Contents

Message from the CEO  5

Highlights 2013  7

IBBL Activities  11
  Overview
  Partners & Clients
  Reaching beyond the borders– biobanking for Europe
  Why every step before analysis matters

PMC Activities  23
  Overview
  Linking gut bacteria to diabetes
  An electronic friend to manage chemotherapy side effects

Facts & Figures  35
A key focus of 2013 has been the investment in areas that make IBBL stand out from other biobanks, such as biospecimen and microbiome research.

Catherine LARUE
PhD, HDR, MBA
Chief Executive Officer
Message from the CEO

In November 2013, as I celebrated my first anniversary at IBBL, I took the time to reflect on what has been a very busy, but rewarding, 12 months. Since the beginning, IBBL’s mission has been to catalyse partnerships and support research that can improve healthcare, through personalised medicine. One of the key components of our success in achieving this goal is the partnership we enjoy with the people and medical institutions of Luxembourg. Without the clinicians’ engagement and the donations of samples from patients and healthy citizens, IBBL could simply not exist. At the same time, IBBL connects multidisciplinary research teams and works hand in hand with Luxembourg’s researchers to help introduce the next generation of healthcare. In addition to our close ties within the biomedical community in Luxembourg, we have spread our wings wider in our efforts to become an international biobanking centre of excellence.

In 2013, we made significant headway in increasing our visibility on an international level and secured service contracts for two projects from large European consortia; the EU Joint Programme for Neurodegenerative Disease Research (JPNd) and the Breast International Group (BIG). We set up a virtual biobank with all sample-related data for the members of JPNd’s BIOMARKAPD project, prepared the sample collection kits and participated in biospecimen research on cerebrospinal fluid samples. In June, the over 50,000 blood and tissue samples from the MINDACT breast cancer trial, developed under the auspices of BIG and coordinated and sponsored by the EORTC (European Organisation for the Research and Treatment of Cancer), arrived at IBBL for long-term storage. The trust these prestigious organisations have put in us is the result of our efforts to build an international reputation for high quality biobanking services and we intend to strengthen our relationship with these organisations by acting as the central biobank for other projects. Similarly, we have recently signed several new contracts with one of our existing clients for the processing of biospecimens from clinical trials, underlining client satisfaction. These service contracts are also the main reason for the substantial increase in the number of samples in our collection; from 67,000 in 2012, to 195,000 in 2013. We have almost doubled the number of sample derivatives from our collaborative projects within the PMC (Personalised Medicine Consortium), through an increase in patient recruitment for existing studies and the launch of two new projects within the cancer programme.

Another key focus of 2013 has been the investment in areas that make IBBL stand out from other biobanks. One is biospecimen research, as very few biobanks world-wide carry out their own research. Our biospecimen research team has been working tirelessly to determine the best ways to collect, process and store human biological samples and develop quality control assays, and this has led to multiple publications in scientific journals. Another area is the programs successfully run by IBBL in 2013 that are endorsed by the International Society for Biological and Environmental Repositories (ISBER); the Proficiency Testing Programme for biobanks to assess the accuracy and effectiveness of their laboratory techniques, and the Principles of Biobanking continuing education course with the University of Luxembourg. Finally, we strive to become the leading biobank for stool samples, which are extensively used in research into the gut microflora, an area that has been getting a lot of attention as links have been established with many diseases. To this end, our Biorefinery team has been working on the development and validation of automated stool sample processing throughout the year.

Looking ahead, I am particularly excited about the new NCER grant for Early Diagnosis and Stratification of Parkinson’s disease, for which IBBL has submitted a joint proposal with a consortium of national and international research partners. The proposed project would strengthen the partnership between collaborators, increase the visibility of Luxembourg’s biomedical research sector, and, most importantly, potentially have a significant impact on the healthcare for Parkinson’s disease patients. In addition, we will continue to increase our activities over the coming years, by expanding our collection sites to hospitals and pathology laboratories in the Greater Region, expanding our service offer and, hopefully, participating in European consortia funded through Horizon2020 or the Innovative Medicines Initiative (IMI).
Highlights
2013
195,474 biological samples

10,657 donors

8 new service contracts

28 active projects

26 international partners & clients

9 scientific publications
Quality Management System

- 178 active procedures

Proficiency Testing programme

- 90 participants
- 24 countries

Biobanking

- 18 participants
- 10 countries

University Certificate

- 40 articles in the press
- 37 highly qualified staff
IBBL Activities
Overview

Sample Collection & Storage

IBBL has agreements in place with the five major hospitals in Luxembourg (Centre Hospitalier de Luxembourg, Centre Hospitalier Emile Mayrisch, ZithaKlinik, Centre Hospitalier du Kirchberg, Centre Hospitalier du Nord) for the collection of fluid and tissue biospecimens from patients after informed consent has been obtained. In addition, IBBL collects tumour and adjacent healthy tissue from a pathology laboratory in Thionville, France, for internal biospecimen research projects. In 2013, IBBL initiated collection agreements with other pathology laboratories and hospitals in France, Germany, and even in Asia. For the last project, a feasibility study has been carried out to validate logistics and tissue fixation protocols. First samples from all of these new collections are expected to arrive at IBBL in 2014. A support system, which includes the preparation of collection kits and the organisation of logistics and electronic Case Report Forms (eCRFs) that capture clinical data related to the samples, has been put into place. One of the key achievements in 2013 was IBBL’s selection as central biobank for two large European studies. For the BIOMARKAPD project in the EU Joint Programme - Neurodegenerative Disease Research (JPND), IBBL will store cerebrospinal fluid and blood samples for the 25 European collection sites and has already set up a customised web-based IT platform. The second multi-national study is a clinical trial for breast cancer patients recruited from 111 European institutions. IBBL now hosts the extensive collection of blood and tissue samples from this trial. Overall, IBBL’s collection is comprised of over 190,000 samples from more than 10,000 donors.

