis and treatment of cancer patients.

Team and infrastructure

The team includes 1 Director, François Fuks, 2 senior scientists (PhDs), 4 post-doctoral scientists, 10 PhD students, 4 technicians, and 1 administrative assistant. The Cancer Epigenetics Laboratory consists of 2 research units, Fundamental Cancer Epigenetics at Erasme Campus and Translational Cancer Epigenetics at IJB, which work closely together with the aim of quickly translating new findings from basic research into clinical use. Both laboratories are equipped with all the tools needed to study modifications in DNA, RNA, and proteins at the molecular and cellular levels. Notably, the laboratories feature an epigenomic profiling platform, a life-cell analysis platform, and various epigenetic in vitro and in vivo models. LCE has expertise in developing state-of-the-art epigenomic profiling technologies and bioinformatics tools for the related analyses as well as in adapting these technologies for their use with tumor biopsies.

Aims

- To characterize the epigenomes of cancers, most notably breast cancer
- To study the role of epigenetic alterations in cancer progression and therapy resistance
- To explore epigenetic alterations as new biomarkers or therapeutic targets to improve the diagnosis and treatment of cancer

Main projects

- Developing technologies for transcriptome-wide mapping of novel modifications on mRNA
- Generating in vitro and in vivo models (mouse) of new epigenetic regulators using CRISPR-technology
- Mapping novel mRNA modifications (e.g., m6A, hm5C), identifying their regulators (writers, erasers, readers), and characterizing their functions and biological roles in development and cancer
- Investigating the role of m6A in (breast) cancer progression and therapy resistance
- Optimizing m6A mapping technologies for use in tumor biopsies
- Mapping changes in m6A abundance in breast cancer and exploring their value as disease markers
- Exploring the role of DNA modifications (5mC, 5hmC) in tumor heterogeneity and tumor immunity

Recent achievements

- Established transcriptome-wide m6A profiling technology (m6A-RIPseq) and adapted it for use in (breast) cancer biopsies
- Identified the wide-spread downregulation of FTO m6A RNA demethylase in epithelial cancers and showed that this changes m6A abundance at transcripts of cancer pathways, most notably the oncogenic Wnt pathway
- Demonstrated that downregulation of FTO promotes EMT-mediated cancer progression of epithelial tumors and sensitivity to Wnt inhibitors
- Discovered that Tet proteins, by marking RNA with hm5C, regulate differentiation of ES cells, a finding that could be relevant in cancer stem cells
- Revealed that Tet2 reduces melanoma initiation and progression by promoting epigenetic plasticity via 5hmC deposition on DNA
- Discovered genome-wide 5hmC changes in basal-like breast cancers that are related to TET1 repression by NF-κB and correlate with immune marker/immune cell abundance

SELECTED PUBLICATIONS

[31] [32] [33] [34] [35]
MRI Physics & Radiophysics Laboratory

The activities of the MRI Physics and Radiophysics Laboratory, which was set up in 2020 and combines clinical and basic research, are developed in close collaboration with the departments of Nuclear Medicine, Radiology and Radiotherapy and, more recently, with the BCRL. Given the varied expertise of our researchers and our intrinsic collaborations, our research topics are highly diversified.

The Laboratory also coordinates IJB’s imaging core lab, ORILAB, performing the quality control and medical review of images included in prospective trials. Between 2020 and 2022, ORILAB provided services to 16 academic and industry sponsored clinical trials.

**Aim**
To develop novel treatment modalities and optimize existing clinical workflows across multiple departments and laboratories, with the ultimate goal of improving patient clinical outcomes

**Team and infrastructure**
The team includes 1 Director, Nick Reynaert, 1 lab manager (PhD), 6 senior scientists (2 PhDs and 4 MScs), 5 post-doctoral scientists (PhDs), 6 PhD students, and 1 administrative assistant.

The laboratory features a 3D printing platform (consisting of 4 3D printers with different technologies and applications) and CPU and GPU-based computational units to perform big data analysis and deep learning experiments. Currently, the laboratory is developing a unit to assess the radiobiology of boron neutron capture therapy (BNCT) and FLASH with dedicated equipment and is actively working to implement the PIRaTH (preclinical imaging and radiation therapy) platform, which comprises a micro-PET, micro-SPECT, micro-CT, micro-MRI, and micro-irradiator for preclinical studies.

**Main projects**
- Developing data sciences, including artificial intelligence techniques (as described elsewhere, “Pillar II”)
- Optimizing radiotherapy techniques: using artificial intelligence for automatic image delineation (CT, MRI and PET images), absorbed-dose prediction, generation of pseudo-CT from MRI images, and TCP/NTCP modelling. We will focus on integrating multimodality imaging as part of precision radiotherapy approaches (MR-Linac, Theranostics, notably 68-Gallium/177-Lutetium PRRT and PSMA, etc).
- Working with the EORTC: The director of the lab serves as a physicist responsible for the Radiotherapy Quality Assurance/Radiation Oncology Science Council (RTQA/ROSC) group at EORTC and is thus highly involved in clinical studies with a radiotherapy component at the European level.
- Contributing to FLASH radiotherapy: Zebrafish experiments are being performed to provide a better understanding of the FLASH effect when using very high dose rates, because normal tissues seem to be better protected in this case (influence of oxygen depletion/immune system).
- Undertaking radiobiology collaborations with the Brussels RadioTheranostics Platform (BRTP) and PIRaTH
- Collaborating closely with SCK-CEN on radiobiology and microdosimetry of PRRT (Nuclear Medicine, Theranostics) is currently ongoing (focusing on kidney toxicity).
- 3D printing of bolus materials for radiotherapy, phantoms for nuclear medicine and radiology and also simulations of surgical interventions.
- Launching a Biowin project of proton and hadrontherapy in collaboration with IBA (D-CAF project), modelling new detectors for carbon ion beams. IJB’s medical physics laboratory will also be involved in providing treatments in the new proton facility in Charleroi (Protherwall).
- Installing and developing BNCT (as described elsewhere, “Pillar III”)

**Recent achievements**
- Created a datascience and 3D printing platforms within the BCRL
- Signed a letter of intent between Neutron Therapeutics and HUB, expressing the interest to install a BNCT facility next to and linked with IJB
- Contributed to the PHERGAIN clinical trial, (see page 37) with ORILAB playing an important role in the quality control and medical review (in partnership with IJB’s Nuclear Medicine Department) of all the baseline and follow-up 18F-FDG PET/CT of the 356 patients included in the trial

**SELECTED PUBLICATIONS**
[36] [37]
PILLAR II · Contribution to “precision oncology”

There is significant heterogeneity in the risk of developing cancer, and this heterogeneity extends to cancer patients themselves, who show markedly different outcomes despite receiving identical histopathological diagnoses and identical therapies. The “one size fits all” approach to screening and treatment as applied today in most circumstances is therefore largely unsatisfactory.

“Precision oncology” is rapidly reshaping cancer care, and it is the ambitious goal pursued by most comprehensive cancer centers nowadays: it means exploiting modern technologies in order to better individualize cancer screening, diagnosis, and treatment in the fields of surgery, radiotherapy, and medical oncology.

IJB has launched precision oncology initiatives in these fields at national and international levels, using modern tools such as genotyping, liquid biopsies, molecular imaging with FDG-PET, MRI-Linac, radiomics, and artificial intelligence algorithms. The Institute’s ambition is to upgrade the efficiency of this research by creating a “learning healthcare system” through the application of artificial intelligence and big data analysis.
28 USING A RISK-STRATIFIED BASED STRATEGY TO IMPROVE OUTCOMES OF STANDARD BREAST CANCER SCREENING: THE EU MYPEBS TRIAL

29 LIQUID BIOPSY

30 NUCLEAR IMAGING

31 RADIOMICS IN PANCREATIC CANCER

32 PRECISION MEDICAL ONCOLOGY

33 PRECISION RADIOTHERAPY

34 PRECISION SURGERY

35 CREATING A LEARNING HEALTHCARE SYSTEM THROUGH THE APPLICATION OF ARTIFICIAL INTELLIGENCE AND BIG DATA ANALYSIS

Data Science Board
Implementing data farming to enable big data analysis
Artificial Intelligence applications to optimize the clinical workflow
Applied image and data analysis to personalize treatment and improve patient outcomes
Using a risk-stratified based strategy to improve outcomes of standard breast cancer screening: the EU MyPeBS trial

Team & infrastructure
This EU-funded, international, multicentric study involves a 27-partner consortium and 6 recruiting countries. The Unicancer network of cancer centers (France) serves as the sponsor, and IJB is the national coordinator for 10 Belgian sites (Principal Investigator: Jean-Benoît Burrion). MyPeBS in Belgium is supported by the Fondation Contre le Cancer.

Aims
Risk-stratified breast cancer screening (BCS), integrating both personal and familial variables and a polygenic risk score (PRS), is a promising strategy that may improve current BCS outcomes. Real-time risk assessment and field implementation are some of the main challenges for such an approach. MyPeBS is a European research project that aims to assess the effectiveness and feasibility of a risk-stratified BCS program, one that is based on individual risk of developing breast cancer.

Main project
At the core of MyPeBS is a trial in which eligible women aged 40-70 are randomized 1:1 between continuing standard BCS as recommended in their participating country/region or switching to risk-stratified BCS, where BCS schedule and modalities are adapted to the individual predicted 5-year risk of invasive BC (IBC). The primary endpoint is 4-year incidence of stage 2 and higher BC. The 5-year IBC risk is estimated using a BCSC-derived or Tyrer-Cuzick risk score and centrally-determined PRS313 (saliva sample), adjusted for national BC incidence.

Recent achievement
Among 16,550 women randomized as of September 2021, 36% were estimated to be at low risk (<1% risk of IBC at 5 years), 29% at average risk, and 35% at high (34%) or very high risk (1%) (>1.67% and >6% risk, respectively) of developing IBC. Only 2.5% of DNA extractions were not usable for genotyping, due to insufficient DNA concentration or quality; and 98.8% of the eligible DNA samples were successfully genotyped. Median turnover time from saliva sampling to risk result availability was 11 weeks despite the COVID pandemic. This preliminary achievement shows that real-time BC risk assessment based on a large set of polymorphisms, on family, screening and hormonal history, and on breast density is feasible within organized screening programs. Participants so far represent different strata of the general population with some over-representation of highly educated participants.

SELECTED PUBLICATIONS
[38]
Liquid Biopsy

Team and infrastructure
Michail Ignatiadis’ team is part of the J.-C. Heuson Breast Cancer Translational Research Laboratory (BCTL).

