

2017 ANNUAL REPORT

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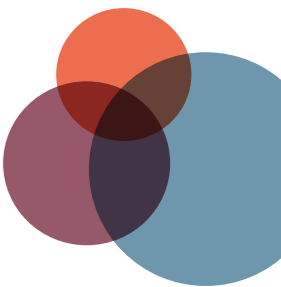
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“We have grown into a fully-fledged research infrastructure, playing a pivotal role both nationally and internationally.”

CATHERINE LARUE
PhD
Chief Executive
Officer

MESSAGE FROM THE CEO

The year 2017 has been eventful, to say the least. We could define it as the year of evolution towards a stronger corporate identity. The winds of change have pervaded every aspect of IBBL's operations, from our activities to our people. Not even the management has been immune to it. It is my pleasure to briefly walk you through the major milestones of the year and give you a taste of the surprising achievements you will encounter throughout the report.

As had been anticipated over the last couple of years, IBBL needed a larger 'shell'. We had grown to an extent that simply required more space. The milestone came in November 2017, when we relocated our entire staff and operations from Luxembourg City to Dudelange. The new facilities open up a wealth of new opportunities, owing to the tenfold increase in storage capacity and the doubling in floor area, allowing us to expand our services. Needless to say that the smooth transition was enabled by the impeccable organisational work of our team.

From the quality perspective, we witnessed the international approval of the ISO/DIS 20387 biobanking standard draft and made important steps forward in our contribution to the development of the draft ISO/AWI 21899 norm. Indeed, the standardisation of biobanking practices is one of our top priorities, which we have been nursing and working on for several years. Owing to our increased space, we were also in a position to start all necessary actions to become an authorised GMP storage infrastructure, which will allow us to store human cells and tissues for therapeutic applications.

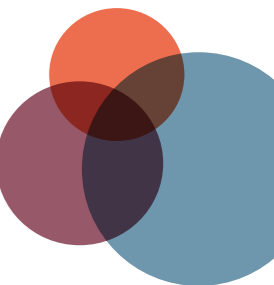
We keep two main fields of action in mind in everything we do, in line with our two strategic objectives: the national and the international dimensions. At the local level, IBBL has been a longstanding partner of all major Luxembourgish research actors, lending its expertise to support advances on Parkinson's Disease (NCER-PD), Personalised Medicine (through the Personalised Medicine Consortium of Luxembourg) and Cancer (under the National Cancer Plan). We are particularly proud of our partnership with the University of Luxembourg, the Luxembourg Institute of Health (LIH) - of which IBBL is a part - the Luxembourg Centre for Systems Biomedicine (LCSB) and the National Health Laboratory (LNS) in the SOCS project, which saw the discovery of a new colorectal cancer biomarker in 2017.

At the European level, IBBL has been nurturing numerous relationships with international players, which resulted in our participation in the consortia of several EU-funded projects. One such instance is SPIDIA4P, under which IBBL is leading the activities to develop and implement External Quality Assessment schemes, with a view to bring about the standardisation of the pre-analytical workflows applied to personalised medicine. We are honoured to have been recognised among other EU partners for our expertise in this field.

We also pride ourselves on being one of the few biobanks that carries out biospecimen research. This year again, our team of devoted scientists has reaped the fruits of their hard work, having discovered two markers that will allow researchers to assess the quality of their biological samples.

All in all, 2017 could not have been a better time for me to retake the reins of IBBL. I extend my heartfelt gratitude to Marc Vandelaer for his dedication and leadership in my absence, to the Ministry of Higher Education and Research for its unwavering support and, most importantly, to all the IBBL staff, both the research and administrative teams, for their passion and commitment. As much as we enjoy the start-up flair of our institution, we now have to accept the fact that we have grown into a fully-fledged research infrastructure, playing a pivotal role both nationally and internationally. As such, we cannot rest on our laurels, but we need to keep delivering on our promises, particularly in light of the renewed 2018-2021 performance contract with the Ministry. Looking forward, 2018 will see the relocation of the samples currently hosted in various partner organisations to IBBL, as well as the continuation of our activities to strengthen our European presence through collaborations and participation in EU consortia. We will also be pursuing our accreditation and certification efforts to uphold our position as a quality-driven biobank. Finally, 2018 will mark the tenth anniversary of IBBL's foundation... Another busy year ahead!