Sample Processing & Testing

IBBL does not simply store biological samples. For most projects, biospecimens are broken down into their components, processed, characterised and then quality tested. In addition to these standard testing services, IBBL performs specific assays, if desired for a particular study. IBBL routinely processes whole blood, serum, plasma, buffy coat, urine, stool, saliva and tissues. Tissue samples are frozen or formalin-fixed and paraffin-embedded; some are also used for the construction of tissue microarrays. Sample testing services offered by IBBL include histology, immunohistochemistry, nucleic acid quantification and assays for RNA integrity, cell viability or cystatin and creatinin concentration in urine. In addition, the development and validation of new assays and workflows are key components of IBBL’s laboratory activities. In 2013, IBBL’s Biorefinery scientists completed, amongst others, the validation of methods for DNA extraction from stool. Overall, increasing importance is placed on the automation of sample processing. As sample numbers increase, IBBL’s recent investment in high throughput equipment, such as liquid handling robots, and the development of appropriate protocols and assays will prove instrumental in sustaining both efficiency and quality.
**Proficiency Testing**

Proficiency Testing (PT) is a critical part of a laboratory’s Quality Management System (QMS), because it allows laboratories to compare their analytical performance to that of other laboratories using similar methods. Potential problems affecting quality assurance, such as issues with calibration, test interpretation or staff competencies can be identified through PT. It can also fulfil requirements from regulatory bodies in the context of an accreditation process. Each year, IBBL’s PT programme, endorsed by ISBER (International Society for Biological and Environmental Repositories), the largest international forum for multidisciplinary issues relevant to biobanking, IBBL sends a series of blinded samples to participating laboratories, which perform their routine tests. IBBL then assesses the participants’ results against values determined by reference laboratories, and provides a measure of the performance of individual participants, as well as the group as a whole. The 2013 PT programme featured a total of 5 schemes: DNA Quantification and Purity, RNA Integrity, Cell Viability, Tissue Histology, and DNA Extraction Efficiency from Whole Blood. With a growing reputation in the international biobanking community, IBBL’s 2013 PT programme drew a total of 90 participating laboratories from 24 different countries.

**Biospecimen Research**

More than a traditional biobank, IBBL carries out its own research on biospecimens. To be able to ensure that biological samples are of the highest quality, IBBL studies which pre-analytical factors during collection, processing and storage impact sample quality, and how they can be managed. In 2013, IBBL’s biospecimen research team, led by Dr Fay Betsou, worked on over 10 pre-analytics projects. In addition, the team has been collaborating with industrial partners on a number of projects to evaluate and validate new technologies and equipment and develop novel workflows. Many of the pre-analytics projects have led to publications in scientific journals, such as the assessment of lithostatin as a quality control tool for urine sample integrity. Other projects have shown promising early results and are now being expanded, such as the identification of quality control (QC) markers in white blood cells (PBMCs) or for plasma metabolomics. To learn more about biospecimen research at IBBL and these QC projects, read the article “Why every step before analysis matters” on page 20.
IBBL Activities

IBBL is working towards being accredited according to the ISO17025 norm, which describes the general requirements for the competence of testing laboratories. IBBL’s Quality Management System (QMS) is divided into 4 chapters covering all aspects related to the quality of samples and services: General Management, Quality Management, Infrastructure, Operations. At the end of 2013, a total of 178 procedures had been put into place, including 23 new assays protocols and 20 new processing methods. IBBL also completed a successful external audit, with auditors showing full confidence that IBBL is establishing a Quality Management System compliant with the above norms. IBBL’s Quality Manager, Dr Sabine Lehmann, and Chief of Biospecimen Science, Dr Fay Betsou, actively contribute to international standardisation projects in the biobanking field. Appointed as “normalisation delegates” by ILNAS, Luxembourg’s national organisation for normalisation, accreditation and product and service quality, Dr Lehmann and Dr Betsou participate in two ISO committees covering Biotechnology (ISO TC276) and reference materials (for biobanks) (REMCO). Importantly, these committees work on tools and standards for certification and accreditation of biobanks and biobank operations.

Information Technology

IBBL continues the exploitation of an eCRF (electronic Case Report Form) solution for the management of clinical data related to the collected samples. At the end of 2013, eCRFs for 5 studies were operational and fully integrated with the TTP (Trusted Third Party). This TTP ensures confidentiality through “pseudonymisation” of the samples, so that researchers and the biobank do not have access to any personal identifying information. Throughout the year, IBBL’s IT team has been collaborating with LABVANTAGE on the configuration and customisation of a new LIMS (Laboratory Information Management System). A beta version of the LABVANTAGE LIMS was delivered at the end of 2013 and IBBL started its own developments and validation on this version. A final version, customised for IBBL, is expected and will be put in production early 2014. Finally, IBBL also developed a reporting tool, which enables the simultaneous analysis of data from the different databases (eCRF, LIMS etc) and provides summaries on the numbers and types of samples that are stored at IBBL or have been distributed to researchers.

Quality Management

IBBL is seeking certification for ISO9001 and for NF S96-900, a French national norm for the quality of biological resource centres (BRCs) and biological resources. IBBL is also working towards being accredited according to the ISO17025 norm, which describes the general requirements for the competence of testing laboratories. IBBL’s Quality Management System (QMS) is divided into 4 chapters covering all aspects related to the quality of samples and services: General Management, Quality Management, Infrastructure, Operations. At the end of 2013, a total of 178 procedures had been put into place, including 23 new assays protocols and 20 new processing methods. In 2013, IBBL also completed a successful external audit, with auditors showing full confidence that IBBL is establishing a Quality Management System compliant with the above norms. IBBL’s Quality Manager, Dr Sabine Lehmann, and Chief of Biospecimen Science, Dr Fay Betsou, actively contribute to international standardisation projects in the biobanking field. Appointed as “normalisation delegates” by ILNAS, Luxembourg’s national organisation for normalisation, accreditation and product and service quality, Dr Lehmann and Dr Betsou participate in two ISO committees covering Biotechnology (ISO TC276) and reference materials (for biobanks) (REMCO). Importantly, these committees work on tools and standards for certification and accreditation of biobanks and biobank operations.
Public Outreach

Part of IBBL’s role as a research infrastructure consists in engaging the public and increasing their knowledge of biomedical research in Luxembourg. One key component of this venture is a regular stream of press releases, blog articles and posts on social media. In 2013, the local press published 40 articles and media programmes about IBBL’s activities. IBBL expanded its social media presence by doubling the number of followers and page “likes” over the course of the year. In addition, the Media Centre page on IBBL’s website was updated and a new RSS feature was implemented to facilitate the stream of information to stakeholders, the press and the public. Finally, in an effort to increase knowledge about biobanking, IBBL opened its doors to the public on three occasions in 2013. IBBL is also committed to educating and inspiring the younger generations to pursue biomedical science as an interest or even a career. To achieve this, IBBL staff participated in the 2013 Science Festival with an interactive workshop of three activities revolving around different forms of ice and methods of freezing, as employed in a biobank. For the festival, IBBL’s Communication team produced a brochure that explains the principles of biobanking and preservation science to non-scientific audiences, as well as educational videos based on the three experiments.

