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In a rapidly-evolving field like biomedical research, an entrepreneurial attitude is a great asset. At IBBL, we have always fostered this start-up spirit in an effort to push innovation. In 2015, this approach has allowed us once again to create and seize new opportunities and to reach some major milestones.

At the beginning of the year, IBBL merged with the Centre de Recherche Public - Santé to form the Luxembourg Institute of Health (LIH). Within this new institute, IBBL has a certain autonomy as it kept its own CEO, management committee, budget and performance contract with the Ministry of Higher Education and Research, even if it now operates under the responsibility of a single Board of Directors of the Luxembourg Institute of Health. As a biobank, it has been crucial for us since the beginning to collaborate with biomedical research institutes like the Centre de Recherche Public - Santé / LIH. The merger has made us work even closer together and led to the creation of synergies on various levels, particularly within the administrative department. In December 2015, the LIH’s Board of Directors decided to appoint Catherine Larue, until then CEO of IBBL, as interim CEO of LIH. Until a new CEO of LIH is recruited, Catherine ensures the general management of LIH, while Marc Vandelaer, until then CIO of IBBL, assumes the role of IBBL’s interim CEO.
Independently of these organisational changes, we have been able to achieve important goals, launch new large-scale projects, expand our service offer, increase our external revenues and even organise a major conference in Luxembourg. The fifth International Human Microbiome Congress (IHMC) attracted experts from 32 countries and received great feedback from presenters, exhibitors and participants alike. With our ISO 9001 and NF S96-900 recertifications and our new ISO 17025 accreditation, we hit a major milestone for our quality management system. On top of that, we won the Luxembourg Quality and Excellence Award, another great reward after six years of hard work. We have also launched a number of new projects with both our national and international partners. One project that we are particularly proud of is the CANCER-ID consortium, funded by the Innovative Medicines Initiative (IMI), a collaboration between the European Union and the European pharmaceutical industry. In Luxembourg, we started collecting biospecimens and clinical data for the new National Centre of Excellence in Research – Parkinson’s Disease (NCER-PD), as well as for the National Cancer Plan.

“WE HIT SEVERAL MAJOR MILESTONES IN 2015, PARTICULARLY FOR OUR QUALITY MANAGEMENT SYSTEM”

Catherine Larue, Chief Executive Officer in 2015

Our primary role within the National Cancer Plan is to optimise the logistics of cancer biospecimen collection with the ultimate goal of including 70% of all biopsies and resected tumours in Luxembourg in IBBL’s cancer research collection. While this is highly ambitious, we have made important strides towards this goal in 2015. The pilot project to determine the best logistical setup for the biospecimen collection was carried out with our partners at the Laboratoire National de Santé (LNS) and the Centre Hospitalier Émile Mayrisch (CHEM). The concerted effort of everyone involved meant that we were able to include the first biopsies in the scope of the Cancer Plan at the CHEM. Our move to the new building annexed to the LNS in Dudelange is planned for 2017. These new facilities will not only give us the additional space we need as we are growing, but also allow us to intensify our collaboration with the LNS.

“WE HAVE A NUMBER OF EXCITING AND CHALLENGING NEW PROJECTS IN OUR PIPELINE FOR THE COMING YEARS”

Marc Vandelaer, Chief Executive Officer (current)

Besides our move, we have a number of exciting and challenging new projects in our pipeline for the coming years. Among those projects, some will allow us to foster once more synergies with existing or new partners. We plan to considerably increase the size and diversity of our sample collection through the National Cancer Plan and the Luxembourg microbiome cohort, as well as through new tissue collections in France and Vietnam. We will also continue our efforts to increase third party funding by gaining new service contracts and grants from national and European research funding agencies. Finally, we plan to expand the scope of our accreditation to more testing methods while maintaining our current certifications. Our plans for the future are ambitious, but, with our government’s and partners’ support and a highly qualified team that has always embraced new opportunities, there is nothing stopping us from reaching our goals.

CATHARINE LARUE
Chief Executive Officer in 2015

MARC VANDELAER
Chief Executive Officer (current)
HIGHLIGHTS

CORE BUSINESS

- 16 new service contracts
- 63 active projects
- 41 partners & clients
- 10 new scientific publications

QUALITY

- 2 certifications: ISO 9001 and NF S96-900
- 1 accreditation: ISO 17025
- 4 testing methods accredited

COLLECTION

- 258,099 samples in collection
- 28,059 samples distributed
INTERNATIONAL HUMAN MICROBIOME CONGRESS

- 520 participants
- 289 abstracts
- 32 countries

PROFICIENCY TESTING PROGRAMME

- 12 schemes
- 107 participating laboratories
- 28 countries

UNIVERSITY BIOBANKING CERTIFICATE

- 22 students
- 17 countries
HAT-TRICK FOR IBBL’S QUALITY MANAGEMENT SYSTEM

IBBL’s strategy to build its operations around a formal Quality Management System (QMS) paid off on 3 levels in 2015: the biobank gained ISO 17025 accreditation, won the Luxembourg Quality and Excellence Award and successfully passed its follow-up audits for ISO 9001 and NF S96-900.