Aim
To explore the role of circulating tumor DNA for breast cancer diagnosis and monitoring of early disease

Main projects
- Developing a liquid biopsy assay for breast cancer diagnosis based on patterns of plasma cell-free DNA fragmentation:
- We aim to address the limitations of the current liquid assays based on cell-free DNA fragmentation patterns (such as their inability to determine the fraction of ctDNA among total cell free DNA) by developing a ctDNA detection and quantification Algorithm that captures Fragmentation patterns of plasma cell-free DNA using machine learning approaches (“ctDNA ALFA” assay). We will develop this assay by comparing the plasma from healthy women and women with breast cancer and further validate the assay in women with breast cancer.
- Identifying associations between plasma ctDNA detection using personalized assays and clinical outcome in patients with early breast cancer:
- The RaDaR™ personalized assay has been used for ctDNA detection in patients enrolled in the NeoRHEA study. This phase 2 trial enrolled 100 patients with ER+/HER2- breast cancer who received 4 months of neoadjuvant endocrine treatment in combination with the CDK4/6 inhibitor palbociclib. The association between ctDNA detection at different time-points and clinical outcome will be explored.

SELECTED PUBLICATIONS
[39] [40] [41] [42] [43]
Nuclear Imaging

Team and infrastructure
The Nuclear Imaging Department is headed by Patrick Flamen.

Aim
To explore the role of functional PET imaging to monitor treatment response and impact patient management in a positive way.

Main projects
- **OSCAR**
  Outcome prediction and response assessment using molecular biomarkers (PSMA receptor expression, metabolic activity, and circulating cell-free DNA) in patients with metastatic castration-resistant prostate cancer treated with taxane-based chemotherapy

Achievements
- **PHERGAIN**
  This trial demonstrated that patients with early HER2+ breast cancer showing a good FDG-PET response after 2 cycles of trastuzumab + pertuzumab can continue this chemo-free regimen for a total of 8 cycles and achieve a pathological complete response close to 40%.
  
  This was the striking result of the elegant PHERGain de-escalation study designed by Spanish investigators and for which the IJB nuclear medicine team played an important role by reviewing all the FDG-PET scans.

- In development and validation cohorts, demonstrated the independent prognostic value of whole-body, metabolically active, tumor volume and early metabolic response in patients with advanced, chemo-refractory colorectal cancer

SELECTED PUBLICATIONS
[12] [44] [45] [46]
Radiomics in Pancreatic Cancer

Team and infrastructure
This is an international collaboration led by the Radiology Department (Maria Bali), the Gastrointestinal Medical Oncology Department (Jean-Luc Van Laethem and Alain Hendlisz), and Philippe Lambin (University of Maastricht).

Aim
To provide clinicians with a radiomics-based model to better stratify patients with pancreatic adenocarcinoma (PDAC) according to disease prognosis and prediction of responsiveness to treatment.

Main projects
The project has the following objectives:

- To extract radiomic features and identify radiomics signatures from conventional CT and MRI images, at no extra cost to the healthcare system, in order to provide comprehensive information about the genotype-phenotype of the tumor.
- To assess performance of the radiomics model (association of clinical findings, radiomics features, and genomic tumor characteristics) to predict overall survival (OS) / progression-free survival (PFS).
- To assess the predictive value of radiomics signatures for tumor response to systemic treatment.

Recent achievements
This study is a retrospective analysis involving a population of patients with PDAC who have their folders and radiological exams available. Patients included in the databases of the Hopital Erasme (80 cases/year) and IJB (25 cases/year) between January 2010 and December 2019 with histologically proven PDAC were considered. The data from selected patients were analyzed and allocated to one of the following groups according to NCCN classification: primary resectable, borderline resectable, and locally advanced unresectable/metastatic tumors. Oncoradiomics research software (Liège, Belgium) was used for feature extraction. A sub-cohort of recruited patients (about two-thirds of them) were included in the feature selection and model training. The remaining patients contributed to model validation or testing. During the feature selection, statistical analysis was performed to assess the relationship between extracted PDAC radiomics features and the previously mentioned clinical outcomes. Once the most important radiomics features had been identified, machine learning classifier models were built to predict the aforementioned clinical end-points. Standard machine performance metrics such as accuracy, precision-recall, and calculation under the curve (AUC) of the receiver operating characteristic curve (ROC) were used to evaluate the performance of the classification models. After obtaining ethical committee approval, 253 pathology-confirmed cases of PDAC were analysed, from which 171 radiomics features were extracted. Six different subgroups of features were selected (clinical-radiomics features, clinical features, and radiomics features) both for OS and PFS. Subsequently, 6 RF models were trained and tested. The clinical-radiomics model was the most predictive for both OS (AUC=0.75) and PFS (AUC=0.76). Other models reached lower AUCs.

SELECTED PUBLICATIONS [47] [48]
Precision Medical Oncology

Team and infrastructure

Investigators at the CTCU serve as principal investigators of multi-institutional programs that provide molecular screening to patients with metastatic breast cancer (AURORA: NCT02102165) and other solid tumors (GeNeo: NCT04641676). Their work will be supported by the Pathology Department’s acquisition of 2 sequencing machines (NextSeq and MiSeq).

Aim

To offer IJB patients tools to identify genomic targets in their tumors and to actively participate in clinical trials of new drugs directed at these genomic alterations.

Projects

- Equip the Pathology Department with hybrid capture-based NGS in order to be able to identify all classes of genomic alterations (SNVs, indels, CNVs, and gene rearrangements).
- Continue to play a central role in the Breast International Group’s molecular screening program (AURORA), specifically during its second phase focused on metastatic lobular cancers, triple negative breast cancer, and late relapses (> 10 years).
- Expand GeNeo with the GeNeo 2 investigator-initiated trial that will allow comprehensive genomic profiling to be implemented locally.
- Continue discussions with government and industry stakeholders for a framework of access to molecular-guided therapeutic options.

Recent achievements

- Opened a portfolio of clinical trials covering a wide range of genomic alterations, including ERBB2-3, EGFR, HRD genes, RET fusions, PTEN mutations, NF1 mutations, FGFR1-3 fusions, CCNE amplification, and MET amplification, among others.
- Co-created the Belgian Molecular Tumor Board to facilitate patient referrals all over Belgium.

SELECTED PUBLICATIONS

[4] [49] [50] [51]
Precision Radiotherapy

Team and infrastructure
Radiotherapy Department led by Dirk Van Gestel. Medical Physics Department led by Nick Reynaert.

Aim
To improve radiotherapy treatment standardization and to develop more tumor targeted approaches (see Pillar 3)

Projects
• ProCaLung

The main objective of the ProCaLung project, endorsed by the Belgian College of Physicians for Radiation Oncology Centers of the Federal Public Health Service, is to standardize across Belgium the radiation treatment of mediastinal node-positive, locally advanced, non-small-cell lung cancer (NSCLC), with a specific focus on nodal target definition and delineation.

• STEREOPAC trial

This is a Belgian nationwide randomized phase II trial led by the Radiotherapy-Oncology Department (Christelle Bouchart), the Hepato-Biliary-Pancreatic Surgery Department (Julie Navez) and the Gastrointestinal Medical Oncology Department (Jean-Luc Van Laethem). It will evaluate the impact and efficacy of adding iHD-SBRT to preoperative neoadjuvant chemotherapy (mFFX or Gem-Nab-P) in patients with borderline resectable pancreatic adenocarcinoma. The hope is to improve both the R0 resection rate and prognosis (DFS as co-primary end point).

SELECTED PUBLICATIONS
[52] [53] [54] [55]
**Precision Surgery**

**Team**
Surgery: Gabriel Liberale, Ali Bohlok, Antoine El Asmar, Sophie Vankerckhove, Vincent Donckier  
Pathology: Pieter Demetter, Ligia Craciun, Denis Larsimont  
Immuno-oncology: Etienne Meylan

**Infrastructure**
The team has access to translational research experts in the BCTL.

**Aim**
The development of distant metastases, and of liver metastases (LM) in particular, represents the main cause of mortality in patients with solid tumors. Surgery could be curative in some patients with isolated metastases. Currently, however, due to the lack of accurate clinical selection criteria, most patients operated for metastatic disease recur postoperatively, including a significant proportion with rapid and diffuse relapses. There is therefore a major need to better adapt oncosurgical management to individual tumor profiles and to reduce the risk of futile interventions.

**Projects**
- Developing a model of colorectal LM in mice: Using 2 different colorectal cancer cell clones, establish distinct models of desmoplastic- and replacement-type LM and characterize the tumor microenvironment in these different patterns, with a particular focus on immune cells infiltrates  
- Investigating how drug and radiotherapy could modulate the microenvironment of LM and how these interventions could alter tumor progression  
- Validating and extending our initial data from patients operated for colorectal peritoneal metastases: first, by collecting from a large, multicentric, international biobank an extended series of samples from these patients; second, by evaluating if similar patterns could be identified in peritoneal metastases of ovarian origin

**Recent achievements**
In liver metastases (LM) of several cancer types (including colorectal, breast, melanoma) we observed that the tumor microenvironment, described by the histopathological growth pattern (HGP), is a strong predictor of the benefit of surgery: we showed that postoperative outcomes are significantly better in patients with desmoplastic HGP (e.g., metastasis surrounded by a fibrous rim and presence of immune cells) than in those with replacement HGP (e.g., infiltration of the liver parenchyma with cancer cells and minimal immune infiltrate). We also identified distinct HGP in peritoneal colorectal metastases that seem to predict survival outcomes.

**SELECTED PUBLICATIONS**
[56] [57] [58] [59]
Creating a learning healthcare system through the application of artificial intelligence and big data analysis

Artificial intelligence and big data are omni-present in the current medical research landscape and are slowly but surely being introduced into clinical practice.

At IJB, a data science research team was created in the Department of Medical Physics, fully dedicated to the development and clinical implementation of artificial intelligence and big data. The ambition of the data science experts is to bridge the different disciplines within the institute and enable and perform modern data analysis, generating evidence with the aim to improve patient care.
1. Data Science Board

Team and infrastructure
The data science team includes 2 data science experts and 1 research coordinator, headed by Nick Reynaert. The team’s infrastructure consists of both CPU and GPU-based computational units to perform big data analysis and deep learning experiments.

Aims
To support current and future artificial intelligence and data science projects throughout IJB, to standardize the workflow, and to ensure high quality research.

Main projects
Monthly data science board meeting open to all IJB departments:

- The main aim of the data science board meeting is to share knowledge, guarantee high quality research, and provide support to ongoing and future research projects in which modern data science is involved.