Biobanking University Certificate

IBBL is dedicated to contributing to education and professional development within the research and biobanking community by sharing knowledge and expertise. This goal is achieved through the training of BSc, MSc and PhD students, and through the “Certificate on Principles of Biobanking for Clinical, Biological and Environmental Biospecimens and Bioresources”. The second edition of this course, which is co-organised by IBBL and the University of Luxembourg took place in June 2013. As the only continuing professional development course of its kind in the world, the course and the certificate are endorsed by the International Society of Biological and Environmental Repositories (ISBER). Taught by international experts, the course covers a variety of topics to provide a strong theoretical background in the science and management of biobanks. In particular, the interdisciplinary teaching of approaches used in repositories for both human and environmental biospecimens gives the course its strength and uniqueness. Additionally, the participants gain hands-on experience in the conservation, storage and processing of biological samples through practical sessions in IBBL’s laboratories. This year’s edition was again successful, attracting participants from 10 different countries including Australia, Germany, Egypt and Qatar. A satisfaction survey conducted at the end of the course showed that 94% of students thought it allowed them to accomplish their objectives and rated the individual modules as good or excellent.
As is the nature of a biobank, IBBL collaborates on the one hand with clinicians for the collection of biospecimens, and on the other hand with the researchers who ultimately use the samples collected, processed and stored by IBBL. Under the umbrella of the Personalised Medicine Consortium (PMC), IBBL works particularly closely with hospitals and research institutes in Luxembourg to help introduce the next generation of healthcare to its citizens. Recognising that international partnerships are key to build a world-renowned centre of excellence in biobanking and biospecimen research, IBBL is continuously expanding its list of international clients and partners. In 2013, IBBL has engaged with several new clients, for whom IBBL delivers biobanking services, including sample collection and storage. In addition, IBBL has worked on establishing close relationships with industry partners worldwide for the evaluation of products and equipment, and the development of novel or optimised workflows.
SWEDEN
- Hospital of Helsingborg
- EU Joint Programme for Neurodegenerative Disease Research (JPND) - BIOMARKAPD
- Denator

LUXEMBOURG
- Centre Hospitalier de Luxembourg (CHL)
- ZithaKlinik
- Centre Hospitalier Emile Mayrisch (CHEM)
- Centre Hospitalier du Nord (CHdN)
- Centre Hospitalier du Kirchberg (CHK)
- Laboratoire National de Santé
- Centre de Recherche Public - Santé
- Luxembourg Centre for Systems Biomedicine
- University of Luxembourg

SWITZERLAND
- TECAN
- PreAnalytiX
- University Hospitals Geneva

FRANCE
- Pathology Laboratory Thionville
- SPLIMS

GERMANY
- Otto von Guericke University of Magdeburg
- Qiagen

ISRAEL
- Novellus

locations of headquarters indicated
In 2013, IBBL was selected for two Europe-wide research projects, one on neurodegenerative diseases and one on breast cancer. Its research support infrastructure and central location in Europe make IBBL a valuable partner for the collection and storage of biological samples from such large-scale international studies.

After the successful participation in and completion of a project from the European Union’s (EU) seventh framework (FP7) programme in 2012, IBBL continued its strategy to partner in pan-European research projects and clinical trials. IBBL’s sustained efforts to build its reputation for providing samples, technologies, project management and logistics, of high quality, bore fruit in 2013, in the form of two new contracts for large international studies.

**Biomarkers for neurodegenerative diseases**

The first project is part of the EU Joint Programme - Neurodegenerative Disease Research (JPND). As a EU member state-led initiative, JPND aims to tackle one of the ‘grand challenges’ our society is facing in the coming years, that of neurodegenerative diseases such as Parkinson’s and Alzheimer’s disease. The programme is the largest global initiative focused on neurodegenerative diseases and brings together research agencies, ministries and centres of excellence from 25 European countries. One major aim of the programme is to improve the scientific understanding of neurodegenerative diseases by promoting research to uncover new genetic and environmental risk factors and assess their interplay. This requires Europe-wide population-based studies, biobanking of DNA and human tissues, and data sharing. To create an enabling environment for neurodegenerative disease research, there is also a need to encourage integration and harmonisation of data and materials, and promote an open-access approach to their use.
In 2013, IBBL was chosen as the sole European biobank to provide the infrastructure necessary for hosting a centralised collection of samples and data as part of the BIOMARKAPD project of JPND. Cerebrospinal fluid and blood samples from 25 European collection sites will be stored at IBBL and made available to the 55 individual members. Besides taking care of the physical storage of biological samples for the project, IBBL has set up a web-based IT platform that captures all data related to the BIOMARKAPD samples stored at IBBL. In addition, this platform gives information on the samples available at the local biobanks of each project partner. Finally, IBBL is also participating in biospecimen research on cerebrospinal fluid samples collected by the consortium and in the development of the BIOMARKAPD Proficiency Testing programme.

Demographic changes mean that neurodegenerative diseases are becoming an ever more important health burden. At the same time, so does cancer, as the second leading cause of death in Europe. In addition to actively supporting cancer research through the projects of the Personalised Medicine Consortium (PMC), IBBL was chosen in 2013 to host an extensive breast cancer collection from a European clinical trial.

**Predicting cancer recurrence to guide treatment decisions**

Although chemotherapy can be a life-saving treatment, it has important side effects. It is therefore essential to be able to identify those patients who will really benefit from the treatment. The MINDACT (Microarray In Node negative Disease may Avoid ChemoTherapy) trial was set up to improve the accuracy of treatment-decision-making in breast cancer patients in order to avoid chemotherapy whenever safely possible. The study’s main objective is to assess the safe use of Mammaprint® to more accurately predict recurrence without affecting patient survival. Commercialised by Agendia, this tool measures the expression (level of activity) of a set of 70 genes to categorise patients into high or low risk of relapse. It is believed that the concomitant use of this type of tool with common clinical and pathological factors will allow clinicians to better select patients needing chemotherapy.

MINDACT is partially supported by the European Commission. It was developed under the TRANSBIG network, a consortium of the Breast International Group (BIG), which is a non-profit network of breast cancer research groups from around the world. The trial is sponsored and coordinated by the EORTC (European Organisation for Research and Treatment of Cancer), the largest independent cancer research organisation in Europe, regrouping over 300 institutions. More than 11,000 patients were screened and 6,600 patients were recruited for this study from 111 European institutions. In 2013, the over 52,000 samples derived from these patients, including tissue, blood and serum, were moved to IBBL for long-term storage.

Being selected for two large-scale European research projects within a year, is clearly a reason to be proud, according to Dr Catherine Larue, Chief Executive Officer of IBBL: “Given that IBBL had been operational for less than four years, it is very satisfying to have been chosen for international studies by prestigious organisations. Given that IBBL had been operational for less than four years, it is very satisfying to have been chosen for international studies by prestigious organisations. We are constantly searching for new avenues to enhance our activities and will be looking to actively partner in European consortia in the coming years.”
Variations in the way biological samples are collected, processed and stored can greatly impact downstream research results. To avoid this and ensure sample quality, IBBL invests in internal biospecimen research. Two flagship projects in 2013 focused on investigating the impact of these variations on blood sample analysis.

High-throughput analyses that facilitate or enable the simultaneous study of thousands of genes, proteins or metabolites, have substantially advanced biomedical research in recent years. Importantly, they have led to the discovery of a number of biomarkers for diagnosis, prognosis or drug response. However, new technologies also bring along new challenges. The large scale of these technologies means that samples from many different patients need to be processed in exactly the same fashion before they are analysed to ensure that observed differences in genes or proteins reflect differences between patients rather than differences in the pre-analytical process. This is especially crucial in biomarker research. Variations in the way in which samples are collected or processed can lead to molecules being misidentified as biomarkers. Similarly, scientists may fail to identify biomarkers if small differences between patients are masked by the variations due to processing.