CATHERINE LARUE
Chief Executive Officer



A MOVE FOR THE BETTER

In November 2017, IBBL relocated its entire staff and operations from Luxembourg City to a permanent location in Dudelange. The precision and rigour of the underlying management ensured a seamless transition. The newly built facilities, in the Laboratoire National de Santé (LNS) building Phase 2, boast a 2,000 m² floor area and a storage capacity of about 5 million samples. The bespoke building is already allowing IBBL to expand its operations and service offering.

No longer a 'start-up'

A prefabricated building and 6 visionary scientists. That was IBBL at its inception in early 2010, perfectly embodying the spirit of the budding life-science community in Luxembourg. However, the significant success it achieved in just a few years and the remarkable growth of its activities meant that a larger building was needed to sustain the biobank's development in the medium term. It was time to look forward and make a move...literally! In 2015, having recognised this need, the Ministry of Health and the Ministry of Higher Education and Research offered IBBL the opportunity to move permanently to Dudelange into a building then under construction. Fast-forward to November 2017, the relocation of IBBL's staff, equipment, samples and operations was completed. "Moving from a temporary building to permanent facilities shows that IBBL is no longer a "start-up": IBBL has grown into an established player in the Luxembourgish and

European scientific landscapes. Our new high quality facilities are witness to that", proudly states Dominic Allen, Chief Operating Officer at IBBL. The new LNS Phase 2 building, shared with the Laboratoire de la Médecine Vétérinaire de l'Etat and the LNS itself, further strengthens IBBL's ties with these two national research players.

A rigorous project plan

The rigour and precision that characterise IBBL's approach to the management of scientific projects were also evident in the way the relocation to Dudelange was handled. The move was treated as a project in its own right, with its own project manager and associated project management methodology. A first plan was written in May 2017, detailing the main steps involved, the individual sub-tasks to be performed and the respective responsible actors.

Weekly meetings among members of the project team also took place from the beginning, together with regular site visits to ensure the construction works were advancing as planned. "It was truly a 'crowd move'", comments Estelle Sandt, the Project Manager at IBBL responsible for the move. "The drawings of the new building were made available to the entire staff well in advance, giving everyone the chance to familiarise themselves with the changes and be actively involved throughout the entire process". In addition, a quality plan was established and a risk assessment carried out, allowing the identification of risks and the implementation of related preventive actions. This resulted in a comprehensive and solid move plan, stemming from the close cooperation between IBBL's biorefinery, biorepository, IT, quality and marketing and communication departments. The move took place in two phases. In October 2017, the biorepository, with its freezers and liquid nitrogen tanks, was the first to be relocated, with IBBL staff and laboratory equipment following suit in November.

A specialised moving company ensured the integrity and safety of the 500,000 samples throughout the move, by using trucks with generators to power the freezers and maintain the appropriate temperature. For an additional level of security, the Luxembourgish police escorted the biospecimens.

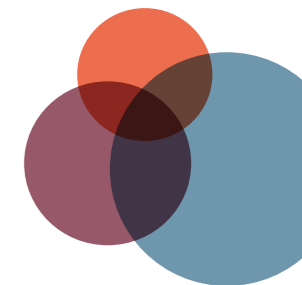
A seamless transition

Such a momentous change has its risks. However, the meticulous planning bore its fruits. The move proved to be a smooth process, with no significant service interruptions and no damage caused to any of IBBL's samples or equipment. Given the significant impact of such a change on its operational infrastructure, IBBL voluntarily suspended its ISO 17025:2005 accreditation, but its Quality Management System (QMS) continued without interruption. Not only was the process seamless, but also efficient - all staff and laboratory equipment were relocated in 4 days, 1 day ahead of schedule. "Preserving sample integrity during the move was of course our number one priority, but making sure the staff was happy was a close second!", explains Estelle Sandt. "Client satisfaction is paramount, but so is that of our people. Without their buy-in and cooperation, none of it would have been possible". A move survey was in fact part of the plan, reporting that 8 in 10 people were satisfied or very satisfied with the move and its internal communication.