Artificial intelligence is often described as a “black box,” and the amount of data involved in modern data science easily renders the process rather abstract. It is therefore not that surprising that plug-and-play commercial solutions are rapidly gaining in popularity. However, while the wide-spread application of machine- and deep-learning is promising, these solutions do not protect their users from common pitfalls. The latter is illustrated by several papers highlighting the many AI-related studies whose results are not reproducible or shown to be a consequence of data bias or questionable statistical methods, despite undergoing peer-review.

During the data science board meetings, specific research projects or clinical trials can be discussed. Based on their experience, the data science experts can answer questions related to data registration, storage and infrastructure, data visualization, data analysis, risk of bias, minimally required amount of data, etc.

- In-house educational seminars on artificial intelligence related topics, open to all IJB departments

2. Implementing data farming to enable big data analysis

Team and infrastructure
The data science team is headed by Nick Reynaert, and the Radiotherapy Department is headed by Dirk Van Gestel, with the input of Philippe Lambin (Consultant in the Radiotherapy Department).

Aims
To collect real-world data and develop prediction models based on applied treatment parameters, recorded toxicities, and patient outcome, and to apply these models in clinical decision support systems for personalized radiotherapy treatment. In addition, to collect real-world data to generate evidence for the validation of novel technologies.

Main project
The Radiotherapy Department is participating in the Multi-OutcoMe EvaluatioN of radiation Therapy Using the MR-Linac (MOMENTUM) study, an international academia-industry partnership involving several hospitals and the industry partner Elekta. The aim of MOMENTUM is to demonstrate formally the added value of the MRI-guided, on-line adaptive workflow that can be applied on this machine. Through the collection of real-world data and the development of clinical decision support systems, we aim to optimize the objective selection of patients who will benefit the most from being treated on the MR-Linac.
3. Artificial Intelligence applications to optimize the clinical workflow

Team and infrastructure
The data science team headed by Prof. Nick Reynaert. The team’s infrastructure consists of both CPU and GPU-based computational units for big data analysis and deep learning experiments. Both research and stand-alone software like DOSIsoft and MiM Protégé are available.

Aim
To automate (parts of) the clinical workflow in the Radiotherapy and Nuclear Medicine Department by implementing both commercial artificial intelligence applications and those developed in-house.

Main projects
- **AI-based Fast Dose Calculation and Delivery Reconstruction, an Elekta research agreement concerning the MR Linac Unit.**
  Monte Carlo (MC) dose calculation is the gold standard in terms of precision, but too slow to be used routinely in the clinic. This study aims to develop a deep learning dose calculation mimicking MC accuracy in a matter of seconds. We may link the results to MC to calculate dose in a fraction of the current time and speed up the segment shape and weight optimization process.

In addition, Elekta Linacs currently log delivery data at a frequency of 40ms. We will use these data to estimate the dose received by the patient. This will be combined with online MR imaging. By synchronizing the online imaging and the estimated dose delivered, one can assess the accumulated treatment dose (and treatment course).

- **MR-only radiotherapy planning with synthetic CT.**
  While MR provides excellent soft-tissue imaging, CT is still essential for providing electron density information for dose planning, which MR images cannot deliver. Establishing an MRI-only workflow in radiotherapy depends on the ability to convert the MRI intensities to get attenuation properties. Many different methods have been proposed in the literature to solve this problem, often referred to as synthetic CT (sCT) generation. With the emergence of deep learning, these methods have recently undergone significant changes. Accuracy and generation speed have dramatically increased. Generative Adversarial Networks (GAN) have introduced new impulses, with their ability to learn to generate any data distribution. Our goal is to improve the generalizability of MRI-to-CT synthesis using GAN. This process has the capability to tackle the image variability problem in clinical practice, since changes can happen in image acquisition parameters or, for instance, with machine replacement.

**SELECTED PUBLICATIONS**
[60] [61] [62]
4. Applied image and data analysis to personalize treatment and improve patient outcomes

**Team and infrastructure**

The data science team headed by Nick Reynaert + others (including CTSU, UGI, MIU).

**Aim**

To personalize the treatment of patients across different departments through the analysis of multi-modality data collected in the context of clinical trials and enriched with real-world data.

**Main projects**

- **AURORA**
  
  In collaboration with the BCTL, big data and image analysis of the Breast International Group’s AURORA database to unravel the genomic landscape of breast cancer primaries and matched metastases.

- **Refractory Advanced Colorectal cancer; big data analysis of aggregated data**
  
  In collaboration with Alain Hendlisz and Erwin Woff, development of a patient outcome prediction model to stratify patients using data collected through the clinical trials REGARD, SoMore and Coriolan. Model validation will be done on real-world data. ESTRO Working Group on clinical target volume CTV definition in early breast cancer patients. This study is sponsored by Intra-Op and aims to analyze the MOBETRON database created by Catherine Philippson and Stephane Simon. The database comprises patient clinical and intraoperative radiotherapy treatment data. Additional pathological data related to the distribution of recurrences will be explored in order to optimize the CTV definition for patients with early breast cancer.

Radiomics is the method to extract a large number of quantitative features from medical images that are meant to non-invasively provide important phenotypic information about the entire tumor region and the surrounding tissues. However, a vast majority of current studies lack robustness and external validation. Our goal is to improve the generalizability of radiomic models across multiple datasets from different institutions. This covers the evaluation of feature implementation in different radiomic software and the assessment of feature repeatability and reproducibility based on phantoms acquired on different scanners and for different imaging modalities (18F-FDG PET and DW-MRI). It provides a first investigation of feature selection to develop robust predictive models in clinical trials, demonstrating the added value of quality assurance processes to select conventional and radiomic features in prospective multicenter trials.

**SELECTED PUBLICATIONS**

[47]
PILLAR III • Fostering Innovation in Cancer Management

Providing cutting-edge treatment options has always been in the DNA of IJB. Many of these innovative therapeutics are delivered within the Clinical Trials Conduct Unit (CTCU) in collaboration with industry for pharma-sponsored clinical trials, academic collaborative groups for academic trials, and the Academic Trials Promoting Team (ATPT)/Clinical Trials Support Unit (CTSU) for IJB-sponsored academic trials. The scope of activity of the CTCU encompasses medical oncology (breast, gastrointestinal, genito-urinary, gynecological, sarcomas, and rare tumors), radiation oncology, and hematology. Members of the CTCU are study coordinators (early phase and later-phase clinical trials), data managers (including an imaging officer), a tissue officer, an administrative team, a start-up coordinator, an operational head, and a quality manager drafting the standard operating procedures while working to get the unit accredited by 2026. The CTCU team will soon manage the Novel Treatment Unit (NTU) in concert with the Nursing Department. The NTU is an inpatient unit of 12 beds, where patients will be hospitalized for first-in-human therapies, studies requiring multiple PK blood draws, or procedures requiring overnight stays. Biosafety level 2 accreditation allows studies to be conducted with viral agents and cellular therapies.

A protocol review committee (PRC) is responsible for selecting the protocols to be implemented within IJB according to three criteria: innovation, unmet need, and feasibility. The principal investigators are selected based on expertise. Recruitment of patients is intra-institutional and inter-institutional via a network of referring physicians. The creation of the “national” molecular tumor board (MTB) has facilitated the accrual of patients with rare genomic alterations across Belgium and has increased the visibility of IJB in the field of precision medicine.

IJB has recently acquired an MR-Linac, thanks to the support of “Association Jules Bordet”: this modern machine increases the precision needed for radiotherapy delivery using a daily MRI-based, online adaptive procedure, and it will be prioritized as a means to explore new radiotherapeutic approaches to cancer management.

IJB also features a modern radiotheranostic center with a fully 6MP-compliant clinical radiopharmaceutical production unit. It will produce and test new radiotheranostics within well-designed clinical trials in close collaboration with medical oncologists and has the ambition to become a “radiotheranostic center of excellence”

IJB has also invested in a vast GMP-Unit (UTCH) in its new building in order to take up the challenge of new cellular and gene immunotherapies. After a pause in the early 2000s linked to diagnoses of secondary leukemia in treated children, the optimization of vectors and genetic manipulation techniques have facilitated a new clinical boom in the field of gene therapies. Chimeric Antigen Receptor (CAR) T-cell therapy is undoubtedly driving a revolution in cancer treatment. The recent successes of CAR T-cell therapy in the fight against hematological malignancies have led to a considerable increase in interest in the field of cellular immunotherapy.
42 INNOVATIVE CANCER THERAPIES PRIORITIZED AT IJB

Cell therapies
Immunotherapy beyond PD-1/PD-L1 immune checkpoint blockers
Radiotheranostics
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BNCT

46 CONTRIBUTING TO ACADEMIA-LED RESEARCH WITHIN THE BIG AND ONCODISTINCT NETWORKS

Contributing to Academia-led research within the BIG network
Contributing to Academia-led research within the ONCODISTINCT network
Innovative cancer therapies prioritized at IJB

Teams and infrastructures

- The CTGU and CTSU clinical research units play a pivotal role in the implementation, conduct and analysis of innovative clinical trials run at IJB.
- The Academic Promoting Team gives advice and support to young investigators interested in designing innovative academic trials for which IJB will be the sponsor.
- The cell therapy platform is an entity meeting GMP standards for the collection, processing (including the selection, expansion, and freezing of cells), control, storage, and delivery of several types of cells, including hematopoietic stem cells, mesenchymal cells, lymphocytes, and dendritic cells. The new Cellular Therapy Unit built in IJB is equipped with 4 independent clean rooms, 5 laminar flows, 4 incubators, 2 temperature-controlled freezing devices, 4 -80°C freezers, and 35 nitrogen tanks containing human body material.

It includes 3 banks accredited by the FAMHP (Federal Agency for Medicines and Health Products):
- The hematopoietic stem cell bank
- The cell bank for therapeutic purposes
- The ULB umbilical cord blood bank

- As explained above, IJB now hosts a modern radiotheranostic center with a GMP radiopharmacy laboratory.
- A letter of intent has been signed between Neutron Therapeutics and HUB, expressing the interest to install a Boron Neutron Capture Therapy (BNCT) facility next to and linked with IJB. A business model is currently being elaborated. The main initial investment will be provided by Neutron Therapeutics. HUB and ULB will be involved in conducting basic research in new tracers (such as tracers based on antibodies or nanoparticles) to replace BPA.

This BNCT research project involves many disciplines, requiring specialized expertise in chemistry, biology, physics, and pharmacy, as well as clinical fields.