Tools to assess sample quality

As one of a few biobanks to carry out their own research, IBBL, specifically the team around its Chief of Biospecimen Science, Dr Fay Betsou, focuses on studying the impact of these pre-analytical variations on the down-stream results. One of the team’s main aims is to discover and validate markers for biospecimen quality control (QC). These QC markers are molecules (DNA, RNA, protein, metabolites) that are sensitive to the method of sample collection, processing or storage, allowing researchers to detect when samples have not been handled correctly. QC markers are especially important for biobanks, which need to ensure that their samples are fit-for-purpose, meaning that they have a level of qual-
ity suitable for the specific type of analysis they are intended for. Indeed, the parameters that need to be controlled during processing depend strongly on the type of downstream analysis and the type of sample. In 2013, IBBL’s biospecimen research team focused on two main research projects to determine the best ways to handle and process blood samples.

Camille Bellora completed a project as part of her BSc studies at IBBL, supervised and supported by Dr Olga Kofanova, IBBL’s Biospecimen Research Scientist. The project aimed to investigate what impact pre-analytical variations have on the levels of gene expression (activity) in white blood cells. When a gene is active it produces gene-specific RNA. So gene expression is generally assessed by measuring the amount of specific RNA extracted from the cells. IBBL’s scientists decided to focus on 4 genes and evaluate how different anti-coagulants, temperatures and times before processing affect their expression in white blood cells. Their results show that the expression of these 4 genes starts changing as early as 3 hours after the time blood is taken from the patient. As the time increases, so does the change in gene expression. One gene in particular was strongly activated the longer the processing was delayed, making it a candidate pre-analytical biomarker. In general, the expression of these 4 genes was altered by differences in all of the tested parameters (anti-coagulants, temperatures and delay), underlining the importance of controlling all variables during collection and processing. Dr Kofanova and Ms Bellora are currently validating their initial results in additional samples to determine if that particular gene can indeed be used as a QC marker to identify samples with compromised pre-analytical conditions.

**Time and temperature are critical**

IBBL’s second big pre-analytics project in 2013 is a collaboration with the Metabolomics research group at the Luxembourg Centre for Systems Biology (LCSB). For his joint PhD at IBBL and the LCSB, Jean-Pierre Trezzi studies the effect of pre-analytical variations on blood plasma metabolomics. Metabolomics is a fairly new but exciting field that systematically studies the output of all biochemical reactions in cells by measuring their end-products, so-called metabolites. Being downstream of genomics, transcriptomics and proteomics, metabolomics analyses the final phenotype of a cell. Since metabolites can tell us more precisely what is happening within cells, they are excellent candidate biomarkers. However, they are also less robust and more time-sensitive than genes or proteins, thus making the control of pre-analytical variation even more important. For the collaborative project, blood samples from volunteers were collected and processed at IBBL and the metabolites were analysed at the LCSB by Gas chromatography–mass spectrometry (GC-MS). Jean-Pierre Trezzi’s results suggest that, if researchers intend to study metabolomics on plasma, the blood should be stored on ice immediately after blood collection, in tubes with EDTA as anti-coagulant and be processed within 90 minutes to avoid any detrimental effect on the end results. Indeed, the concentration of 28 metabolites, most of which play a crucial role in the body’s energy metabolism cycle, was altered when samples were stored at room temperature, even for a short time. On the other hand, almost all metabolite levels were stable for up to 90 minutes when stored on ice.

Both of these projects underline the importance of tightly controlling every step a biological sample goes through; from the patient, to the biobank, to the researcher. By implementing the results from biospecimen research into efficient Standard Operating Procedures (SOPs), IBBL can ensure all samples are of high quality and fit-for-purpose.
3

PMC Activities
Overview

Personalised medicine means that patients’ treatment and care are tailored to their individual needs, all the way from diagnosis right up to the specific medication and management of therapy. As our understanding of the underlying causes of diseases has increased, it has become clear that a single approach to treatment for all patients is generally not the best course of action. Because every patient is genetically different, the defects underlying the diseases also vary. By analysing these differences, personalised medicine can help identify patients at an increased risk of developing a disease. Following diagnosis, patients’ genetic profiles can be used to predict whether their disease will progress fast, or help determine which treatment is likely to be most effective.

Recognising the great promise of personalised medicine, the Luxembourgish government decided to invest heavily, leading to the formation of the Personalised Medicine Consortium (PMC) in 2010, with the aim of making Luxembourg a world leader in the adoption of personalised medicine into the national healthcare system. As an initiative to foster collaborative research, the PMC regroups the major hospitals in Luxembourg, IBBL, the Centre de Recherche Public – Santé (CRP-Santé) and the Luxembourg Centre for Systems Biology (LCSB) at the University of Luxembourg. The consortium serves to coordinate research activities between different groups, to encourage sharing of technologies, equipment and information, and to avoid the duplication of effort. The participating institutions currently work hand in hand on various projects in their priority domains: cancer, Parkinson’s disease and diabetes. Moreover, a national cohort study to obtain important demographic information about the development of diseases in Luxembourg is planned and pilot studies are well under way. In addition to providing samples, data, project management and funding for the research projects under the umbrella of the PMC, IBBL acts as the consortium’s administrative home.

Advancing Healthcare in Luxembourg
The Diabetes Programme

The prevalence of diabetes mellitus has been increasing exponentially over the last decade, and diabetes is rapidly becoming a global problem. Current estimates suggest that 6.9% of Luxembourg’s population between 20 and 79 years of age have diabetes. Sadly, this number is projected to further increase. Indeed, international diabetes experts predict that, in the absence of major interventions, 592 million people will live with diabetes by 2035. This constitutes 10% of the global population. Diabetes represents a daily burden to the patients who have to scrupulously watch their diets, monitor their blood sugar levels and administer insulin injections. The disease can also lead to serious complications affecting the eyes, heart, kidneys and feet and is estimated to cause 11% of deaths in Europe. In addition, the increasing number of patients means that diabetes is becoming a growing burden on healthcare systems. In fact, in Germany, about 10% of all healthcare costs are spent on diabetes treatment and care.

While it is clear that both genetic predisposition and environmental factors play important roles in the development of type I and type II diabetes, many of the exact mechanisms underlying its development are still unknown. To improve our understanding of diabetes and identify novel therapeutic and diagnostic approaches, the PMC currently supports three diabetes projects.