'Building' new opportunities

The idea behind the move being to increase IBBL's service capacity, it was pivotal to ensure that the operational needs of its departments were translated into architectural and technical specifications. "The public buildings administration (ABP) and all the architects and technical design offices working for them have done a very good job in adapting the design of the building to our requirements", comments Dominic Allen. A good example is the installation of a lift entirely dedicated to the transport of samples from the biorepository department on the first floor to the biorefinery on the third, not initially foreseen in the original design.

The completed building boasts a total area of 2,000 m², of which 500 m² for the biorepository alone and 1,000 m² for the laboratories. This represents a doubling in floor area compared to the previous facilities and a tenfold increase in storage capacity, meaning that IBBL is now able to accommodate up to 5 million biospecimens, compared to the previous capacity of 500,000. The new building also provides additional space for new equipment, new facilities such as a walk-in freezer room and more automation in the laboratory. Moreover, it has enabled IBBL to separate its laboratories according to different activities, such as DNA and RNA extraction, to prevent cross-contamination. "Thinking that all our biorepository activities alone used to be performed in a single 90 m² room really puts the importance of the move into perspective" states Katy Beaumont, Biorepository Team Leader at IBBL. "The flexibility that comes with the new facilities is already enabling IBBL to expand its operations and services to support an increasing number of partners and clients internationally". Indeed, IBBL is preparing to become compliant with GMP storage regulations for the storage of stem cells for use in therapeutic applications (see chapter "A pioneer in quality and standardisation").



“We are delighted that IBBL could contribute to the advancement of biobanking operations.”



SABINE LEHMANN
PhD
Quality Manager

A PIONEER IN QUALITY AND STANDARDISATION

2017 was marked by four important steps with regard to quality. Internationally, the ISO/DIS 20387 biobanking standard draft was approved and the draft ISO/AWI 21899 norm published. Internally, IBBL successfully passed the recertification audit for ISO 9001:2008 and started preparing to become an authorised GMP storage infrastructure.

International collaboration

Since 2013, IBBL has been working with international experts on the development of dedicated biobanking norms. Specifically, IBBL's Quality Manager Dr. Sabine Lehmann and project co-leader Dr. Georges Dagher contributed to the elaboration of the official 'new work item proposal' (NWIP) for the ISO 20387 biobanking standard. The document, being devised under Working Group 2 of the ISO technical committee TC 276 'Biotechnology', has been conceived as an 'umbrella standard' detailing the general requirements for biobanking, under which other more specific standards will be elaborated. The year 2017 saw the collaborative efforts of the working group's 150 experts pay off, with the Draft International Standard (ISO/DIS 20387) being released in July to the international community for voting and comments. The result of the ballot was an almost unanimous approval. "We could not be more satisfied with this outcome! Not only does the vote highlight the international dimension of the approval of the document, but it also further proves the case for developing a tailored biorepository standard. We are delighted that IBBL could contribute to the advancement of biobanking operations", comments Dr. Lehmann.

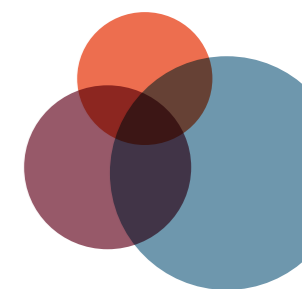
Standards... and more standards!

This strong international cooperation has also been paving the way towards the development of yet another ISO standard. Indeed, Dr. Fay Betsou, Chief Science Officer at IBBL, has brought her experience to the conception of the draft version of ISO/AWI 21899, a complementary norm aiming to establish the general requirements for the validation and verification of processing methods for biological material in biobanks. The draft document was prepared and revised in November 2017, and will undergo a similar ballot once finalised. "The work of the international biorepository community towards the standardisation of its activities must go on. We are making enormous progress in terms of ensuring the quality and fitness-for-purpose of biospecimens through evidence-based

experimental method validation. However, being accredited and certified to existing norms is not of itself enough. We would like to see the development of international biobanking technical standards supporting improved reproducibility of research results", explains Dr. Betsou.