Following a successful audit in 2015, IBBL is now one of the very few biobanks worldwide to be accredited according to ISO 17025:2005, the norm that specifies the general requirements for the competence of testing and calibration laboratories. IBBL’s accreditation was issued by OLAS (Office Luxembourgeois d’Accréditation et de Surveillance) for an initial period of five years and currently covers the following testing methods:

1. Complete Blood Count with ABX Micros CRP 200
2. DNA Quantification by Spectrofluorometry
3. Nucleic Acid Quantification by Spectrophotometry
4. RNA Integrity Measurement

In addition to these methods, the biobank plans to have the scope of its accreditation expanded and further biospecimen testing methods included in the future. All of the testing methods included in the scope will be assessed yearly during follow-up audits. The news of IBBL’s accreditation was equally celebrated by its partners, clients and staff. “Being one of only a handful of biobanks in the world that is accredited according to ISO 17025 underlines our competence in providing well-annotated samples, data and services of the highest quality. It is a great reward for the team that has worked tirelessly over the last few years”, proudly commented Marc Vandelaer, IBBL’s current CEO.

And the winner is...

The continuous effort of IBBL to ensure the high quality of its samples and bioservices was further rewarded when the biobank was chosen as the winner of the Luxembourg Quality and Excellence Award in the category for small companies. Supported by the Ministry of Economy, the award is presented annually by a member of the government to recognise the great performance of organisations across a range of sectors. The participating organisations are evaluated based on a neutral process, led by trained auditors in a context devoid of any conflict of interest. The winners are then selected on the basis of their positive results and continuous improvement. In their report, the auditors noted that IBBL stood out amongst all the candidates for its excellent performance in the areas of leadership, strategy, personnel, resources and processes.

Building on sustainability

For IBBL’s Quality Manager, Dr Sabine Lehmann, winning the Luxembourg Quality and Excellence Award was the cherry on the cake. “It is extremely satisfying to be recognised, not only for our QMS, but also for our efforts in terms of sustainability”, she declared. Indeed, a large part of the evaluation process for the award focused on sustainability. The main purpose of IBBL’s QMS is to ensure its services, which include biobanking,
sample processing, sample analysis and quality control, are of the highest quality, meeting customer satisfaction. It has also allowed the management to put in place mechanisms that foster both social and environmental sustainability. IBBL aims to be energy efficient, protect the environment, establish a culture of knowledge-sharing, engage the next generation of researchers, give back to society and promote diversity.

**Quality as strategy**

Since the beginning, quality has been a key focus for IBBL. The quality management system was set up by Dr Lehmann and has been developed under her supervision as the biobank’s activities have grown. By validating and standardising every process that can affect the quality of biological samples, the biobank ensures that researchers receive samples that are fit for purpose and of uniform quality. This allows both the biobank and the researchers to work more efficiently and save time and money. At the same time, donors know that the greatest care is taken of their samples to maximise their contribution to research.

**Keeping it up**

In addition to passing its first accreditation audit and winning the quality award, IBBL celebrated another important achievement for its QMS in 2015. In November, the biobank successfully passed the follow-up audits for its ISO 9001 (general quality management) and NF S96-900 (quality of biological resource centers and biological resources) certifications. “All in all, 2015 has truly been an outstanding year for us in terms of quality”, summarises Marc Vandelaer: “But for us, quality is not just a project that gets put to the side now that we have achieved certification and accreditation. We will continuously improve the quality of our bioservices, expand the scope of our accreditation and make sure we are ready if and when an international norm related to biobanking is published.”
FINDING BETTER WAYS

Led by Dr Fay Betsou, IBBL’s Biorefinery department is recognised as one of the leading research groups focusing on the quality of biospecimens. In 2015, two of IBBL’s main biospecimen research projects evaluated new technologies to improve processing of tissue biospecimens with the goal of getting the most out of the tissue that is voluntarily donated by patients.

While everyone agrees that biospecimens need to be collected and processed in a standardised way to eliminate bias introduced during pre-analytical steps, in many instances the best way to handle these biospecimens is simply not known. In reality, most researchers do not have the time to optimise each step of their processing and analysis protocols or develop alternative methods. IBBL sees one of its roles as a biobank, in investigating these kinds of questions and has over the years become an international leader in the field of biospecimen research. Other organisations that are interested in optimizing the way biospecimens are processed and analysed are equipment, consumable and assay suppliers. IBBL works closely with these companies to optimize and evaluate their products and workflows. In 2015, IBBL’s biospecimen researchers carried out two independent evaluations of new methods to improve the utilisation of tissue biospecimens.

An alternative to formalin

The first project evaluated the use of the PAXgene tissue fixative system as an alternative to formalin fixation, which is currently used, in combination with paraffin embedding, as the gold standard for tissue preservation. While formalin fixation is routine in pathology laboratories around the world, it has one major shortfall, which is the poor quality of molecules (DNA, RNA, protein, etc.) extracted from the tissue. For this reason molecular biologists favour frozen tissue over formalin-fixed paraffin-embedded tissue (FFPE). Unfortunately, though, frozen tissue preserves the morphology less well than fixed tissue. The PAXgene tissue fixation system was developed to address this dilemma.