In collaboration with the Otto von Guericke University of Magdeburg in Germany and the Luxembourg Centre for Systems Biomedicine (LCSB), IBBL collects, processes and stores fat tissue and purified blood monocyte samples from patients that display multiple risk factors for developing heart disease, stroke or diabetes. This study aims to determine how a lifestyle-mediated weight loss programme can affect a specific type of regulatory molecules (microRNAs), in an effort to identify new therapeutic targets.

The two other diabetes projects investigate if and how the microbial environment in our gut is involved in the onset of diabetes. These national pilot studies were initiated in 2012 and are led by Dr Paul Wilmes, Head of the Eco-Systems Biology Laboratory at the LCSB, and Dr Carine de Beaufort, consultant in paediatric endocrinology and diabetology at the Centre Hospitalier de Luxembourg (CHL).

To find out how our intestinal flora has been linked to a number of diseases and how the two PMC projects plan to address their role in diabetes, read the article “Linking gut bacteria to diabetes” on page 30.
The Parkinson’s Disease Programme

Worldwide, approximately 6.3 million people live with Parkinson’s disease (PD), a chronic and progressive neurodegenerative disease. Even though the risk of developing a neurodegenerative disease increases as we grow older, up to 10% of PD patients are already diagnosed before they turn 50. At the time of diagnosis, PD patients usually exhibit typical motor symptoms including rigidity, tremors and bradykinesia (slowness in initiating movement). However, up to 10-20 years before this, most patients will exhibit problems with their vision, constipation, sleep disorders, or a reduction in their sense of smell. These symptoms are today considered pre-motor risk factors for developing PD. Since PD takes years to develop and progress, the damage to neurons is already extensive by the time motor symptoms appear. In order to treat patients as early as possible, it is imperative that accurate early diagnostic tools or biomarkers are found.

Understanding this urgency, IBBL supports a collaborative project with Dr Nico Diederich, neurologist at the Centre Hospitalier de Luxembourg (CHL) and the Luxembourg Centre for Systems Biomedicine (LCSB) under the leadership of Prof. Rudi Balling. This first PD project within the framework of the PMC aims to verify the hypothesis that dysfunctions in the dynamic properties of mitochondria may be used as a biomarker for PD. IBBL collects blood, colon biopsies or skin biopsies from idiopathic PD patients and healthy donors so that differences in mitochondrial dynamics can be compared in three different tissues: platelets, fibroblasts and neurons.

The collaboration between IBBL, CHL and LCSB, as well as the CRP-Santé, will be further strengthened by their potential participation in the new National Centre of Excellence in Research (NCER) research programme, created by the FNR (Fonds National de la Recherche). Indeed, in collaboration with international experts, members of the PMC have recently submitted an ambitious project proposal to the NCER’s first funding call on the topic of “Early Diagnosis and Stratification of Parkinson’s Disease”.
The Cancer Programme

With approximately 2,400 new cases of cancer diagnosed each year in Luxembourg, cancer remains one of today’s main health burdens, both in terms of personal suffering and healthcare cost. Cancer is responsible for about a quarter of all deaths in the country. Members of the PMC are currently working on several projects to improve diagnosis, treatment and care for Luxembourg’s cancer patients.

Led by Dr Guy Berchem, oncologist at the Centre Hospitalier de Luxembourg (CHL) and Head of the Laboratory of Experimental Hemato-Oncology at CRP-Santé, and Prof. Bruno Domon, Head of the Clinical Proteomics Centre at CRP-Santé, the main aim of the PMC’s cancer programme is to discover, evaluate, and verify biomarkers in the blood or tumour tissue of cancer patients. The PMC’s flagship lung cancer study compares survival between patients that received targeted therapy, based on a set of specific mutations, and those that received standard therapy. To date, about 200 patients have been recruited for the study, a third of which are treated taking into account the results of mutations tests. First results from this long term follow-up study are expected by the end of 2014.

In 2013, IBBL launched two new pilot cancer studies under the umbrella of the PMC, which focus on a direct improvement of patients’ quality of life. For the first new study over 100 patients suspected of having prostate cancer have been recruited with the support of Luxembourg’s urologists. To get a definitive diagnosis for prostate cancer, patients currently have to undergo one, sometimes several, prostate biopsies. In an effort to avoid this, the biobank collects blood and urine samples from patients and performs a novel diagnostic test that is based on the presence of a cancer-specific protein in the urine.

The second new study, led by Dr Stefan Rauh from the Centre Hospitalier Emile Mayrisch (CHEM) is co-financed by the Fondation Cancer and IBBL. Half of the patients in the study use an interactive assessment device to determine if this can improve the management of their chemotherapy side-effects.

To find out how the Bosch Health Buddy helps patients evaluate their symptoms, educates them on their medication and tells them when it is time to seek further medical advice, read the article “An electronic friend to manage chemotherapy side effects” on page 32.
The National Population Cohort Programme

Epidemiological changes in developed countries represent a significant challenge to pensions and healthcare systems. To be able to take appropriate and, if possible, preventive action, it has become increasingly important that governments have access to accurate and up-to-date information about the structure of the population and about the health needs of different subgroups. This is one of the goals behind Luxembourg’s national population cohort, a collaboration between IBBL and CRP-Santé. In addition to monitoring the state of health in Luxembourg’s population and helping prepare the population and healthcare system, the cohort will be an important resource for research. Indeed, the data and samples collected from healthy donors in the scope of a cohort study can serve as control samples for disease-specific studies.

Led by Dr Daniel Witte, epidemiologist at CRP-Santé, the Luxembourg cohort plans to recruit participants over 10 years and is structured into three levels, each one going into more detailed analysis in a subgroup of participants. The cohort will focus on studying healthy development, healthy ageing and integrating new technologies into healthcare. In preparation for the national cohort, IBBL has been collecting a substantial number of healthy donor samples with the support of Dr Marc Keipes from the “Gesondheetszentrum” at the ZithaKlinik. In addition, the biobank works with CRP-Santé on the European Health Examination Survey (EHES), an EU-wide study that aims to provide indicators on major chronic diseases and their risk factors. In 2013, the EHES-LUX study was restructured to be similar to the cohort, to facilitate integration later on. The national cohort itself is currently in the planning phase with protocols, budgets and a business plan drafted in 2013. Meanwhile pilot studies to identify the most appropriate measuring devices were carried out and a series of further targeted pilot projects is planned over the coming year.
Events

Lung Cancer Conference
On 14th & 15th March 2013, IBBL and CRP-Santé organised the second edition of an international lung cancer conference in Luxembourg-Kirchberg. The conference brought together a large number of international expert speakers to discuss recent advances and explore new avenues for lung cancer research in the era of personalised medicine.

PMC Retreat
The 2013 annual PMC retreat took place on 21st & 22nd November in Mondorf-les-Bains, Luxembourg. Coordinated by IBBL, the event gathered around 70 national and international researchers and medical professionals, currently working under the umbrella of the PMC. This year, the PMC was not only joined by its Scientific Advisory Board of international experts, but also by Dr Irene Norstedt, Head of the Personalised Medicine Unit at the European Commission, who presented the EU’s new funding programme “Horizon2020” launched in December 2013.