A biobank like no other

Having a solid Quality Management System (QMS) in place pays off in every respect. Not only does it build customer trust, but it also allows IBBL to expand its activities. In 2017, work started on ensuring compliance with Good Manufacturing Practices (GMP), according to the Grand-Ducal Regulation of 30 August 2007 determining technical requirements for the distribution, procurement and control of tissues and cells of human origin (which is in turn based on EU Directive 2004/23/EC). Compliance with this legislation will enable IBBL to offer a new type of service, namely the storage of human cells and tissues to be used in downstream therapeutic purposes ("GMP storage"), adding to the traditional biobanking service of tissue and cell storage for research applications. This will allow IBBL to become an authorised GMP storage infrastructure (known as an authorised "tissue bank") and be positioned at the interface between research and the clinic. In practical terms, 2017 saw the extension of IBBL's QMS to address customer needs, as well as the purchase of the relevant equipment and the design of dedicated storage facilities in the new building to fully align with GMP storage requirements.



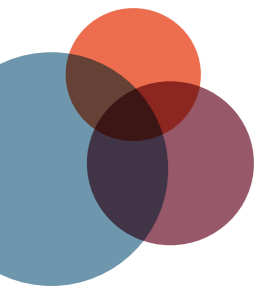
Quality is particularly critical when it comes to the storage of samples of human origin for therapeutic applications, due to the potential repercussions on human health, therefore requiring the repository room to possess a specific ventilation system to keep it isolated and impeccably clean. “The storage of human cells and tissues according to GMP requires a very complex QMS and is not an activity that biobanks typically pursue. However, our QMS was mature enough, requiring only a few modifications to be compliant, so it felt like a natural progression of our activities”, explains Dominic Allen, Chief Operating Officer at IBBL.

Client satisfaction in our DNA!

Finally, the year ended with an additional achievement to put under the belt. In Q3 2017, IBBL successfully passed the recertification audit for ISO 9001:2008 (quality management systems - requirements) at the conclusion of the third surveillance year, with its entire QMS being reassessed. The certification was issued by the TÜV Rheinland group in December 2017. “ISO 9001 is an appropriate standard for the certification of a biobank’s QMS, since it ensures the consistency of its core processes. As a highly customer-oriented institute, IBBL wants to officialise its dedication to client satisfaction and continuous improvement. Obtaining the recertification is therefore an earned recognition of our efforts”, states Dr. Betsou.

The future through the ‘quality lens’

Looking forward, prospects for IBBL in terms of quality are bright, with the Final Draft International Standard (ISO/FDIS 20387) set to be released for voting in Q2/2018. Moreover, in line with the requirements of the national legislation, IBBL will seek authorisation from the Luxembourg Ministry of Health in 2018 to become an authorised GMP storage facility (“établissement de tissus”). Finally, the ISO 17025:2005 reaccreditation audit will take place in Q1 2018.



“We will now be able to determine whether the quality of samples with undocumented preanalytics, such as historical collections, is good enough to allow their use in downstream research applications.”

FAY BETSOU
PhD, HDR
Chief Scientific Officer



DIAGNOSING SAMPLE ‘HEALTH’

In 2017, IBBL’s Biorefinery Department took yet another step forward in advancing biospecimen research. The team published the results of a study that identified and validated two cytokine biomarkers to be used as an assay to evaluate the quality and fitness for purpose of serum and plasma samples. This discovery bears important implications for the accuracy and reliability of downstream biomedical research.

No precision preanalytics, no precision medicine

It is nowadays universally acknowledged that the success of biomedical research and precision medicine requires precision preanalytics. When preanalytical variables – parameters that influence the sample before it is processed – are unknown and uncontrolled, they can negatively affect the accuracy and reproducibility of downstream analytical results. When it comes to serum, plasma and peripheral blood mononuclear cells (PBMCs) – white blood cells containing one nucleus, such as lymphocytes and macrophages – some of the most critical variables include pre-centrifugation conditions, namely the temperature and time during which the blood cells have been in contact with plasma prior to being centrifuged. Indeed, prolonged pre-centrifugation times, particularly at room temperature, mean greater chances of protein degradation, extended metabolic activity in the blood cells and ensuing oxygen depletion, in turn leading to a series of alterations within the sample, with repercussions on its quality attributes. IBBL’s Biorefinery Department, led by Dr. Fay Betsou, has therefore been actively investigating ways to assess the pre-centrifugation times of biospecimens of undocumented preanalytical history. In 2017, the team made a significant discovery that will enable the objective qualification of biological samples.