Collaborating with the Imperial College London, the University of York and the Wales Cancer Bank, IBBL’s researchers performed a comprehensive independent evaluation of the system. They compared the morphological preservation, the performance of immunohistochemistry and the quality of molecules extracted from frozen, FFPE and PAXgene-fixed paraffin-embedded tissue (PFPE) tissue. They found that the PAXgene system preserved nucleic acids better than FFPE preservation, but not as well as cryopreservation. Thus, while the PAXgene system is unlikely to replace formalin in the routine clinical setting, because of the cost associated with switching to a new system, it is a valuable alternative for molecular diagnostics.
Enhancing the value of biospecimens

IBBL’s second tissue biospecimen research project of 2015 evaluated the CryoXtract CXT350 Frozen Sample Aliquetter, which can be used not only to take cores of frozen tissue, but also liquid biospecimens, like stool, urine or blood. Unlike a cryostat, which slices frozen tissue, coring allows researchers to target a specific section of the tissue, thus enabling the separate analysis of molecules from different parts of a biospecimen (e.g. tumoral and adjacent normal tissue). IBBL’s researchers used a total of 614 cores from different types of tissue in their evaluation of the CryoXtract equipment. They found that the technology was easy to use and integrate into the workflow of a tissue biobank. It provided reproducible cores without nuclease- or cross-contamination. The quality of RNA extracted from cores was marginally poorer than that of RNA extracted from tissue slices, thus not representing a barrier for the effective utilisation of the technology. Overall, the researchers concluded that the CryoXtract system enhances the value of frozen tissue biospecimens, because one can get a lot more data out of each biospecimen.

Ideally, researchers and biobanks would have a frozen specimen for coring with the CXT350 for molecular analysis and a mirrored FFPE tissue block for histological analysis. “While IBBL has applied this principle to its routine processing of tissues, this may not always be feasible”, comments Dr William Mathieson, the scientist at IBBL who led both projects. “Particularly when dealing with rare tumours or remote collection locations, the PAXgene system is a viable alternative.”

Sharing knowledge

While Dr Mathieson and his team focused primarily on tissue biospecimen research, other researchers within IBBL’s Biorefinery department investigated aspects relating to the quality of other types of biospecimens. In 2015, IBBL’s researchers evaluated the impact of different collection tubes on biospecimen quality, compared RNA quality assessment methods, investigated different aspects of RNA extraction protocols, developed new quality control assays and validated a number of processing and analysis methods, including 16S rRNA gene sequencing (see page 14) and the nucleic acid extraction from whole blood. These various projects led to 10 scientific publications in peer-reviewed journals. These publications are not only a reward for the researchers who worked for months on their projects, but also a crucial tool for IBBL to share its knowledge with the biobanking and the biomedical research community.
In order to respond best to its clients’ needs, IBBL reformulated its service offer in 2015 and introduced a new service for the pre-clinical validation of biomarkers. With 16 new service contracts, increased participation in the Proficiency Testing programme and great feedback from the students of the University Biobanking Certificate, the year proved fruitful for IBBL’s bioservices.

For a number of years IBBL has been offering biospecimen-related services to clients in industry, academia and EU consortia, particularly for large-scale studies such as multi-centre clinical trials and international research projects. In 2015, the biobank decided to reformulate its service offer and launch a comprehensive package of bioservices specifically tailored to the needs of its clients. Highlighting its expertise, its research-driven approach to quality and its compliance with international standards, IBBL now offers the following six bioservices:

- Biobanking
- Sample Processing
- Sample Analysis & Quality Control
- Biomarker Validation
- Biospecimen Proficiency Testing
- University Biobanking Certificate

**New service and website**

The updated service package includes the brand new Biomarker Validation service, which was launched officially in early 2016 with a call for proposals. Researchers from industry or academia can submit a proposal for their biomarkers, with the hope of receiving IBBL’s pre-clinical biomarker validation service free of charge. IBBL will select the most promising biomarker candidate and undertake the pre-analytical and analytical validation, as well as the clinical verification, key steps towards a marketable product. In parallel with the launch of the service offer, IBBL updated its corporate website, which is now clearly centred around bioservices, while www.biobank.lu remains IBBL’s multilingual website for the general public.

**Increasingly popular programme**

IBBL has also expanded the scope of its existing services. In 2015, IBBL signed 16 new service contracts, most of which are for sample and data storage, and processing of blood and tissue samples. IBBL also doubled the number
of schemes it offered in the 2015 edition of its Biospecimen Proficiency Testing (PT) programme, based on the feedback from previous years. The PT programme provides an external quality assessment to participating laboratories and allows them to compare their performance to that of other biobank laboratories all around the world. As the only PT programme in the world that is focused on biospecimens, IBBL’s programme is endorsed by the International Society for Biological and Environmental Repositories (ISBER) and has become increasingly popular over the last five years. In 2015, a total of 107 participants registered for 332 PT schemes, an increase of 78% for participants and 66% for schemes compared to 2014.