EUSTM-2013
IBBL supported and participated in the Annual Congress of the European Society for Translational Medicine (EUSTM) & Global Network Conference on Translational Medicine, co-organised by EUSTM and CRP-Santé on 14th & 15th October 2013 in Mondorf-les-Bains, Luxembourg.

EIC
Members of IBBL’s Management Committee participated and presented at the 3rd Euromediag International Convention (EIC) on 5th & 6th July in Montpellier, France. Organised by the French Health Competitive Cluster, the EIC is an international partnering event for technology transfer, business and collaboration in the medical diagnostic sector.
Recent scientific studies have revealed how the billions of bugs in our gut influence our Body-Mass-Index (BMI) and immune system. To establish links between our genes, the bacterial environment in our gut and diabetes, Luxembourg’s researchers have embarked on two pilot research projects.

**Linking gut bacteria to diabetes**
It is widely accepted that a combination of the environment and our genes is responsible for many diseases. In recent years a third player has come to light: the microbiome. This term is used to describe all the microorganisms living in a given environment, for example the human gut. Given that the number of microbial cells far outweighs the number of human cells, it is not surprising that the former actually play an important role in human health. Indeed, over the last five years links between the microbiota in the gut and diseases such as *Clostridium difficile* infections, irritable bowel syndrome (IBS), Crohn’s disease, colorectal cancer and even obesity have been established.

**Diversity affects waistline**

Even though the field of human microbiome research has made major progress, it is still not fully understood how and why these microorganisms cause diseases. However, it seems that the composition of the whole microenvironment and the balance between different species can make the difference between health and disease. This is especially true for the gut, where, the higher the bacterial diversity, the healthier the individual, at least when it comes to his waistline. Indeed, a study by the MetaHIT consortium, published in a top scientific journal, linked reduced diversity in the gut microbiome to obesity and inflammation. The authors reported that individuals with low bacterial diversity in their gut had a higher percentage of body fat, abnormal amounts of lipids in the blood and were more insulin-resistant. The combination of these factors puts these individuals at a higher risk for diseases such as diabetes or cardiovascular diseases. A second study from the same consortium showed that dietary intervention in overweight people improves diversity in some individuals.

These studies underline the great promise of research on the human microbiome, in particular, because it can potentially be modified through intervention (diet, probiotics, fecal transplants). However, before any of these interventions make their way into the clinic, it is important to further elucidate the complex network of interactions between the bacterial communities and human cells. IBBL supports two microbiome research projects, led by consultant in paediatric endocrinology and diabetes, Dr Carine de Beaufort (Centre Hospitalier de Luxembourg, Luxembourg Centre for Systems Biomedicine - LCSB), and research fellow, Dr Paul Wilmes (LCSB). Through different approaches, both of these projects try to identify links between the gut microbiome and diabetes.

The first study tries to find the relationship between the microbiome and the genomic background of people with and without diabetes. To this end, families, where more than one member has diabetes, have been recruited with the help of the Clinical and Epidemiological Investigation Center (CIEC). IBBL has been collecting blood, urine, stool and saliva specimens, which were then processed at IBBL and the LCSB. Using high-throughput technologies, the DNA, RNA and metabolites of human or bacterial origin in these samples are then analysed to compare variations in the human genome and the composition of the microbiome between individuals with and without diabetes.

**How the bacterial environment develops**

The second project, called COSMIC, studies the development and evolution of the microenvironment in the gut of babies to determine how this might influence the development of diabetes later in life. Indeed, children with a low birth weight are at an increased risk to develop chronic metabolic disorders, including diabetes. It is currently not well understood why this is the case, but the way in which the microbiome develops in new-borns might have something to do with it. To identify potential links, the COSMIC study analyses babies’ gut floras at different time points after birth and looks for differences between normal healthy new-borns and new-borns with low birth weight.

IBBL co-funds both projects and collects samples from voluntary participants. In addition, in 2013, IBBL focused on establishing and validating workflows for automated processing of stool samples, in an effort to become THE biobank for microbiome research projects. Dr Catherine Larue, CEO of IBBL, explains: “We understand the great potential our second genome holds, not just for diabetes, but for many other diseases. The microbiome is a fundamental part of IBBL’s strategy in the coming years. Therefore, we are focusing intensely on initiating other microbiome projects and investing in the continuous increase of our expertise.” Looking to the future, Dr Larue further comments: “With the knowledge and expertise at IBBL and the LCSB, we are in a unique position to become a centre of excellence in microbiome research and we will be working hard with our partners to achieve that goal.” In this spirit, IBBL has been chosen among other international candidates to co-organise the 5th International Human Microbiome Congress in Luxembourg from 31st March – 2nd April 2015.
In 2013, IBBL and the Centre Hospitalier Emile Mayrisch (CHEM) started recruiting patients for a new clinical trial, co-financed by the Fondation Cancer. The study will determine if pro-active daily surveillance, using the Bosch Health Buddy©, could lead to better control and management of chemotherapy side effects.

Despite the considerable progress in cancer treatments, most available chemotherapy kills not only tumour cells, but is also toxic to healthy cells. Hence, most patients undergoing these life-saving treatments experience common side-effects including hair loss, fatigue, pain, nausea and diarrhoea/constipation. Many of these side-effects are still unavoidable and it is virtually impossible for clinicians to forecast them on an individual patient basis. Other, generally rarer, complications that affect the circulation, kidney, liver or heart can potentially be quite severe, requiring immediate medical attention.

Judging the severity of symptoms

Out-patient treatment has become the standard of care for chemotherapy but, at home, it can be difficult for patients to determine whether the symptoms they are experiencing are acceptable “normal” reactions to chemotherapy or whether they could be first signs of major side effects that later will warrant hospitalisation. This means that the early signs are sometimes missed and symptoms advance to a point where hospitalisation is unavoidable. Previous studies have determined that in cases
of severe side-effects patients tend to contact their physicians late, possibly because of a mix of resignation and fear of hospitalisation. To address and potentially improve on this issue, the PRO-ELECTS (PROspective randomised ELectronic Evaluation of ChemoTherapy Side effect in oncology out-pa-tients) study was launched in 2013.

The study was initially conceived at the Luxembourg Health Summit in 2012, organised by the Personalised Medicine Consortium (PMC) in partnership with the Ministry of Health. This conference gathered over 50 international and national healthcare and research experts to discuss new initiatives to make Luxembourg a hub for testing and implementing medical innovations. Following the Health Summit, funding for the PRO-ELECTS study was secured from IBBL and a generous contribution of €75,000 from the Fondation Cancer. The study was implemented as a collaboration between IBBL and Dr Stefan Rauh, oncologist at the Centre Hospitalier Emile Mayrisch (CHEM), and patient recruitment started in spring 2013. Recently, this has been expanded to include patients from the Centre Hospitalier Régional Metz-Thionville.