Main projects

Besides precision oncology (see Pillar 2), five axis of development are currently being prioritized:

- Cell therapies
- Immunotherapy beyond PD-1 / PDL1 immune checkpoint blockers
- Theranostics
- MR-Linac for individualized radiotherapy
- BNCT

43 CELL THERAPIES
44 IMMUNOTHERAPY BEYOND PD-1/PD-L1 IMMUNE CHECKPOINT BLOCKERS
44 RADIOTHERANOSTICS
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46 CONTRIBUTING TO ACADEMIA-LED RESEARCH WITHIN THE BIG NETWORK
47 CONTRIBUTING TO ACADEMIA-LED RESEARCH WITHIN THE ONCODISTINCT NETWORK
1. Cell therapies

**Aim**

To offer patients at IJB access to an accredited cell therapy unit that will facilitate their inclusion in innovative clinical trials of new cellular / gene immunotherapies in accordance with the new regulations:

Prior to the adoption of Regulation (EC) No 1394/2007, some of the therapeutic products now classified as advanced therapy medicinal products (ATMPs) were produced and distributed on a small scale by facilities housed within hospitals such as cell therapy units (CTUs) and tissue banks. CTUs and tissue banks are specialized laboratories providing cell or tissue engineering and the conservation, often by cryopreservation, of cells or tissues of human origin. These are infrastructures that do not have the status of a pharmaceutical establishment and that work within the framework of an establishment permit issued by the AFMPs. Initially, the CTUs distribute cell therapy preparations (CTP) that are not medicinal products, but fall under tissue/cell regulations. However, many CTUs and tissue banks, such as the one at IJB, are now engaged in processes to improve their professional practices and participate in biomedical research protocols aiming to evaluate the clinical interest of therapeutic products derived from cell or tissue engineering, formerly classified as CTP, now considered ATMPs.

**Team**

Director : P. Lewalle - CTU, 1 lab director, 1 Quality Manager, 1 administrative assistant, 5 technicians.

Director : P. Lewalle - Apheresis Unit, 1 Quality Manager, 1 administrative assistant, 4 nurses.

**Projects**

- Collaborate with the children’s hospital (HUERF) on gene therapy in haemoglobinopathies; a phase 1/2 study to evaluate the safety and efficacy of a single dose of autologous crispr-cas9 modified cd34+ human hematopoietic stem and progenitor cells (CTX001 - Vertex Pharmaceuticals) in subjects with severe sickle cell illness is ongoing.
- Open a treatment protocol with allogeneic antiviral lymphocytes after transplantation
- Collaborate closely with Celyad Oncology for clinical phase 1 protocols for autologous and allogeneic CAR T-cell treatments, both in hematology and in solid tumors. A protocol for treatment with anti-mage lymphocytes is ongoing in melanoma.
- Collaborate with the liver transplantation unit on CAR T reg to induce better tolerance after transplantation
- Generate genetically modified T-cells in a standardized and automated process in an academic setting. This on-site academic production represents a breakthrough in cell manufacturing and a leap into the next generation of processing. IJB has initiated a collaboration with Oregenes to implement the on-site production of CART-cell in CD19+ lymphoid hemopathies, and discussions are underway with Miltenyi Biotech for the same on-site approach.

**Recent achievements**

Recent protocols:

<table>
<thead>
<tr>
<th>Allo-depleted T-Lymphocytes</th>
<th>ATIR</th>
<th>Allo transplant in hematology</th>
<th>Kiadis Pharma</th>
<th>Closed</th>
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<tbody>
<tr>
<td>Allo-depleted T-Lymphocytes</td>
<td>HATCY</td>
<td>Allo transplant in hematology</td>
<td>Kiadis Pharma</td>
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<td>NKG2-D CAR-T cell</td>
<td>THINK</td>
<td>AML and solid tumors</td>
<td>Celyad</td>
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<td>Colorectal cancer</td>
<td>Celyad</td>
<td>Closed</td>
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<tr>
<td>NKG2-D CAR-T cell</td>
<td>DepleTHINK</td>
<td>AML</td>
<td>Celyad</td>
<td>Closed</td>
</tr>
<tr>
<td>Anti-BCMA Allogeneic CAR-T cells</td>
<td>IMMUNICY</td>
<td>Multiple myeloma</td>
<td>Celyad</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Antiviral T cell</td>
<td>TRACE</td>
<td>Allo transplantation</td>
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<tr>
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<td>Allo transplantation</td>
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<tr>
<td>Ag specific T cell</td>
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<td>T-Knife</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Genetically modified stem cells</td>
<td>CTX001</td>
<td>Drenpancytosis B-Thallassemia</td>
<td>Vertex Therapeutics/CRISPR</td>
<td>Ongoing</td>
</tr>
<tr>
<td>CAR-Treg</td>
<td>QEL001</td>
<td>Liver transplantation</td>
<td>Quell Therapeutics</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

**SELECTED PUBLICATIONS**

[63] [64] [65] [66] [67]
2• Immunotherapy beyond PD-1/PD-L1 immune checkpoint blockers

Aims
To develop combinations of immunotherapeutic strategies with new compounds targeting immune checkpoint receptors and other components of the immune system or with other treatment modalities such as radiation therapy in order to counteract resistance to immune checkpoint inhibitors and expand the proportion of patients who will ultimately benefit from this exciting treatment modality.

Projects
NEO-CHECKRAY is an ongoing randomized academic neoadjuvant trial that hopes to transform the immune cold luminal B breast cancer, characterized by a high risk of late relapses, into a hotter cancer that is more responsive to immune checkpoint blockade. To achieve this, radiation therapy to the primary tumor (3x8 Gy using an SBRT technique) and an anti-CD73 (oleclumab) are combined with chemotherapy and durvalumab.

ACHIEVEMENTS
- The SYNERGY trial, which tested the addition of oleclumab (anti-CD73) to carboplatin-paclitaxel and durvalumab as first line therapy for metastatic TNBC, was stopped by the IDMC after 127 patients had been randomized. The basis for the recommendation was identical clinical benefit rates of 42% that crossed the futility boundary. This trial was initiated and sponsored by IJB following the translational research discovery of the poor prognosis associated with the overexpression of CD73 in this disease. CD73 is responsible for generating immunosuppressive adenosine in the tumor microenvironment. The tumor and blood biosamples collected during the trial will soon undergo in-depth analyses in the BCTL.

SELECTED PUBLICATIONS
[68][69]

3• Radiotheranostics

“We have everything in our midst to be able to support and execute radiotheranostic research at the highest level.”

Patrick Flamen
Zéna Wimana

Team and infrastructure
The multidisciplinary team (composed of nuclear medicine specialists, medical physicists, biologists and technologists) has undergone expansion since 2020, with the arrival of new recruits, including a full time radiopharmacist for the fully GMP-compliant clinical radiopharmaceuticals production unit. The move to the new facility prompted the inauguration of the first radiotheranostic center of excellence in Belgium. This opens the door to new collaborations with academia and industry.

Aims
- To generate innovative radiotheranostics for bench-to-bedside use
- To understand the radiobiological dynamics
- To identify radioresistance biomarkers
- To offer a fully integrated solution to produce and test radiotheranostics in phase1-2 studies for third parties

Projects
- Understanding the radiobiology of peptide receptor radionuclide therapy with 177 Lu-Dotatate (completed)
- Developing an imaging biomarker for immunotherapy monitoring, namely a granzyme B specific PET-tracer (currently in preclinical testing)
- Investigating the pan-cancer radiotheranostics 68Ga/177Lu-FAPI, targeting the tumor microenvironment
- Preclinical study on anti-CEA (radio-)labelled nanobodies for hybrid imaging (fluorescent and PET) (in collaboration with VUB)

Recent achievements
- Partial qualification of the GMP radiopharmacy lab
- 177Lu-PSMA for therapy of prostate cancer
- Installation of the first equipment in the Preclinical Imaging and Radiation Therapy unit (PIRaTh) (see Pillar 1, page 18)
4• MR-Linac for individualized radiotherapy

**Aim**
To use high-precision MRI-guided radiotherapy to tailor treatment to individual tumor characteristics and anatomical variations during treatment, with the hope to improve patient outcome.

**Projects**
- Daily functional imaging to adapt radiotherapy treatment: we aim to use daily MRI imaging to localize the target and organs at risk more precisely and reduce the population-based safety margins. In addition, study of interfraction and intrafraction motion may allow population-based margins to be replaced by personalized ones.
- Participate in the International MR-Linac consortium’s “Momentum study”, together with 10 other cancer centers in the USA and in Europe: this observational study will collect all the data of treated patients into a single platform, with the possibility for consortium members to access the data for approved research projects.
- Explore the role of daily functional MRI as a tool to identify patients with rectal cancer who will benefit from presurgical radiotherapy dose-escalation.

**SELECTED PUBLICATIONS**
[60] [62] [70]

5• BNCT

**Aim**
To offer to selected patients this biologically targeted form of cancer radiation therapy designed to target cancer tissues specifically while minimizing damage to healthy tissues (following injection of boronophenylanine – BPA – which contains boron-10, the target area is exposed to thermal neutrons that are absorbed by boron-10; the neutron capture reaction leads to the emission of high-energy charged particles).

**Projects**
- Launch a search for new tracers to replace BPA (such as nanoparticles)
- Irradiate highly infiltrating tumors (e.g., brain or pancreas)
- Re-irradiate a recurrence in a previously irradiated field (e.g., head and neck tumors)
- Combine BNCT with immunotherapy (as the high-energy charged particles emitted can cause clustered DNA damage effects that can be immunogenic)

**Recent achievements**
A letter of intent has been signed between HUB and Neutron Therapeutics.
Contributing to Academia-led research within the BIG and ONCODISTINCT networks

1. Contributing to Academia-led research within the BIG network

Many IJB staff are founders and/or committee members of collaborative groups/networks such as BIG, EORTC, IBCSG, OncoDistinct, actively promoting and empowering collaborative academic research internationally.

BIG network

“Our goal is to facilitate breast cancer research at international level by stimulating cooperation between its members and other academic networks, and collaborating with but working independently from the pharmaceutical industry.”

Team and infrastructure

Today the Breast International Group (BIG) is composed of almost 60 academic research groups from around the world. Its headquarters, comprising about 45 staff members, report to a board of directors and general assembly of members.

The headquarters staff works closely with BIG’s member groups to develop, support and run clinical trials and research programs. Many of its pivotal (adjuvant) trials are conducted in co-partnership with IJB’s CTSU, which has acquired unique expertise in managing international registration trials over the last two decades.