A diverse audience

Though not considered a “service” in the traditional sense of the word, IBBL also offers a continuing education course on biobanking every 2 years. In June 2015, IBBL and the University of Luxembourg ran the third edition of the “Principles of Biobanking” certificate, which uniquely combines environmental and clinical aspects of biobanking. 22 participants from 17 different countries in Europe, Africa, Asia and South-America made their way to Luxembourg to attend the biobanking course endorsed by ISBER. Over a period of three weeks, the students had the opportunity to tap into the expertise that comes from running a certified and accredited state-of-the-art biobank, as well as the experience of internationally-renowned lecturers in domains like pre-analytical research, cryobiology, stem cell or museum biobanking. This wide range of topics is part of what makes this course unique. It is thus no surprise that the participants come from very diverse fields; this year’s student list included fellows from cancer, fish and invertebrate and Arabidopsis biorepositories.

All of the students said that the course accomplished their overall objectives and 89% rated the content of the lectures as good or excellent. The course is however not only an enriching experience for the students but also for the teachers and organisers. “Personally, I feel it is our responsibility and actually a privilege to share our knowledge.” comments Dr Fay Betsou, Chief Scientific Officer at IBBL and the coordinator of the course. “Through this course we can indirectly help set-up and run biobanks efficiently all around the globe, especially in countries where biobanking is still relatively new.”

Beyond Luxembourg

While the success of IBBL’s bioservices helps to cover some of the costs of the biobank, it principally contributes to the global quality of biobanking and biomedical research, increases the biobank’s visibility and contributes to the positive image and reputation of Luxembourg’s biomedical research sector. All of these aspects are crucial key performance indicators in IBBL’s performance contract with the Luxembourg Ministry of Higher Education and Research.
A GUT FEELING

Over the last few years, IBBL has become deeply invested in microbiome research, the field that studies the interactions between the human body and the billions of microorganisms that share it. 2015 was no exception: IBBL co-organised the fifth International Human Microbiome Congress (IHMC) in Luxembourg, studied the best ways to process and annotate gut microbiome samples and prepared to launch the first Luxembourg gut microbiome cohort.

Even though we have made great strides in deciphering the complex interactions between human and microbial cells, microbiome research remains relatively new and much more research will need to be done to really lift the fog. As IBBL prepares to launch the Luxembourg gut microbiome cohort, microbiome research groups from around the globe are starting to decipher how exactly the microbes in our gut are influenced by our lifestyle and how they in turn influence our health.

Luxembourg takes centre stage

To push the field forward, microbiome experts from all around the world come together every 18 months at the IHMC to discuss their latest discoveries. In March 2015, Luxembourg took centre stage when IBBL welcomed hundreds of researchers for the fifth edition of the IHMC, which was supported by the FNR (Fonds National de la Recherche). Over the course of 3 days, more than 500 researchers, engineers and clinicians gathered at the LuxExpo exhibition centre. Under the theme “Future Directions for Human Microbiome Research in Health and Disease”, the congress participants enjoyed presentations from
50 internationally-renowned speakers, as well as the Luxembourg Minister of Health and Secretary of State for Higher Education and Research. The congress was organised into three plenary and six concurrent sessions, with multiple poster sessions and a panel discussion. The comprehensive programme included topics like microbiome biobanking, new technologies and models to study the microbiome, therapeutic interventions, the role of the microbiome in human evolution and its role in a variety of human diseases, from cancer to metabolic disorders and cardiovascular diseases. On top of that, the Luxembourg Centre for Systems Biomedicine (LCSB) organised two workshops on computational analysis for microbiome research, on the day before the congress and the day just after the congress.

A national cohort

The Luxembourg research community as a whole has been active in the field of microbiome research for a number of years. In addition to IBBL’s involvement in the field, the LCSB runs several research projects to elucidate the role of the microbiome in human health, a number of which are collaborations with IBBL. Recently, IBBL has teamed up with clinical laboratories in Luxembourg to prepare the launch of a cohort of microbiome samples from healthy volunteers in an effort to further foster microbiome research. Samples from this well-annotated cohort will be used as a reference for both national and international microbiome research projects. The cohort is currently in the setup phase and active recruitment is expected to begin in 2016.