Qualifying serum and plasma

The challenge that the IBBL Biorefinery team embarked on was to identify an easy and reliable way to assess whether serum and plasma samples had been subject to long pre-centrifugation times, in the order of magnitude of 24 hours. Such delays have an impact on the downstream quantification of several proteins and metabolites in the serum and plasma. By leveraging on simple and readily available ELISA kits, Dr. Olga Kofanova, Biospecimen Quality Team Leader at IBBL and project coordinator, together with Estelle Henry, successfully devised an accurate method to address this research question. They screened twenty cytokines – cell signaling

proteins that regulate several biological functions including immunity and inflammation – in serum and plasma samples for variations in their concentration as a result of extended pre-centrifugation delays at room temperature.

Two cytokines, namely interleukin 8 (IL-8) and interleukin 16 (IL-16), showed the largest changes in concentration. These were subsequently validated for their ‘diagnostic ability’ to detect serum or plasma samples altered by significant pre-centrifugation delays. The validation was performed on 7 independent sample collections from both healthy and diseased donors, in close collaboration with members of the ISBER Biospecimen Science Working Group. “Our work allowed us to identify the two most promising cytokine markers to be used in the characterisation of pre-centrifugation delays of over 24 and 48 hours. We can now offer a robust and accurate quality control tool to diagnose the ‘preanalytical health’ of serum and plasma samples”, explains Dr. Kofanova. “We will now be able to determine whether the quality of samples with undocumented preanalytics, such as historical collections, is good enough to allow their use in downstream research applications” adds Dr. Betsou.

In parallel, Dr. Kofanova and Camille Bellora have been working on a related assay focusing specifically on the assessment of the quality of PBMC samples. The research looked at the ratio of the expression of two target genes, namely IL-8 and EDEM3, as an indicator of pre-centrifugation delays. The results of the study will be published in 2018 and are set to revolutionise PBMC sample qualification for downstream applications such as gene expression and functional assays, in turn enabling new and more accurate insights into disease mechanisms and experimental immunology.



CHRISTELLE BAHLAWANE
PhD
Project Manager

“We are delighted that the sample collection set up at the national level has been put to the service of Luxembourgish researchers to feed additional colorectal cancer studies. It is exactly what it was intended for!”

COLORECTAL CANCER: A NATIONAL PRIORITY

IBBL works in close collaboration with national players to support research across a variety of areas, from Parkinson's Disease (under the National Centre for Excellence in Research in Parkinson's Disease) to personalised medicine (through the Personalised Medicine Consortium of Luxembourg) and cancer (under the National Cancer Plan). An instance of successful cooperation is the SOCS (Suppressor Of Cytokine Signaling) project which saw the discovery of the protein MYO5B as a colorectal cancer biomarker in 2017.

A winning partnership...made in Luxembourg

The concerted action against colorectal cancer (CRC) in the Grand Duchy started back in 2011 when researchers from the University of Luxembourg, clinicians and IBBL launched the SOCS (Suppressor Of Cytokine Signaling) study, supported by the Fondation Cancer. Led by Prof. Serge Haan and Dr. Elisabeth Letellier from the Life Sciences Research Unit at the University of Luxembourg, the SOCS study revealed that two members of the SOCS family of proteins*, namely SOCS2 and SOCS6, can serve as diagnostic biomarkers to help the early-stage diagnosis of CRC. Since then, the vast sample collection created under SOCS has given life to a variety of new projects in collaboration with researchers from the Luxembourg Institute of Health (LIH) and the Luxembourg Centre for Systems Biomedicine (LCSB), in a joint effort to further elucidate the mechanisms of CRC and its links to diet and environmental factors such as pesticides. In 2017, the National Health Laboratory (LNS) also joined the SOCS study team, further reinforcing the national collaborative efforts and providing increased opportunities to collect samples from local hospitals.