Aims

- Today the Breast International Group (BIG) is composed of almost 60 academic research groups from around the world. Its headquarters, comprising about 45 staff members, report to a board of directors and general assembly of members.
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Main projects (in collaboration with the Clinical Trials Support Unit)

- Coordinating the first worldwide, large adjuvant trial to explore adding a PD-L1 inhibitor to chemotherapy in triple negative breast cancer (ALEXANDRA / IMpassion 030 trial)
- Setting up an international, academic BIG trial exploring chemotherapy de-escalation in selected patients with HER2-positive hormone receptor negative early breast cancer (DECRESCENDO). Decrescendo is sponsored by IJB and managed by its CTSU.
- Conducting AURORA, an ambitious translational research program aimed at understanding the clonal evolution of metastatic breast cancer in over 1000 women from across 12 European countries; the study compares molecular data from primary and metastatic biopsies, collects plasma for ctDNA analysis at 6-monthly intervals and at each disease progression, and follows patients for up to 10 years

Recent achievements of the BIG network involving IJB include the following:

- Launched the IJB-sponsored DECRESCEndo trial prospectively testing the hypothesis that CT can be safely de-escalated from an anthracycline + taxane backbone to a taxane-only regimen in women with HER2+, hormone receptor negative breast cancer who achieve a pathological complete response after 3 months of a taxane combined with subcutaneous trastuzumab + pertuzumab (PHESGO). This single arm de-escalation trial aims to achieve excellent 3-year IDFS rate in responding patients, while women with residual disease at surgery receive the “salvage” regimen with T-DM1.
- Analyzed and published the first results of the AURORA molecular screening program conducted in patients with metastatic breast cancer, with leadership from IJB.
Through the genomic and transcriptomic analyses of matched primary and metastatic samples from the first 381 enrolled patients, the AURORA program identified genomic alterations involved in metastases and new candidate biomarkers. Of interest is the detection of ESCAT tier I/II alterations in 51% of the patients.

Another important BIG achievement in 2021, with a more modest contribution of IJB, was the publication of the first results of the OlympiA trial.

A total of 1836 patents with HER2-negative BC with BRCA1-2 germline pathogenic variants and high risk clinical-pathological factors were randomized to receive 1 year of olaparib or placebo following (neo)adjuvant chemotherapy. Olaparib was shown to improve IDFS (HR 0.58 p<0.001) with an 8.8 percent absolute benefit at 3 years; more recently an OS improvement was also demonstrated (HR 0.68; 3.4% absolute benefit), leading to changes in clinical practice.

SELECTED PUBLICATIONS
[4][71][72][73]

2• Contributing to Academia-led research within the ONCODISTINCT network

“Our goal is to accelerate oncology drug development in the era of molecular oncology with closer attention paid to patients’ essential needs”

Nuria Kotecki, Ahmad Awada

Team and infrastructure

Twenty-eight cancer hospitals or departments across 8 countries have signed the ONCODISTINCT consortium agreement. They include academic and non-academic centers with expertise in early or late-phase clinical trials, sharing a common enthusiasm for innovation in clinical trial methodology in the era of molecular oncology.

The network functions with a steering committee and rotating data centers coordinated by IJB, and benefits from the input of a patient advisory panel.

Aims

- To address unmet medical needs such as brain metastases, rare tumors, oligometastases, and inflammatory breast cancer
- To conduct proof-of-concept studies with innovative designs, as well as biomarker driven trials
- To accelerate the conduct of phase I-II-III trials alongside new collaboration models with pharmaceutical and biotechnology companies
- To develop new models of clinical research organization such as the “spiderweb” model: this consists in setting up a permanent collaboration in form of a master agreement between all participating centers, which enables patients from a given site to be treated at this site in any biomarker-driven clinical trial opened in another center, regardless of the center location and country borders.
Main projects

Four clinical trials are up and running, of which 3 are managed by the CTSU:

- **PELICAN**, testing the addition of immune checkpoint inhibitors to cytotoxic chemotherapy in inflammatory breast cancer (Oncodistinct 003)
- **REGINA**, testing the combination of neoadjuvant regorafenib in combination with nivolumab and short-course radiotherapy in intermediate-risk stage II/III rectal cancer (Oncodistinct 009)
- **BRAINSTORM**, aiming to constitute a brain metastases research platform to tackle the challenge of CNS metastases in solid tumors, including an analysis of ctDNA in the CSF of patients with CNS metastases (Oncodistinct 006)
- **CHANCES**, (first-in-human) evaluating an anti CD43 IDH5301 alone or in combination with chemotherapy and trastuzumab (Oncodistinct 011)

Recent achievements

- Performed the first translational analyses in the BRAINSTORM program, including the sequencing of ctDNA from the CSF of patients with CNS metastasis from solid tumors
- Presented interesting results of the neo-adjuvant AURA trial that investigates an immune checkpoint inhibitor – avelumab – with or without chemotherapy in patients with CT2 na No-2 Mo bladder cancer. For the 56 “cisplatin-eligible” patients a very good pathological complete response (PCR) rate of around 50% was documented when avelumab is combined with either cisplatin + gemcitabine or MVAC; for the 56 “cisplatin ineligible” patients a PCR rate of 36% was obtained with avelumab alone, while a PCR of 18% was seen for the combination of avelumab with paclitaxel and gemcitabine.
- Launched a first-in-human study of the anti CD43 IDH5301 alone or in combination with chemotherapy and trastuzumab, coordinated by Institut Paoli Calmettes (Marseille)

SELECTED PUBLICATIONS

[74]
PILLAR IV • Developing New Approaches to Patient Empowerment and Well-being

IJB has worked for many years to accompany patients for the duration of their cancer journey. This patient-centered approach, as it is implemented in care, is embedded in the way our researchers design and lead research.

IJB has reinforced its international reputation through pivotal clinical trials studying the management of febrile neutropenia, establishing the Multinational Association of Supportive Care in Cancer (MASCC), and being among the first to set up an intensive care unit (ICU) fully dedicated to cancer patients. At a national level it has played an important role in supporting Belgian legislation on euthanasia. And, today, IJB recognizes that research is not only a matter of researchers. In various initiatives, researchers are involving patient-partners, patient-experts, artists, and others to explore new ways of caring for patients, as well as respecting and valuing the work of healthcare professionals.

This pillar comprises 6 domains:

- Research on oncological complications, including infectious diseases and intensive care
- Psycho-oncology and supportive care research
- Geronto-oncological research
- Nursing research
- Survivorship clinic
- Patient involvement and empowerment
Research in oncological complications

“Our goal is to minimize the cancer patient’s risk of death as a result of anticancer treatment complications.”

Team and infrastructure

- 5 emergency rooms dedicated to oncological emergencies
- 8 beds dedicated to short hospitalization for the management of acute complications
- Infectious disease team comprising 3 full time physicians, 1 research nurse, and 1 administrative assistant.

Aims

- To provide state-of-the-art treatment of febrile neutropenia, sepsis, acute respiratory failure, tumor lysis syndrome, and severe complications of targeted therapies and immune therapies, as well as to continuously re-assess the rates of success and failure in managing these complications
- To benchmark clinical outcomes of IJB cancer patients experiencing severe complications with the ones of other European cancer centers and departments
- To participate in international clinical trials testing new intensive care approaches or new antimicrobial, antiviral, and antifungal agents

Main projects

For the ICU Team

- COHESIS study assessing collaboration between intensivists and hematologists in the ICU

For the Infectious Disease Team

- Fever of unknown origin in cancer patients (a unicentric study)

Recent achievements

- Published a conference consensus statement on oncohaematological resuscitation
- Used the PARIS score to evaluate the probability of SARS-CoV2 infection in cancer patients
- Participated in RETRO-TARGETICU, a multicentric study assessing when targeted therapy for cancer leads to ICU admission
- Studied the outcomes of ICU patients with and without perceptions of excessive care: a comparison between cancer and non-cancer patients

SELECTED PUBLICATIONS

[75] [76] [77] [78] [79]
Psycho-oncology and supportive care research

“Our goal is to preserve, restore or enhance the quality of life of cancer patients all along their journey (from diagnosis to end of life). In parallel we aim to enhance the communication skills of IJB healthcare professionals, hoping to improve patient wellbeing and satisfaction.”

Team and infrastructure

The team is composed of 1 psychiatrist, 2 postgraduate psychiatrists and 11 psychologists fully dedicated to cancer patients and their relatives, and to the physicians and nurses caring for them.

The Acute Supportive Care Unit comprises 2 physicians, and 15 nurses responsible for 8 beds.

Aims

- To develop psychological interventions supported by written manuals and to assess their efficacy on cancer patients and their relatives at different stages of the disease, using rigorous methodologies (such as randomization between early versus late intervention)
- To develop communication skills training programs for cancer physicians to avoid burnout and to improve their wellbeing, and consequently improve patients’ satisfaction with their medical care and compliance with their physicians’ advice
- To develop studies that improve understanding of the difficulties encountered by patients throughout the course of the disease (such as cognitive fatigue, anticipated care planning)
- To develop supportive care interventions allowing better control of pain, mucositis, skin toxicities, and sleep disturbances

Main projects

Several new projects have been launched:

- Re-Boost: A randomized controlled trial of an intensive, ecologically-boosted group intervention focused on emotion regulation for cancer patients in the early survivorship period
- e-Motion: A randomized study assessing the efficacy of an intensive, ecologically-boosted group intervention to promote emotion regulation in patients with metastatic cancer
- Efficacy of a parenting-support intervention to improve communication between patients with advanced cancer and their adolescents
- Cognitive fatigue and its associated factors in women with breast cancer
- Cross-sectional, observational study of patients with advanced cancer and their primary caregivers’ willingness to communicate about advanced care planning

Processes of code status transitions in hospitalized patients with advanced cancer cared for by a supportive care unit
- Satisfaction with supportive care among patients with advanced cancer: a longitudinal prospective study based on an innovative method combining multiple perspectives

Recent achievements

- Developed and assessed the efficacy of a communication skills training program addressing uncertainty and hope
- Improved emotion regulation in breast cancer patients in the early survivorship period: developed and assessed the efficacy of a brief, ecologically-boosted group intervention, with a first paper under review
- Developed and assessed the efficacy of a support intervention designed to improve parents’ communication with their children dealing with parental cancer: a randomized pilot trial
- Assessed psychological factors associated with clinical fear of cancer recurrence in breast cancer patients in the early survivorship period
Geronto-Oncologic Research

Our goal is to offer the best possible cancer care to older patients, taking into account their degree of frailty and their comorbidities.

Team and infrastructure

Five leading physicians (2 geriatricians, 1 medical oncologist and 2 haemato-oncologists), and 1 fully dedicated nurse supported by members of the psycho-oncology team (including a neuro-psychologist) constitute this group.