Annotating samples to add value

IBBL has spent a lot of effort to become specialised in the optimisation and validation of stool sample processing and annotation methods to become “the biobank” adapted to microbiome research. The initial phase of the validation study focused on the extraction of DNA from stool samples and was completed in 2014. IBBL is currently finalising the report for the second phase, which focuses on the annotation of microbiome samples. A standard operating procedure for 16S rRNA gene sequencing of microbiome samples has been implemented and validated for factors like accuracy, precision, interference, robustness and stability. The data analysis pipeline was developed in-house and also validated for its accuracy. The combination of a validated wet lab protocol and bioinformatics pipeline provides a comprehensive workflow for the annotation of microbiome samples with 16S rRNA gene sequencing data. In addition, IBBL will test the samples in its microbiome collection for calprotectin, a protein that indicates intestinal inflammation. In 2015, IBBL completed a feasibility study on the calprotectin assay and is currently fine-tuning the assay protocol. Both the sequencing and calprotectin annotation add tremendous value to the samples, because they inform researchers on the health of the patients and the composition of the microbial community within the sample. Hence, with the launch of the Luxembourg gut microbiome cohort around the corner, everything is set up to ensure IBBL can collect and deliver valuable and high-quality samples for gut microbiome research.
JOINING FORCES WITH EUROPE’S BEST LABORATORIES

In recent years, IBBL has contributed its expertise to European research consortia through biospecimen research and through its bioservices. One of IBBL’s biggest successes in 2015 was its membership in the CANCER-ID consortium, where IBBL joined the ranks of 33 partners from prestigious academic and clinical research institutions, Small-and-Medium-sized Enterprises (SMEs) and the pharmaceutical industry.

When you bring together people that tackle a problem from different angles, you are more likely to find an innovative solution. That is the idea behind initiatives that call for large-scale research consortia, such as the Horizon2020 programme of the European Commission or the Innovative Medicines Initiative (IMI), a collaboration between the European Union and the European pharmaceutical industry. Recognising the potential such collaborations across different countries and sectors have in pushing science and innovation forward, IBBL contributes both its biobanking and biospecimen research expertise to several EU research projects.

Liquid biopsies

IBBL is a member of the CANCER-ID consortium, which was created in 2015 with the goal of validating the use of blood-based biomarkers for cancer. Blood-based biomarkers such as circulating tumour cells, circulating free tumour DNA and microRNAs are potential indicators for the tumour burden of patients living with cancer. The use of these markers from blood may offer an additional invaluable tool for modern cancer therapy. Apart from being of high importance when biopsies of the tumour are not accessible, blood-based tests may allow continuous determination of disease markers - a means to monitor the efficacy of treatment and potentially improve the choice of treatment options. The CANCER-ID project is an ambitious public-private partnership that was selected for funding by the IMI. It brings together 33 partners from 13 countries from academia and industry, providing a unique setting for establishing the clinical utility of “liquid biopsies”. As one of the world leaders in biospecimen research, IBBL works within the CANCER-ID consortium on the validation of laboratory methods, the development of standard operating procedures and the development of a proficiency testing programme.

A valued partner

As Dr Catherine Larue, CEO of IBBL in 2015, explains, the IMI programme is highly competitive on two levels: “First you have to become part of a mounting consortium, preferably with internationally recognised partners. Then the project that the consortium submits has to go through a rigorous review process before being accepted for funding”. Despite the competition, IBBL has been pursuing the strategy of obtaining European funding for a number of years now, because of the big potential rewards. “Being part of an important European consortium is great news for IBBL and for Luxembourg, not just in terms of securing funding from the European Commission, but also in terms of visibility for our research sector and personalised medicine. Our participation in CANCER-ID shows that IBBL is considered a valued partner and recognized as a first-class research support infrastructure in Europe”, says Dr Larue.
Virtual biobanking

In addition to participating in EU consortia by carrying out biospecimen research, IBBL also contributes its biobanking activities, including logistics, sample and data storage, to a number of European projects. One of these projects is BIOMARKAPD (Biomarkers for Alzheimer’s disease and Parkinson’s disease). Funded by the EU Joint Programme – Neurodegenerative Disease research (JPND), the BIOMARKAPD project was designed to standardise the assessment of existing assays and validate new fluid biomarkers for Alzheimer’s and Parkinson’s disease. In 2015, the consortium members published a paper (see page 20) in Frontiers in Neurology describing how IBBL was used as a central biobank for BIOMARKAPD. Cerebrospinal fluid and blood samples were collected from 14 centres across Europe according to standardised pre-analytical procedures. Samples were then processed and stored at IBBL in compliance with international standards and best practices. To simplify logistics, one of the biobank’s project managers oversees the collections and sample requests from consortium partners and external parties. Together with the consortium partners, IBBL has also developed a web-based IT platform that captures all the clinical and biological data related to the BIOMARKAPD samples stored at IBBL. The platform works as a virtual biobank by providing information on the samples available at the local biobank of each consortium partner.

The benefit of a central biobank

In addition to the 8,600 participants in the virtual biobank, BIOMARKAPD now has a collection of standardised samples and data from over 400 participants, which are all available for validation studies for new biomarkers and assays. This is a prime example of the added value a central biobank can bring to a large-scale consortium and the importance of getting a biobank on board from the start. Having a reliable partner that can support the standardisation of samples and provide long-term storage allows researchers to make the best use of the samples, an important issue for both funding bodies and sample donors. In the coming years, IBBL will continue to offer its know-how in biospecimen research and biobanking to international consortia and to contribute through its other bioservices, in particular its newly developed biomarker validation service.
LARGE NATIONAL EFFORT TO BEAT PARKINSON’S DISEASE

In 2015, IBBL and its national partners ventured into an 8-year research programme with the aim of diagnosing and stratifying Parkinson’s disease better and earlier. The public and patients embraced the ambitious but promising programme, leading to a remarkable number of participants and collected samples.