Three cheers for Luxembourgish research

In 2017, the SOCS project yielded a remarkable result. Based on the collection of tumor samples originating from several Luxembourgish hospitals, such as the Centre Hospitalier Emile Mayrisch (CHEM) and the Centre Hospitalier de Luxembourg (CHL), Prof. Haan and Dr. Elisabeth Letellier identified a new prognostic CRC marker, bringing the number of discovered CRC biomarkers to three. Namely, protein MYO5B of the Myosin V family – a group of proteins involved in cell trafficking and polarisation – was found to have a high potential for the identification of a patient's risk of relapse. The team used

a previously conducted meta-analysis of publicly available gene expression data to analyse the expression of different members of the Myosin V family, specifically MYO5A, 5B, and 5C, in CRC. Subsequently, an independent study was also performed on the Luxembourgish patient cohort. Together, the two studies revealed that the expression and, consequently, the concentration of MYO5B decreases as the disease progresses. Specifically, CRC patients with low MYO5B expression were found to report a weaker chance of survival. “The prognostic ability of MYO5B is especially valuable in the early stages of CRC, helping clinicians match patients with the most effective and appropriate treatment options”, explains Prof. Haan. “The strength of the study lies in the joint effort of an interdisciplinary team of partners, involving bioinformatics and state-of-the-art experimental techniques. Our discovery further consolidates Luxembourg's reputation as a centre of excellence in cancer and biomedical research in general”, adds Dr. Letellier, principle investigator of the study. The research team is currently in the process of applying for funding for a proof of concept to validate the new MYO5B prognostic biomarker, together with IBBL, and bring it to market. The validation will be the object of the dedicated MyoRPROG project.

A coveted collection

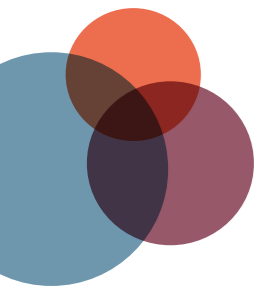
IBBL played an important role in the SOCS project. Working in close cooperation with the other partners, IBBL contributed to establishing an independent cohort of CRC patients. It oversaw all the steps involved in the collection of tumour samples from various Luxembourgish hospitals - 75% of which originating specifically from the CHEM - as well as the storage and redistribution of the specimens and associated medical data.

*SOCS proteins have been recognised for their tumor-suppressor and anti-inflammatory functions

The collection subsequently allowed the researchers from the University of Luxembourg and IBBL to reconfirm the initial results. The collection is of very high value looking ahead, as it sets the foundations for the other research projects on CRC and for the identification of new prognostic biomarkers. “The quality of the samples is the key factor, particularly for this type of research, where the outcome depends on the accuracy of the measurements of very small molecular variations between healthy and malignant tissues”, explains Dr. Christelle Bahlawane, IBBL project manager in charge of SOCS and MyoRPROG. “We are delighted that the SOCS collection has been put to the service of Luxembourgish researchers to feed additional CRC studies. It is exactly what it was intended for!”. Indeed, the collection will be used for the future validation of the novel MYO5B biomarker under the MyoRPROG project.

The road to biomarker validation

The SOCS project illustrates an important concept. The discovery of a biomarker alone does not guarantee its use in a clinical setting, and therefore needs to be supported by a rigorous validation process. This is where IBBL adds value to studies such as MyoRPROG. “By carrying out all the steps of early validation for its partners and clients, IBBL helps assess the robustness of the biomarker, its precision, specificity, sensitivity and stability”, explains Dr. Monica Marchese, Biomarker Validation Scientist at IBBL. Clinical verification – a pilot study on a small sample size to evaluate the performance of the biomarker in a clinical setting – is also performed. “Ultimately, the goal is to develop a test that can one day be used clinically”, she adds. In the case of the MyoRPROG project, such a test could be based on the combined expression of the MYO5B gene and of another CRC-related gene (RAB8A). This could assist oncologists in their post-surgical decision about the need for chemotherapy in early stages of colorectal cancer, as well as in the follow-up of high-risk patients.