Aims

- To avoid overtreatment and undertreatment of the geriatric cancer population with the use of validated tools.
- To develop new tools or refine existing ones in order to improve prognostic estimations, with a particular focus on the role of neurocognition.
- To design or join clinical trials exploring alternative treatment regimens to chemotherapy or “softer” chemotherapy regimes.
- To participate in real-world evidence, phase IV initiatives focussing on the elderly cancer population.

Main projects

- Comprehensive geriatric assessment (CGA) and prediction of postoperative complications and unplanned hospitalizations in older patients with cancer.
- New screening tool for frailty and cognitive impairment in older patients with cancer.
- Evaluation of HRQoL in clinical trials with older patients with advanced breast cancer.
- COVID-19 in older patients with hematological malignancies.

Recent achievements

- EORTC 1745: A Phase II study of Adjuvant PALbocilib as an Alternative to CHemotherapy in Elderly patientS with high-risk ER+/HER2- early breast cancer (APPALACHES).
- RibOB trial: A phase IV study to collect data on the efficacy and safety of ribociclib in combination with letrozole in older women (>=70 years) with hormone receptor-positive (HR+)HER2-negative (HER2-) advanced breast cancer with no prior systemic therapy for advanced disease.
- Fonds Yvonne Boel supported project: « Facteurs neuropsychologiques et biologiques avec impact sur l’adhérence au traitement et la survie des patients âgés porteurs d’une hémopathie maligne : Mise en place d’un score prédictif » in collaboration with the University of Rennes (Dominique Bron & Yves Libert).

SELECTED PUBLICATIONS

[85] [86] [87] [88] [89]
Nursing Research

“Our goal is to improve patients’ outcome, quality of life, and adherence to treatment through evidence-based symptom management and early recognition of potentially severe complications.”

Team and infrastructure

Each care unit at IJB delegates 1 nurse specifically interested in nursing research to the Nursing Research Unit.

Aims

- Improve nursing practices by implementing well-established processes:
  - Identify “Nursing Sensitive Patient Outcomes” (e.g., catheter-related infections)
  - Search for evidence-based guidelines/data describing how to best manage the problem
  - Implement these guidelines in the care units
  - Evaluate the impact of this change in nursing care on patient outcome

Main projects

- Identification of risk factors associated with falling among elderly patients and implementation of evidence-based preventive measures
- Systemic assessment of opioid-induced constipation and early implementation of adequate measures
- Early recognition of signs of neutropenic sepsis and rapid nursing intervention to enable documentation and antibiotic start within one hour
- Study of the feasibility of implementing state of the art palliative care interventions in a general oncology ward

Recent achievements

- Produced an inventory of evidence-based nursing assessment and management of side effects in oncology
- Implemented hypnosis for symptoms according to evidence from the literature and started planning a prospective study
- Implemented systematic assessment for peripheral neuropathy in high-risk patients in the ambulatory anticancer treatment setting (day-clinic)
- Explored reasons for emergency and re-admission of patients and alternative ways to manage these (ongoing)
- Reviewed effective preventive measures for central catheter-related infections

SELECTED PUBLICATIONS

[90]

Patrick Crombez
Survivorship Clinic

“ Our goal is to accelerate recovery from the side effects of therapies given with ‘curative intent’, so that patients can return to a ‘normal life’ and regain autonomy.”

Team and infrastructure

One medical oncologist, Laura Polastro, assisted by a nurse are launching this new program called RESTART.

Aims

- To identify breast cancer patients’ specific needs in the 3 months following completion of primary therapy given with a curative intent (e.g., surgery +/- radiotherapy +/- chemotherapy +/- endocrine therapy)
- To develop a physical rehabilitation program with the help of kinesiotherapists
- To organize educational workshops for “eligible” patients that will allow them to actively participate to their recovery
- Once the program is successfully running, to start addressing research questions related to the potential impact of such patient-centered activities on clinical outcome

Recent achievements

- The RESTART survivorship program has been up and running for breast cancer patients since early 2022.
- A pilot trial, “PRINTEMPS,” was launched for young cancer patients (< 40 years), who suffer from intense fatigue after treatment. The study offers multidisciplinary care with coaching, psychological interventions, and physical activity. A first goal is to determine its feasibility.
Patient Involvement and Empowerment

“Our goals are to involve patients in order to increase the quality of our research and make projects more patient-centric while reducing inequalities in cancer care in a multicultural society.”

Team and infrastructure

The team includes 1 coordinator (PhD) in research promotion and patient partnerships, 1 anthropologist, 1 patient-expert, 1 artist, and a group of patient-partners.

Aims

- To improve clinical and translational research by promoting patient involvement in studies through collaborations and co-creation of projects.
- To pursue the training of patient-partners, integrate patient-experts, and open the hospital to other professionals and skills (artists, coaches, sociologists...).
- To guarantee optimal cancer care to migrants and ethnic minorities, including participation in clinical trials.
- To train health care professionals on migrants’ health and cultural issues.

Main projects

- Conduct research on patient involvement: coordination of the OECI Collaboration for Good Practices with Patients (CGPP) working group, which develops methodologies to launch, support, and evaluate patient involvement initiatives in European cancer centers, and co-chairing the BBMRI.be Stakeholder Involvement group.
- Communicate about clinical research: develop tools and media solutions to engage patients in research.
- Identify risk factors for non-adherence to cancer therapy in migrants with hematological malignancies.
- Compare incidence and mortality rates according to migration patterns in patients with hematological malignancies.
- Conduct a retrospective study assessing imatinib-use patterns across patients treated for a Chronic Myeloid Leukemia (CML) in Belgium between 2004 and 2018.
- Develop a strategic plan to provide linguistically and culturally competent cancer care.

Recent achievements

- B.CaRe project: The team initiated a collaboration with ESP-ULB researchers, patient advocates (Association Travail et Cancer), and 1st-line healthcare professionals (Maison médicale Le Noyer) through a multidisciplinary, co-creation research project focusing on the resilience of the cancer community. Facing the health system crisis, the project explores various paths of investigation to “re-humanize” oncology care pathways and to improve the resilience of the cancer care model and the quality of life of all cancer stakeholders (caregivers, patients, and families).
- MADESIO mixed method study: Intermediate analysis of responses to quantitative study on adherence to oral anticancer medication (OAM) in patients with hematological malignancies (32 migrants and 34 non-migrants).
- OBSIMA: Gathering a cohort of 1236 patients from the Belgian Cancer Registry (BCR) for medical-administrative data linkage and evaluation of demographic characteristics, comorbidities, and patterns of imatinib use.
- BEIS platform: In collaboration with specialized nurses in cosmetic care and well-being, development of a platform to experiment and innovate in well-being and self-image.
- “PISARO”, the patient advisory group in research, celebrating its 3rd anniversary, 15 meetings between trained patient-partners and researchers, 10 full evaluations of research projects, 5 trainings in clinical research for patient-partners, and 4 communications.

SELECTED PUBLICATIONS

[91]
Organization of research

Since its creation, Institut Jules Bordet has always been a major actor in clinical and translational research. Over several decades, a few departments, very active in their respective fields, developed extensive expertise and specific skills in research activities, spanning from the design of ambitious scientific projects to proficiency in operational management.

With the number of clinical trials and research projects increasing significantly throughout Institut Jules Bordet, and having identified the need for professional support in their set-up and conduct, in 2016 Institut Jules Bordet officially established a new centralized research infrastructure by reorganizing its existing structures.

The purpose of this organization, active for over six years, is to stimulate scientific creativity through efficient medical and scientific support to researchers on the one hand and, on the other hand, to provide professional support to clinical research by centralizing and harmonizing the administrative, operational, contractual, and financial management.

Governance

Successful research projects require strong collaboration between medical, scientific, and operational teams. Institut Jules Bordet organizes and conducts research by gathering scientific, medical, and operational skills and expertise from all departments.

Research activities are organized through two main structures working in close collaboration:

- A medical and scientific team, responsible for the development of new research projects and clinical trials, the enrollment and follow-up of patients, data collection and analysis, and the publication of the results in collaboration with the statistical team.
- An operational team supporting the set-up and conduct of the research projects and clinical trials, in compliance with all legal and regulatory obligations and ensuring administrative and financial follow-up.

Laurence Buisseret, Marielle Sautois, Julie Gaye, Martine Piccart
Institut Jules Bordet participates in many clinical trials with external sponsors, both from the pharmaceutical industry and academia, but also runs its own academic trials, many of them being international interventional trials with investigational medicinal products.

With its dedicated structures, Institut Jules Bordet can efficiently carry out the responsibilities of a clinical trial sponsor.

Working in close collaboration with the above, specific decision-making bodies ensure the good governance of research activities:
Institut Jules Bordet Research Board

The Institut Jules Bordet Research Board is composed of the Scientific Director, the General Medical Director, the General Director, the Director of Research Administration, the Heads of the Medical and Research departments, the IT Director, and the Information Management Unit Director. This board carries out the following missions at the institutional level:

- Defines research strategy and budget
- Analyzes research activity reporting and processes.

Research Executive Board

The Research Executive Board is composed of individuals specialized in the operational aspects of research activities and meets on a very regular basis. This board manages global research operations and resources:

- At the site level: external sponsorship (pharma or academic)
- At the sponsor level: Institut Jules Bordet sponsorship (academic) or service provider.

Project Review Committees

Beyond these strategic and operational boards, which aim to optimize, stimulate, and streamline the procedures related to the assessment and set-up of research projects, some specific committees are in place:

- **Protocol Review Committees (PRC)**

  These committees aim to assess in an efficient and timely manner the clinical trial proposals coming from Institut Jules Bordet’s medical departments and that involve external sponsors.

- **Committee for Clinical Research Optimization**

  This committee aims to assess and provide strong scientific support to the research projects proposed by Institut Jules Bordet’s study chairs. These projects, sponsored in-house, can be retrospective (Retrospective Projects Committee) or prospective (Clinical Projects Committee) and may include human biological material.

- **Tumor Board**

  Biobanking activities are regulated by the Tumor Board, a scientific advisory committee. The Tumor Board takes decisions about the facilities, equipment, implementation of guidelines on best practices and, above all, the distribution and sharing of samples and data. The Board is a multidisciplinary team, including pathologists, biostatisticians, researchers, and clinicians, and faces a crucial ethical challenge: improving and maintaining the trust of patients, clinicians, researchers and industry, and across academic medical networks.