Parkinson’s disease (PD) is a chronic and progressive neurodegenerative disease. While the risk of developing PD increases as we grow older, up to 10% of patients are already diagnosed before they turn 50. At the time of diagnosis, PD patients typically exhibit motor symptoms including muscle stiffness, shaking and slowness in initiating movement. PD takes years to develop and the damage to nerve cells is already extensive by the time these motor symptoms appear and the disease is diagnosed. In order to treat patients as early and as efficiently as possible, it is imperative that accurate early diagnostic tests are found and that clinicians get tools to predict the progression of a given patient’s disease. Understanding this urgency, IBBL and its national and international partners work on a number of PD research projects.

Collaboration is key

The biggest initiative in PD research in Luxembourg was launched in 2015: the National Centre of Excellence in Research (NCER) – Parkinson’s Disease. Initiated and funded by the Fonds National de la Recherche (FNR), NCER-PD is an 8-year programme that aims to identify and validate new methods for the early diagnosis of PD and for the stratification of patients in sub-groups. In addition to its scale and scope, the main benefit of the programme is that it brings all the different PD expertise in Luxembourg to one table. The national partner institutes of NCER-PD are IBBL, the Luxembourg Centre for Systems Biomedicine (LCSB), the Luxembourg Institute of Health (LIH) and the Centre Hospitalier de Luxembourg (CHL). On top of that, the local partners have brought international experts from Germany and the UK on board. The NCER-PD programme is led by Prof. Rudi Balling and Prof. Rejko Krüger of the LCSB and comprises multiple related research projects, each investigating different angles to reach the same ultimate goal.

Clinical sample and data collection

One of the central parts of the programme is a clinical study with PD patients and healthy participants from Luxembourg and the Greater Region. For this study, the participants donate biological samples, undergo a neurological and a neuropsychological evaluation and complete questionnaires. Participation in the clinical study is voluntary and participants have the right to withdraw from the study at any moment without giving any justification. The collected data and samples are analysed and compared between patients and healthy controls with the hope of identifying differences that can be exploited for diagnosis and/or stratification. As the biobank of NCER-PD, IBBL plays a key role in this clinical study, taking care of sample collection, processing and storage. IBBL prepares the collection kits and sends them to the CHL or the Clinical and...
Epidemiological Investigation Centre (CIEC) of the LIH. Here, patients and healthy volunteers are asked to give blood, urine and saliva as part of the standard collection, with the option of also donating stool, skin biopsies and cerebrospinal fluid if they wish. The biospecimens are then brought to IBBL, where a laboratory technician extracts various components like cells and nucleic acids, and preserves the samples for long-term storage. Ultimately, these samples are then distributed to the national and international research partners within NCER-PD.

Great support and participation

With the official launch of NCER-PD in April 2015, the partner institutes initiated a large and very active communication campaign, in order to inform the public and specifically PD patients about the programme and recruit as many participants as possible. This proactive approach paid off as the team recruited just over 200 patients and healthy donors in 2015, generating almost 10,000 aliquots of blood, urine, saliva and their components. This number, which is all the more impressive given that the study has been up and running for less than a year, would not have been achieved without the support of numerous associations and, of course, of the participants themselves. Thus, NCER-PD has become a showcase of how doctors, biologists, computer scientists, biobankers, funding agencies and patient associations can come together and collaborate on multiple levels to push towards a common goal that is centred on the patient.
HOW SEVERELY IS DNA QUANTIFICATION HAMPERED BY RNA CO-EXTRACTION?

THE CENTRAL BIOBANK AND VIRTUAL BIOBANK OF BIOMARKAPD: A RESOURCE FOR STUDIES ON NEURODEGENERATIVE DISEASES

TUBE POLYPROPYLENE: A NEGLECTED CRITICAL PARAMETER FOR PROTEIN ADSORPTION DURING BIOSPECIMEN STORAGE

EXOSOMES RELEASED BY CHRONIC LYMPHOCYTIC LEUKEMIA CELLS INDUCE THE TRANSITION OF STROMAL CELLS INTO CANCER-ASSOCIATED FIBROBLASTS

ULTRAVIOLET C RADIATION INFLUENCES THE ROBUSTNESS OF RNA INTEGRITY MEASUREMENT

METHOD VALIDATION FOR AUTOMATED ISOLATION OF VIVABLE PERIPHERAL BLOOD MONONUCLEAR CELLS

METHOD OPTIMIZATION FOR FECAL SAMPLE COLLECTION AND FECAL DNA EXTRACTION

BIOSPECIMEN PROCESSING METHOD VALIDATION
F. Betsou. Biopreservation and Biobanking, Volume 13, Issue 2, Page 79–93