An interactive assessment device

To improve the management of chemotherapy side-effects, half of the 120 patients in the trial will use the Bosch Health Buddy©, on a daily basis between their treatments. This interactive assessment device is programmed with an algorithm developed in collaboration with oncologists and healthcare professionals. It takes patients through a series of questions to evaluate their symptoms, educate them on medication and side-effects and instruct them to seek further medical advice, if required. This approach should ensure that side effects and hospitalisation are minimised, improving patients’ quality of life and ultimately reducing the cost to the healthcare system. The PRO-ELECTS study aims to determine whether the Bosch Health Buddy© is a feasible, cost-effective and beneficial tool for both the patient and the healthcare system so that it can eventually become part of the standard care during chemotherapy.

Participants in the study are also given the option to donate blood to IBBL for future research. However, IBBL’s main role has been to support Dr Stefan Rauh, the principal investigator, with the design and management of the study. Even though such an observational study is beyond the normal limits of a biobank, it underlines IBBL’s commitment in general to support research that could lead to the introduction of new healthcare solutions. The ultimate goal of IBBL and the PMC remains the improvement of patients’ quality of life by personalising, not only diagnosis and treatment, but also patient care.

The ultimate goal of IBBL and the PMC remains the improvement of patients’ quality of life by personalising, not only diagnosis and treatment, but also patient care.
Facts & Figures
Collection Statistics

<table>
<thead>
<tr>
<th>Programme</th>
<th>Cancer</th>
<th>Diabetes</th>
<th>Parkinson’s Disease</th>
<th>Population Studies</th>
<th>Contracts</th>
<th>Biospecimen Research</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donors</td>
<td>462</td>
<td>305</td>
<td>67</td>
<td>2,315</td>
<td>7,331</td>
<td>177</td>
<td>10,657</td>
</tr>
<tr>
<td>Samples (total)</td>
<td>26,196</td>
<td>12,927</td>
<td>2,188</td>
<td>74,023</td>
<td>78,716</td>
<td>1,424</td>
<td>195,474</td>
</tr>
</tbody>
</table>

| Blood and derivatives | 17,926 | 9,633 | 1,927 | 69,331 | 65,928 | 0 | 164,745 |
| Tissue and derivatives | 5,978  | 762   | 261   | 0      | 12,788 | 1,424 | 21,213 |
| Other and derivatives   | 2,292  | 2,532  | 0     | 4,692  | 0      | 0 | 9,516  |

Evolution of sample numbers

Samples per Programme

- 1% Biospecimen Research
- 13% Cancer
- 7% Diabetes
- 1% Parkinson’s Disease
- 38% Population Studies

Blood and derivatives
- 2011: 22,763
- 2012: 60,209
- 2013: 21,211

Tissue and derivatives
- 2011: 4,292
- 2012: 5,436
- 2013: 8,536

Other and derivatives
- 2011: 101
- 2012: 2,016
- 2013: 8,536
1% Parkinson’s Disease
### 2013 Projects

#### Cancer

<table>
<thead>
<tr>
<th>Topic</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomarker validation in lung cancer</td>
<td>Centre de Recherche Public-Santé (CRP-S), 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 (UL), LNS</td>
</tr>
<tr>
<td>A prospective pilot study on the feasibility and clinical evaluation of the PCA3 test in male urology patients in Luxembourg, with constitution of a prostate cancer sample collection</td>
<td>Centre Hospitalier de Luxembourg (CHL) and Luxembourg urologists</td>
</tr>
<tr>
<td>A PROspective Randomised Electronic Evaluation of Chemotherapy Side effects in Oncology Out-patients (PRO-ELECTS)</td>
<td>CRP-S, Centre Hospitalier Emile Mayrisch (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>CIEC (CRP-S), 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</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>CRP-S, 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>
**Biospecimen Research**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biospecimen research project looking at tissue fixation time and type</td>
<td>Laboratoire d'Anatomie et Cytologie Pathologique Thionville, France</td>
</tr>
<tr>
<td><strong>Biospecimen research – Research and validation of micro- and macro-molecular biomarkers for the quality of preservation of biological samples, and the validation of the related methods</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td>Method comparison on RNA integrity</td>
<td>Qiagen</td>
</tr>
<tr>
<td>Intra-individual miRNA stability</td>
<td>Wafergen</td>
</tr>
<tr>
<td><strong>Cell storage – Investigating the effect of storage and shipment conditions on cell viability</strong></td>
<td>ISBER Biospecimen Science Working Group</td>
</tr>
<tr>
<td><strong>Pre-analytical metabolomics</strong></td>
<td>LCSB</td>
</tr>
<tr>
<td>Room temperature storage of whole blood</td>
<td>University Hospitals of Geneva</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, CryoXrtact, Perkin Elmer</td>
</tr>
<tr>
<td>Immunohistochemistry optimisation for PAXgene-fixed, paraffin-embedded tissue</td>
<td>PreanalytiX, Thionville pathology laboratory</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)</td>
</tr>
<tr>
<td>European Health Examination Study extended with local component.</td>
<td>Ministry of Health, EHES, CRP-S</td>
</tr>
</tbody>
</table>

**Contracts & others**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistics, storage and supplies management for an international clinical trial: Target Temperature Management after Cardiac Arrest</td>
<td>CHL, CRP-S, Helsingborg Hospital, Lund University (Sweden)</td>
</tr>
<tr>
<td><strong>Proficiency testing mechanism to standardise the quality control of biospecimens</strong></td>
<td>ISBER and other organisations</td>
</tr>
<tr>
<td>2 projects for PBMC isolation and shipment services for clinical trials</td>
<td>Precision Bioservices</td>
</tr>
<tr>
<td>Long term commercial storage contract for 52,000 samples from a completed European cancer trial.</td>
<td>EORTC, BIG, Institut Bordet</td>
</tr>
<tr>
<td>Wafergen fee for service for miRNA analysis</td>
<td>UL</td>
</tr>
</tbody>
</table>
2013 Scientific Publications

Is There a Protocol for Using the SPREC?
S. Nussbeck, E. Benson, F. Betsou, F. Guadagni, S. Lehmann, N. Umbach
Biopreservation & Biobanking,
Volume 11, Issue 5, Page 260 - 266

Lithostatine Concentration is Not Useful or Assessing the Preanalytical Variations in Biobanked Urine Samples
O. Kofanova & F. Betsou
Biopreservation & Biobanking,
Volume 11, Issue 5, Page 316 - 318

Combined Effect of Tissue Stabilization and Protein Extraction Methods on Phosphoprotein Analysis
O. Kofanova, F. Fack, S. Niclou, F. Betsou
Biopreservation and Biobanking,
Volume 11, Issue 3, Page 161-165