- **Ethics Committee**

  Institut Jules Bordet’s Ethics Committee is an independent body whose role includes:

  - Prior to implementation, giving an opinion on all research projects for experimentation on humans, including interventional trials but also observational studies and retrospective research projects
  - Monitoring and advising on ethical aspects of hospital care practices
  - Assisting in decision-making on ethical aspects of individual cases
Research Support Units

Research Administration Unit
The Research Administration Unit is a centralized unit set up to manage research. Its principal missions related to research projects are the following:

- Budgetary evaluation and financial monitoring of research conducted at Institut Jules Bordet
- Legal and contractual management
- Coordination of human and operational resources.

Clinical Trials Support Unit
The Clinical Trials Support Unit (CTSU) assists researchers from academia and industry in the development and conduct of phase I, II, and III clinical trials:

- In early disease (neoadjuvant, adjuvant) and advanced disease (locally, metastatic)
- For all cancer types
- For all treatment and diagnostic modalities.

The CTSU can manage a clinical study from A to Z or can collaborate with partners on specific activities. CTSU activities include:

- **CLINICAL STUDY MANAGEMENT:** Operational coordination, communication
- **CONTRACT MANAGEMENT:** Legal expertise, financial management
- **REGULATORY AFFAIRS:** EU submissions, regulatory compliance
- **PHARMACOVIGILANCE:** Safety reporting, adverse events oversight
- **SITE MONITORING:** Site initiation visits, on- and off-site visits
- **DATA MANAGEMENT:** eCRF design, data quality control
- **CENTRAL IMAGING:** eCRF design, data quality control
- **BIOSAMPLES MANAGEMENT:** Standardization, sample collection & analysis
- **INFORMATION TECHNOLOGY:** Development and maintenance of software, users support
  Statistics clinical study design and methodology, analysis plan, data analysis, publication

CTSU in numbers (30/06/2022)
Number of trials operationally managed by the CTSU 28 trials sponsored by Institut Jules Bordet. 9 as a service provider for academic or pharmaceutical partners.
Cancer types and settings of the trials managed by the CTSU

Information Management Unit

The Information Management Unit provides support to the clinical departments and the Institute as a whole.

This unit carries out the following missions:

- An epidemiological mission, by developing, managing and operating the hospital cancer registry as well as the clinical data related multidisciplinary oncological consultations. In doing so, it contributes actively to the Belgian Cancer Registry and makes the hospital’s cancer registry available as a research support and care quality evaluation tool. Because it includes all incident tumors since 1 January 2000, now encompassing more than 45,000 records, it is regularly used to plan studies as well as to conduct retrospective research by identifying patients and providing a core dataset to the investigators. It is presently limited to data about the primary tumor episode, but the process of extending it to collect data on relapses for breast cancer or for rare tumors is ongoing. For breast cancer tumor incidents between 1 January 2000 and 31 December 2010, the whole history of the disease including description of all relapses (local, regional, distant) and subsequent treatments is available.

- An analysis and reporting mission related to the Institute’s activities, in particular by developing and maintaining a data warehouse (partially shared with the finances department).

- An oncological clinical research mission in terms of methodology and statistics (single-center and multicenter research, centralized at the Institut Jules Bordet and elsewhere, including contribution to clinical projects and meta-analyses). This mission involves collaboration with the CTSU and participation in the various Project Review Committees, for internal as well as external collaborations.

Projects include:

- Identifying and documenting all data sets collected for each clinical project sponsored by the Institute, including retrospective projects, and to make them available to the wider community of researchers

- Achieving early identification of new patients with rare tumors in order to help clinicians improve the therapeutic management of these cases and developing a specific registry for rare tumors, facilitating research with these patients

- Linking the cancer registry with other data sources. The goal for this last project is to be able to link a medical treatment or a medical investigation to a record in the cancer registry.

Academic Trials Promoting Team

The Academic Trials Promoting Team (ATPT) promotes and initiates new academic studies sponsored by Institut Jules Bordet.
The physicians comprising the ATPT design new clinical studies, supported by the extensive experience of the Institut Jules Bordet’s statisticians for the methodology, statistical considerations, and conduct of their projects. The ATPT and statisticians work closely with the CTSU throughout the study conduct.

**Tumor Bank and Pathology Department Expertise**

The Tumor Bank provides cancer researchers with a diverse selection of high-quality biospecimens and derivatives, comprehensively annotated with clinical data; these materials are used to identify diagnostic molecular markers, prognostic indicators, and therapeutic targets.

Samples and clinical data supplied by the Tumor Bank are handled in accordance with the highest ethical standards and in strictest compliance with all applicable rules and regulations.

Tumor and adjacent normal tissues from donors are available in snap frozen or formalin fixed paraffin embedded formats. More recently matched biofluid sets have been added to tissue collections. More than 25,000 tissue samples and whole blood fractions are available, provided by more than 11,000 patients.

The Tumor Bank is completely integrated into the Pathology Department, enabling full and accurate analysis of tumors by pathologists prior to sample preservation and delivery. It also forms an integral part of the Belgian Virtual Tumorbank (BVT) of the Belgian Cancer Registry, and of two European biobanks: the BBMRI – ERIC and ESBB (European, Middle Eastern & African Society for Biopreservation and Biobanking).

A robust system for sample quality control exists and enables numerous research projects to be supported every year. The Tumor Bank has been ISO 9001 certified since 2012 and is actively working to implement the ISO 20387 biobanking accreditation program. The quality of the tumor samples is very satisfactory and adapted to a large panel of next-generation technologies.

The Pathology Department is a key partner in all of Institut Jules Bordet’s translational research projects. Since 2009, it has invested time and energy to obtain full BELAC accreditation (ISO 15189) and remains deeply involved in the quality testing of all clinically relevant biomarkers (e.g., PD-L1, CD73, NTRK and many others). It is also responsible for Institut Jules Bordet’s NGS platform, an essential tool for tumor molecular characterization and precision medicine.

The Tumor Bank and Pathology Department partnership offers to the research community digital pathology expertise (2 Hamamatsu scanners), including artificial intelligence projects (Visiopharm) and tissue laser microdissection techniques (Zeiss).

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Collaborations

National and international collaborations

National collaborations

- ALWB
- AFMV
- AZ Groeninge Kortrijk
- AZ Sint Marteen
- AZ Turnhout
- BAPCOC
- BBMRI
- Belgian Cancer Registry (BCR)
- BioCINBIOS
- BSMO
- Centre Hospitalier Universitaire Ambroise Paré
- CHR Verviers
- CHU Erasme
- CHU Sart Tilman
- Cliniques de l’Europe
- Cliniques Universitaires St Luc
- D-CAF MecaTech
- ELCWP (European Lung Cancer Working Party)
- EORTC
- ESICM (European Society Intensive Care Medicine)
- GIGA-Cancer, Metastasis Research Laboratory
- Grrr-OH (Groupe de recherche en Réanimation Respiratoire en Onco-Hématologie)
- GZA Hospitals Sint-Augustinus
- IBA (Louvain-La-Neuve)
- IRIBHM
- iTeos Therapeutics
- KU Leuven
- Nine-i multinational network (Caring for critically ill immunocompromized patients)
- Siensano
- UCL
- UCL – MIRO Laboratory (Louvain-La-Neuve)
- UNamur – Laboratory URBC
- University of Antwerp
- University of Ghent
- University of Liège
- University of Mons
- UZ Brussel
- VUB

European Collaborations

- Austria
  - Vienna (MedAustron Centre)
- Finland
  - Helsinki (Helsinki General Hospital)
- France
  - Paris (Institut Imagine, Institut Pasteur, Institut Gustave Roussy, Institut Curie)
  - Rennes (Université de Rennes, CHU)
  - Strasbourg (University of Strasbourg)
  - Dijon (Center Georges Francois Leclerc)
  - Brest (Université de Bretagne Occidentale)
- Germany
  - Hamburg (University of Hamburg)
  - Regensburg (Universität Regensburg)
- Greece (University of Crete)
- Italy
  - Cagliari (University Hospital in Sardinia)
- Latvia
  - Riga (Latvian Biomedical Research and Study Centre)
- Luxembourg (TIME, LIH)
- Netherlands:
  - Amsterdam (NKI)
  - Eindhoven (Philips)
  - Rotterdam (Erasmus MC)
  - Maastricht (Maastricht University)
- Slovenia
  - Ljubjana (Cosylab)
- Spain
  - Barcelona (Vall d’Hebron Institute of Oncology)
  - Murcia (University of Murcia)
  - Josep Carreras Leukaemia Research Institute (IJC), Barcelona, Catalonia, Spain
- Switzerland (SIB, ISREC, SIOG)
- Sweden
  - Stockholm (Karolinska Institute and University Hospital)
- ERS (European Respiratory Society)
- SRLF (Société de reanimation de langue française)
- EHA SWG (European Hematology Association)
- Eurobloodnet
Collaborations outside Europe

- **Canada**
  - Montreal (Lady Davis Institute, Jewish General Hospital, McGill University)
  - Saskatoon (USASK)

- **China**
  - Wuhan (College of Chemistry and Molecular Sciences, Wuhan University)
  - Beijing (Chinese PLA General Hospital)

- **Israel** (The Weizmann Institute of Science)

- **Japan**
  - Kumamoto (University of Kumamoto)
  - Tokyo (University of Tokyo)

- **United Kingdom**
  - London (Guy’s Hospital)
  - London (Institute of Cancer Research)
  - Cambridge (Wellcome Trust Sanger Institute)
  - Oxford (Institute of Molecular Medicine, University of Oxford)

- **USA (NCI, NIH)**
  - Baltimore (National Institute on Aging)
  - Boston (Harvard Medical School and Broad Institute of MIT and Harvard, Neutron Therapeutics)
  - Massachusetts (MIT)
  - New York (Albert Einstein College of Medicine, Montefiore Medical Center)
  - Texas (MD Anderson Cancer Center)
  - Washington (McDonnell Genome Institute)
  - Yale (Yale University)
  - Cincinnati (Rieveschl Laboratories for Mass Spectrometry, Department of Chemistry, University of Cincinnati, OH)

- **CARG (Cancer Aging Research Group)**
WHO IS PART OF BIG?

57 academic research groups

It is the largest international network of collaborative academic research groups dedicated to breast cancer research.

Covering ± 70 countries on 6 continents

Running large multinational trials, such as HERA, (Neo)ALTTO, MINDACT, APHINITY, OLYMPIA, PALLAS, ALEXANDRA/Impassion 030 among others.

WHO IS PART OF ONCODISTINCT?

26 sites in 10 countries
Funding

Association Jules Bordet

For more than 50 years, cancer research at Institut Jules Bordet has been inseparable from the Jules Bordet Association (formerly “Les Amis de l’Institut Bordet”). As the Institute’s first private donor, the Association has raised more than 100 million euros in the past half a century, allowing the Institute to achieve an incalculable number of Belgian, European, and even world firsts in the research and treatment of cancer.