REPLACING β-MERCAPTOETHANOL IN RNA EXTRACTIONS

PLATELET ACTIVATION AND AGGREGATION PROMOTE LUNG INFLAMMATION AND INFLUENZA VIRUS PATHOGENESIS
10 scientific publications were authored by IBBL staff. An additional 8 publications acknowledged IBBL for providing bioservices and biological samples & data.
PARTNERS & CLIENTS

Legend

- Collection Partner
- Industrial Partner
- Research Collaborator
- Client

UNITED KINGDOM
- FluidX
- RNAssist
- Imperial College London

UNITED STATES
- National Cancer Institute
- BD (Becton Dickinson)
- Biolife Solutions
- LABVANTAGE
- CryoXtract
- WaferGen Bio-systems
- Biomatrica
- Precision for Medicine

CANADA
- DNA - Genotek
- International Society for Biological and Environmental Repositories
## PROJECTS

### CANCER

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<td>Biomarker validation in lung cancer</td>
<td>Luxembourg Institute of Health (LIH), Partnership for Personalized Medicine</td>
</tr>
<tr>
<td>Lung Cancer Antibodies - Genetic and immunological risk factors for smokers to develop lung cancer</td>
<td>Laboratoire National de Santé (LNS)</td>
</tr>
<tr>
<td>Suppressor of Cytokine Signalling - Discovery of new therapeutic targets for colorectal cancer</td>
<td>University of Luxembourg, LNS</td>
</tr>
<tr>
<td>Feasibility of implementing good practice in prostate cancer diagnosis in Luxembourg and hence to change medical practice in the country</td>
<td>Centre Hospitalier de Luxembourg (CHL), Luxembourg urologists</td>
</tr>
<tr>
<td>A prospective randomised electronic evaluation of chemotherapy side effects in oncology out-patients</td>
<td>LIH, Centre Hospitalier Emile Mayrisch (CHEM), Bosch</td>
</tr>
<tr>
<td>Collection of skin biopsies for establishment of melanoma cell lines</td>
<td>University of Luxembourg</td>
</tr>
<tr>
<td>Plan Cancer</td>
<td>LNS, CHEM</td>
</tr>
</tbody>
</table>

### PARKINSON’S DISEASE

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>PARTNERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitochondrial dynamics in Parkinson’s disease - A case-control study comparing different post-mitotic tissues from Parkinson’s disease patients</td>
<td>LIH, CHL, Luxembourg Centre for Systems Biomedicine (LCSB)</td>
</tr>
<tr>
<td>Biomarkers for Alzheimer’s and Parkinson’s disease</td>
<td>LCSB, European Joint Programme for Neurodegenerative Disease Research (JPND)</td>
</tr>
<tr>
<td>Metabolomics &amp; neuronal imaging in Parkinson’s disease</td>
<td>LCSB, Uniklinik Köln (Germany)</td>
</tr>
<tr>
<td>National Centre for Excellence in Research on Parkinson’s Disease</td>
<td>LCSB, LIH, CHL, Fonds National de la Recherche (FNR)</td>
</tr>
</tbody>
</table>

### DIABETES

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>PARTNERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Multiplex Family Study – Candidate genes within specific environments in diabetic and non-diabetic family members</td>
<td>LIH, LCSB</td>
</tr>
<tr>
<td>Colonisation, Succession and Evolution of Human Gastrointestinal Microbiome from Birth to Infancy – Investigating the relationship between gut microflora development immediately after birth and diabetes later in life</td>
<td>CHL, LCSB</td>
</tr>
<tr>
<td>Characterisation of changes in microRNA expression in patients with weight loss due exclusively to life style changes</td>
<td>University of Magdeburg (Germany), LCSB</td>
</tr>
</tbody>
</table>

### POPULATION STUDIES

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>PARTNERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collection of control biological samples from the population</td>
<td>Zitha Gesondheetszenter (ZithaKlinik, Hôpitaux Robert Schuman)</td>
</tr>
<tr>
<td>European Health Examination Study (EHES) extended with local component</td>
<td>Ministry of Health, EHES, LIH</td>
</tr>
</tbody>
</table>
### BIOSPECIMEN RESEARCH