Secretion of Prohormone of B-Type Natriuretic Peptide, proBNP1-108, Is Increased in Heart Failure
JACC Heart Failure,
Volume 1, Issue 3, Page 205-212

The ISBER Biorepository Proficiency Testing Program: Two Successful Years Already, and New Features to Come.
F. Betsou & M.E. Sobel
Biopreservation & Biobanking
Volume 11, Issue 4, Page 255-256

Depletion of proBNP1-108 in Patients with Heart Failure Prevents Cross-Reactivity with Natriuretic Peptides
PLOS ONE,
Volume 8, Issue 9, e75174

Integrating Pathways of Parkinson’s Disease in a Molecular Interaction Map
Molecular Neurobiology,
Volume 49, Issue 1, page 88 -102

Translating Cryobiology Principles into Trans-disciplinary Storage Guidelines for Biorepositories and Biobanks: a Concept Paper
E. Benson, F. Betsou, B. Fuller, K. Harding, O. Kofanova
CryoLetters,
Volume 34, Issue 3, Page 277-312

Identification of Evidence-Based Biospecimen Quality-Control Tools
The Journal of Molecular Diagnostics,
Volume 15, Issue 1, Page 3-16
Change in turnover time
# Profit & Loss Account

## CHARGES

<table>
<thead>
<tr>
<th>Item</th>
<th>2013 (EUR)</th>
<th>2012 (EUR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and development expenses</td>
<td>893,474.96</td>
<td>664,642.00</td>
</tr>
<tr>
<td>Consumption of goods, raw materials and consumables</td>
<td>489,721.95</td>
<td>394,015.34</td>
</tr>
<tr>
<td>Other external charges</td>
<td>1,793,853.88</td>
<td>1,530,100.21</td>
</tr>
<tr>
<td>Salaries and wages</td>
<td>3,013,012.90</td>
<td>2,625,777.50</td>
</tr>
<tr>
<td>Social security on salaries and wages</td>
<td>370,671.76</td>
<td>306,933.70</td>
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</table>

<table>
<thead>
<tr>
<th>Staff costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value adjustments on tangible and intangible assets</td>
</tr>
<tr>
<td>Value adjustments on current assets</td>
</tr>
<tr>
<td>Other operating charges</td>
</tr>
<tr>
<td>Interest and financial charges</td>
</tr>
<tr>
<td>Extraordinary charges</td>
</tr>
<tr>
<td>Profit for the financial year</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total CHARGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,383,684.66</td>
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</table>

## INCOME

<table>
<thead>
<tr>
<th>Item</th>
<th>2013 (EUR)</th>
<th>2012 (EUR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grants</td>
<td>1,740,000.00</td>
<td>9,000,000.00</td>
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<tr>
<td>Other operating income</td>
<td>267,003.97</td>
<td>205,789.47</td>
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<tr>
<td>Other interest and other financial income</td>
<td>69,190.85</td>
<td>65,440.16</td>
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<tr>
<td>Loss for the financial year</td>
<td>5,891,185.98</td>
<td>-</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Total INCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>7,967,380.80</td>
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</tbody>
</table>
# Balance Sheet

## ASSETS

<table>
<thead>
<tr>
<th>Description</th>
<th>2013 EUR</th>
<th>2012 EUR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FIXED ASSETS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible assets</td>
<td>288,436.20</td>
<td>313,842.32</td>
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<tr>
<td><strong>Tangible assets</strong></td>
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<td></td>
</tr>
<tr>
<td>Land and buildings</td>
<td>1,038,328.19</td>
<td>1,229,190.11</td>
</tr>
<tr>
<td>Plant and machinery</td>
<td>1,602,359.11</td>
<td>1,477,734.63</td>
</tr>
<tr>
<td>Other fixtures and fittings, tools and equipment</td>
<td>523,636.18</td>
<td>574,596.23</td>
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<tr>
<td></td>
<td><strong>3,164,323.48</strong></td>
<td><strong>3,281,520.97</strong></td>
</tr>
<tr>
<td><strong>CURRENT ASSETS</strong></td>
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<td></td>
</tr>
<tr>
<td>Trade debtors</td>
<td>83,664.58</td>
<td>227,712.50</td>
</tr>
<tr>
<td>Other debtors</td>
<td>594,350.41</td>
<td>9,420,990.75</td>
</tr>
<tr>
<td>Cash at bank</td>
<td>7,477,104.72</td>
<td>3,955,211.69</td>
</tr>
<tr>
<td><strong>PREPAYMENTS</strong></td>
<td>41,617.29</td>
<td>76,110.07</td>
</tr>
<tr>
<td></td>
<td><strong>11,649,496.68</strong></td>
<td><strong>17,275,388.30</strong></td>
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## LIABILITIES

<table>
<thead>
<tr>
<th>Description</th>
<th>2013 EUR</th>
<th>2012 EUR</th>
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<tr>
<td><strong>EQUITY</strong></td>
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<tr>
<td>Initial Funding</td>
<td>4,000,000.00</td>
<td>4,000,000.00</td>
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<tr>
<td>Profit or Loss brought forward</td>
<td>12,133,792.70</td>
<td>9,351,656.40</td>
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<tr>
<td>Profit of Loss for the financial year</td>
<td>(5,891,185.98)</td>
<td>2,782,136.30</td>
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<tr>
<td><strong>CREDITORS</strong></td>
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<td></td>
</tr>
<tr>
<td>Trade creditors</td>
<td>1,406,889.96</td>
<td>1,141,595.60</td>
</tr>
<tr>
<td>Tax and social security debts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tax debts</td>
<td>4.41</td>
<td>107,938.10</td>
</tr>
<tr>
<td>Social security debts</td>
<td>101,786.71</td>
<td>123,060.99</td>
</tr>
<tr>
<td>Other creditors</td>
<td>196,000.00</td>
<td>62,979.38</td>
</tr>
<tr>
<td></td>
<td><strong>11,649,496.68</strong></td>
<td><strong>17,275,388.30</strong></td>
</tr>
</tbody>
</table>
IBBL Governing Board

Josiane ENTRINGER
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Ministry for Higher Education and Research
Chargée de Mission

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Vice-President
Ministry of Economy and Foreign Trade
Head of the Life Sciences and Technologies Department

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Institute of Pathology Charité Berlin
Molecular biologist / Molecular pathologist

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Alpine Partners AG
Managing Partner

Nadine Catherine MARTIN
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Director Translational Medicine

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Fay BETSOU
PhD, HDR
Chief Biospecimen Science

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MA
Marketing & Communication Manager

Karl-Heinz DICK
MSc
Chief Financial Officer

Marie-Paule HOFFMANN
MA
Senior Assistant / Event Manager

Michel LABORDE
MD
Chief Information Officer

Sabine LEHMANN
PhD
Quality Manager
### IBBL Staff

#### Nationality

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#### Staff Category

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37 highly qualified staff
Excellence
Trust
Integrity
Proactivity
Vision
Collaboration