By concentrating its activity exclusively on the Institute, Belgium’s sole integrated cancer center, the Association is situated at the heart of the fight against cancer. This strategy allows the Association to identify the Institute’s needs and to follow the results of its contributions as closely as possible.

True to its mission, the Jules Bordet Association has already provided 18 million euros to support research activities in the New Bordet, including nearly 15.5 million euros to acquire state-of-the-art research equipment.

And because the Institute is entering a new chapter in its history, the Association has decided to set up a scientific committee to meet the expectations of this new environment. Composed of scientists internationally recognized for their expertise in oncology, this committee should enable the Association to help develop major breakthrough projects that will make a difference in the fight against cancer.

Jules Bordet Association Scientific Committee: Prof. Wolf Hervé Fridman (President), Prof. Yvan de Launoit (Vice-President); Prof. Eric Deutsch, Prof. Eric Gilson, Prof. Samra Turajlic, Prof. Niels Halama, Prof. Alberto Mantovani, Prof. Daniela Thommen, Prof. Elisabete Weiderpass.
Research Grants

From 2020 to 2021, Institut Jules Bordet researchers have been awarded highly prestigious research grants provided by the organizations listed below.

Funders Name
- Association Jules Bordet
- Breast Cancer Research Foundation
- Belgian Society of Medical Oncology
- European Society of Medical Oncology
- Fonds de la Recherche Scientifique-FNRS
- Fondation ARC pour la Recherche sur le Cancer
- Fondation Cancer Luxembourg
- Fondation Contre le Cancer
- Fondation Roi Baudouin
- Fonds Ariane
- Fonds Barsy-Laffut
- Fonds Yvonne Boël
- Fonds Gaston Ithier
- Fondation Kisane
- Fondation Lambeau-Marteaux
- Innoviris
- Het Antikankerfonds
- Octobre Rose
- Plan National Cancer
- Télévie (FNRS)
- WALInnov

Visiting Research Fellows (2020-2022)

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>NAME</th>
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<tr>
<td>Algeria</td>
<td>Karim Gourari</td>
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<tr>
<td>Belgium</td>
<td>Imane Bachir</td>
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<td>Sebastien Pennickx</td>
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<td>Christelle Bouchart</td>
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<td>Madaline Michel</td>
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<td>Tycho de Bakker</td>
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<td>Belgium</td>
<td>Thomas Descamps</td>
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<td>Brazil</td>
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<td>Florence Perrault</td>
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<td>Yan Jia</td>
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<td>Alessandro Audision</td>
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<td>Rachele Danieli</td>
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<td>Roberto Casale</td>
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<td>Irene Assaf</td>
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<td>Antoine El Asmar</td>
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<td>Mexico</td>
<td>Grace Gattas</td>
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<tr>
<td>Nigeria</td>
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<td>Portugal</td>
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<td>Sule Mine Ozturk</td>
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<tr>
<td>USA</td>
<td>Edgar Cardenas</td>
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<tr>
<td>Yemen</td>
<td>Ahmed Shagera Qaid</td>
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Awards

2020

- Anaïs Boisson, honorable mention in the 2020 Akoya LinkedIn Usergroup image competition
- Mattia Rediti - ASCO 2020: “2020 ASCO Annual Meeting Merit Award”
- Soizic Garaud, winner of the 2020 Akoya LinkedIn Usergroup image competition
- Stamatopoulos Basile - Prix Bekales: “The light chain IgV3-21 defines a new poor pronostic subgroup in chronic lymphocytic leukemia”
- Christelle Bouchart - Belgian Week of Gastroenterology (BWG) : Prix de la meilleure présentation orale (BGDO)
- Laurence Buisseret - Fondation contre le Cancer : Mandats en Recherche Translationnelle et Clinique

2021

- Bouland Cyril – Prix du Spécialiste de l’année
- Marcela Carausu - ESMO Research Fellowship: “Interrogating triple-negative breast cancer heterogeneity and its microenvironment at the single-cell level”
- Noémie Thomas, Award recipient of the EACR-Akoya Spatial Phenotyping Award
- Francesco Sclafani - Fondation contre le Cancer : Mandats en Recherche Translationnelle et Clinique
- Christelle Bouchart - Belgian Week of Gastroenterology (BWG) : Prix de la meilleure présentation orale (Working Group of Digestive Pathology)

2022

- Martine Piccart – AACR Annual Meeting 2022 – Victoria’s Secret Global Fund for Women’s Cancers 2022 Meritorious Awards, in Partnership with Pelotonia and AACR
- Laetitia Collet - ESMO Research Fellowship: “Molecular characterization of intratumor heterogeneity and tumor microenvironment in high grade serous ovarian cancer and BRCA1/2 mutant breast cancers using spatial transcriptomics”
- Mattia Rediti – ESMO Congress 2022, “ESMO Merit Travel Grant”: “Identification of biologically-driven HER2-positive breast cancer subgroups associated with prognosis after adjuvant trastuzumab in the ALTTO trial”
- XiaoXiao Wang - ESMO Congress 2022 « Best Poster Award »: “Spatial transcriptomics reveals substantial heterogeneity in TNBC tumor and stroma compartments with potential clinical implications”
- Zelda Paquier (PhD student) - BHPA 2022 – Young scientist award
- Rachele Danieli (PhD student) - BELNUC 2022 – Medical Physics best oral presentation
Publications 2020-2022

2020-2022 (Selected Papers)

Breast Cancer Translational Research Laboratory (BCTL)


Gastrointestinal Cancer Laboratory (GI)


Clinical and Experimental Oncology Laboratory (LOCE)


**Molecular Immunology Laboratory (MIU)**


**Lung Cancer & Immuno-Oncology Laboratory (LCIO)**


**Onco-Virology Laboratory**


**Clinical Cell Therapy Laboratory (LTCC)**


**Cancer Epigenetics Laboratory (LCE)**


**MRI Physics & Radiophysics Laboratory**


Using a risk-stratified based strategy to improve outcomes of standard breast cancer screening: the EU MyPeBS trial


Liquid Biopsy


Nuclear Imaging


Radiomics in Pancreatic Cancer


Radionics in Pancreatic Cancer


Precision Medical Oncology


**Precision Radiotherapy**


**Precision Surgery**


Artificial Intelligence applications to optimize the clinical workflow


Applied image and data analysis to personalize treatment and improve patient outcomes


Cell Therapies


Immunotherapy Beyond PD-1/PD-L1 Immune Checkpoint Blockers


IRM-Linac for Individualized Radiotherapy


Contributing to academic-led research within the BIG and ONCODISTINCT networks


Oncodistinct Network


Research in Oncological Complications


Psycho-Oncology and Supportive Care Research


Geronto-Oncologic Research


Nursing Research


Patient Involvement and Empowerment

Publications 2020


Institut Jules Bordet Scientific Report 2022 | PUBLICATIONS 2020-2022


Publications 2021


Institut Jules Bordet


Institut Jules Bordet Scientific Report 2022 | PUBLICATIONS 2020-2022


A. van de Stolpe, W. Verhaegh, J.Y. Blay, C.X. Ma, P. Pauwels, M. Pegram, H. Prenen, D. De Ruyscher, N.F. Saba, S.F. Slovin, K. Willard-Gallo, H. Husain, RNA Based Approaches to Profile Oncogenic Pathways From Low Quantity Samples to Drive Precision Oncology Strategies, Front Genet 11 (2021) 598118.


K. Otmani, P. Lewalle, Tumor Suppressor miRNA in Cancer Cells and the Tumor Microenvironment: Mechanism of Deregulation and Clinical Implications, Front Oncol 11 (2021) 708765.


Publications 2022


**Publications 2022**


K. Gourari, A. Awada, N. Kotekci, Molecular oncology: what is needed to speed access to innovative therapies in clinical research?, Curr Opin Oncol 34(5) (2022) 575-578.


Institut Jules Bordet Scientific Report 2022 | PUBLICATIONS 2020-2022


Institut Jules Bordet Scientific Report 2022 | PUBLICATIONS 2020-2022


Institut Jules Bordet Scientific Report 2022 | PUBLICATIONS 2020-2022


Institut Jules Bordet Scientific Report 2022 | PUBLICATIONS 2020-2022


**Clinical Research Opportunities**

**Translation of Breast Cancer Research (2022) 4 pages.**

**MONARCH-plus: the Evidence of Efficacy and Safety of Abemaciclib in Countries with Limited Access**


**Esophageal cancer: Outcome and potential benefit of esophagectomy in elderly patients**


**COVID-19**


**Translating Breast Cancer Research**


<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AML</td>
<td>acute myeloid leukemia</td>
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<tr>
<td>ATL</td>
<td>adult T-cell leukemia</td>
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<td>ATPT</td>
<td>Academic Trials Promoting Team</td>
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<td>BCTL</td>
<td>Breast Cancer Translational Research Laboratory</td>
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<td>BIG</td>
<td>Breast International Group</td>
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<td>ctDNA</td>
<td>circulating tumor DNA</td>
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<td>CTCU</td>
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<tr>
<td>CTSU</td>
<td>Clinical Trials Support Unit</td>
</tr>
<tr>
<td>CT scan</td>
<td>computerized tomography scan</td>
</tr>
<tr>
<td>EBRT</td>
<td>external beam radiotherapy</td>
</tr>
<tr>
<td>EORTC</td>
<td>European Organisation for Research and Treatment of Cancer</td>
</tr>
<tr>
<td>FDG-PET</td>
<td>fluorodeoxyglucose (FDG)-positron emission tomography (PET)</td>
</tr>
<tr>
<td>HER2</td>
<td>human epidermal growth factor receptor 2</td>
</tr>
<tr>
<td>HTLV-1</td>
<td>human T-cell lymphotropic virus type-1</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>MSC</td>
<td>mesenchymal stromal cells</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>NGS</td>
<td>next generation sequencing</td>
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<tr>
<td>OECI</td>
<td>Organisation of European Cancer Institutes</td>
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<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
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<tr>
<td>PET</td>
<td>positron emission tomography</td>
</tr>
<tr>
<td>SBRT</td>
<td>stereotactic body radiation therapy</td>
</tr>
<tr>
<td>SIRT</td>
<td>selective Internal radiation therapy</td>
</tr>
<tr>
<td>TIL</td>
<td>tumor infiltrating lymphocytes</td>
</tr>
<tr>
<td>TLS</td>
<td>tertiary lymphoid structures</td>
</tr>
<tr>
<td>TNBC</td>
<td>triple negative breast cancer</td>
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