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>PARTNERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer treatment and monitoring through identification of circulating tumour cells and tumour related nucleic acids (CANCER-ID)</td>
<td>Innovative Medicines Initiative (IMI) CANCER-ID consortium</td>
</tr>
<tr>
<td>Biospecimen research project looking at tissue fixation time and type</td>
<td>Thionville Pathology Laboratory (France)</td>
</tr>
<tr>
<td>Research and validation of micro- and macro-molecular biomarkers for the quality of preservation of biological samples, and the validation of the related methods</td>
<td>LCSB, International Society for Biological and Environmental Repositories (ISBER), Biospecimen Science Working Group</td>
</tr>
<tr>
<td>Method Comparison on RNA integrity</td>
<td>QiAGEN</td>
</tr>
<tr>
<td>Intra-individual miRNA stability</td>
<td>WaferGen Bio-systems</td>
</tr>
<tr>
<td>Pre-analytical metabolomics</td>
<td>LCSB</td>
</tr>
<tr>
<td>Automated peripheral blood mononuclear cell extraction from CPT tubes</td>
<td>TECAN</td>
</tr>
<tr>
<td>Fecal sample collection and processing for DNA analyses</td>
<td>LCSB, CryoXtract, Perkin Elmer</td>
</tr>
<tr>
<td>Evaluation of different types of polypropylene storage containers</td>
<td>FluidX</td>
</tr>
<tr>
<td>CSF freeze-drying evaluation</td>
<td>JPND BIOMARKAPD consortium</td>
</tr>
<tr>
<td>Impact of fixation conditions on tissue miRNA</td>
<td>US National Cancer Institute, WaferGen Bio-systems</td>
</tr>
<tr>
<td>Impact of cold ischemia time on tissue miRNA</td>
<td>US National Cancer Institute, WaferGen Bio-systems</td>
</tr>
<tr>
<td>Interactive protocol project for simultaneous DNA, RNA and protein extraction from tissue</td>
<td>Imperial College London (UK)</td>
</tr>
<tr>
<td>Fitness-for-purpose evaluation of 30-year old bladder cancer cohort</td>
<td>Imperial College London (UK)</td>
</tr>
<tr>
<td>Evaluation of a molecular biology-friendly fixative</td>
<td>RNAassist</td>
</tr>
<tr>
<td>Immunohistochemistry optimisation for PAXgene-fixed paraffin-embedded tissue</td>
<td>PreAnalytiX, Thionville Pathology Laboratory</td>
</tr>
</tbody>
</table>

### CONTRACTS & OTHERS

<table>
<thead>
<tr>
<th>TOPIC OR SERVICE PROVIDED</th>
<th>PARTNERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistics, storage and supplies management for international clinical trial: Target Temperature Management after Cardiac Arrest</td>
<td>CHL, LIH, Helsingborg Hospital, Lund University (Sweden)</td>
</tr>
<tr>
<td>Proficiency Testing (7 testing schemes, 5 processing schemes)</td>
<td>ISBER and other organisations</td>
</tr>
<tr>
<td>21 projects for PBMC isolation and shipment services for clinical trials</td>
<td>Precision for Medicine</td>
</tr>
<tr>
<td>PBMC isolation and shipment services for a clinical trial</td>
<td>UniQure</td>
</tr>
<tr>
<td>WaferGen Bio-systems fee for service for miRNA analysis</td>
<td>University of Luxembourg</td>
</tr>
<tr>
<td>Long-term commercial storage contract for 52,000 samples from a completed European cancer trial</td>
<td>European Organisation for Research and Treatment of Cancer (EORTC), Breast International Group (BIG), Institut Bordet (Belgium)</td>
</tr>
<tr>
<td>Pathology processing for the Luxembourg arm of the AURORA breast cancer trial</td>
<td>CHL, LIH, BIG</td>
</tr>
<tr>
<td>Sample storage for 2 ongoing European breast cancer trials</td>
<td>BIG</td>
</tr>
<tr>
<td>Service agreement for sample storage and DNA extraction among others</td>
<td>University of Luxembourg</td>
</tr>
<tr>
<td>Pathology processing for a clinical trial</td>
<td>LIH</td>
</tr>
</tbody>
</table>
FACTS & FIGURES - COLLECTION STATISTICS

SAMPLES PER PROGRAMME

- CANCER: 44,876 (18%)
- DIABETES: 18,342 (7%)
- NEURODEGENERATIVE DISEASES: 20,815 (8%)
- POPULATION STUDIES: 77,776 (30%)

CONTRACTS: 96,290 (37%)
FINANCES

2015 EXPENSES

- RAW MATERIALS AND CONSUMABLES: 579,812 € (8%)
- DEPRECIATION: 1,123,118 € (15%)
- INTEREST AND OTHER FINANCIAL CHARGES: 3,302 € (0.05%)
- STAFF COSTS: 3,906,242 € (54%)
- OTHER OPERATING COSTS: 1,631,510 € (23%)

2015 SOURCES OF FUNDING*

- COMPETITIVE FUNDING: 122,271 € (2%)
- CONTRACTUAL SERVICES: 718,067 € (10%)
- MINISTRY OF HIGHER EDUCATION AND RESEARCH: 6,403,646 € (88%)

* Sources of funding covering 2015 expenses only
13 NATIONALITIES

Australia - 1
Belgium - 7
France - 15
Germany - 3
Italy - 1
Luxembourg - 3
Netherlands - 1
Poland - 2
Portugal - 2
Spain - 1
UK - 4
Ukraine - 1
USA - 1

42 STAFF MEMBERS

- Management & Administration 5
- Biorefinery 16
- Biorepository 4
- Business Information Solutions 7
- Clinical & Pathology 2
- Marketing & Communication 2
- Project & Data Management 5
- Quality Management 1
IBBL is an autonomous institute, organised within the Luxembourg Institute of Health (LIH) and operates under the responsibility of the Board of Directors of the LIH.

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President of the Board
Medical Director
Hôpitaux Robert Schuman
Luxembourg

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Head of Innovation Management
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