THE EXTERNAL QUALITY ASSESSMENT (EQA) PROGRAMME PROVIDER TO EU CONSORTIA

Aside from supplying traditional biobanking services to EU consortia, IBBL has increasingly been strengthening its position as the EU provider of external quality assessment (EQA) schemes through its participation in several EU-funded projects. In 2017, another opportunity to share its expertise in this area saw its official kick off - the project SPIDIA4P (Standardisation of generic Preanalytical Procedures for In vitro DIAgnostics for Personalised Medicine), aiming to promote the standardisation of biobanking operations.

AMÉLIE GAIGNAUX
PharmD, PhD
Project Manager

“Standardising procedures is crucial if we want to reduce the incidence of irreproducible pre-clinical and clinical research results and diagnostic mistakes.”

A double priority

IBBL is one of the few biobanks that carries out biospecimen research and develops quality control assays to ensure that biological samples are suitable for their intended downstream purposes. As such, one of its main matters of concern is the contribution to the standardisation of biobanking practices through the development of global technical standards that will guarantee reproducible results (see the success story 'A pioneer in quality and standardisation'). This also reflects another one of IBBL's priorities, namely its inclination towards the international dimension and willingness to put its expertise at the service of the European scientific community. Indeed, IBBL is striving to consolidate its EU-wide contributions by offering international Proficiency Testing (PT) programmes supporting the various biobanking technical standards. This dual priority culminated in an important achievement.

A natural match

The year 2017 saw the concretisation of an ideal opportunity, in line with IBBL's dedication to standardisation and its European outreach. In January 2017, the SPIDIA4P project kicked off, with IBBL counting among its consortium partners. SPIDIA4P (Standardisation of generic Preanalytical Procedures for In vitro DIAgnostics for Personalised Medicine) is a 48-month support and coordination action funded by the European Commission under the Horizon 2020 programme. It seeks to initiate, develop and implement a comprehensive portfolio of 20 pan-European CEN* Technical Specifications (CEN/ TS) and ISO International Standards (ISO/IS) documents, as well as corresponding external quality assessment schemes (EQAs). These TS - normative

documents in areas where the actual state of the art is not yet sufficiently established for a European Standard - cover the pre-analytical workflows applied to personalised medicine, from documentation of patient information to sample collection, transport, processing and storage. They will also be applicable to research such as biomarker discovery and validation, as well as to biobanks, thus being a topic of particular interest and relevance for IBBL. SPIDIA4P is the follow-up of the earlier SPIDIA project, which set the foundation for the development and introduction of the first CEN/TS for pre-analytical workflows in Europe and for their progress to ISO standards. "Standardising procedures is crucial if we want to reduce the incidence of irreproducible pre-clinical and clinical research results and diagnostic mistakes", comments Amélie Gaignaux, Project Manager at IBBL. "Our participation in this consortium of highly experienced partners could not be a better fit for us. The standardisation of biobanking practices at the European and international level is one of our top priorities".

Quality pre-analytical workflows

As the leader of Work Package 2 (WP2), IBBL's role in SPIDIA4P revolves around the development and implementation of external quality assessment (EQA) schemes that will accompany the pre-analytical procedures. The EQAs will assess the efficiency of sample preparation methods in terms of the quality of the resulting samples, to be used for downstream diagnostic or research purposes.

*CEN : European Committee for Standardisation

Specifically, IBBL's long-standing expertise as the sole provider of Proficiency Testing (PT) programmes for biobanks, entirely dedicated to biospecimens, proves to be an asset for the activities of WP2. IBBL's PT programme – endorsed by the International Society for Biological and Environmental Repositories (ISBER) – acts as an EQA research tool for a variety of institutions handling biological samples (laboratories, biorepositories, etc.), allowing them to validate their routine processing and analytical methods, compare their performance to that of others, comply with normative requirements and strengthen their credibility and visibility. Notably, IBBL has developed both a series of 'processing schemes', which allow the verification and benchmarking of the performance of biospecimen processing methods, as well as 'analytical schemes', focusing on the accuracy of the measurements made to qualify the specimens.

Given its proven effectiveness, IBBL's existing PT programme will provide the basis for the development and deployment of new PT schemes for pre-analytical processing methods. Some of IBBL's existing schemes that will be enriched by the consortium include DNA and RNA isolation from whole blood samples, DNA extractions from saliva and stool, as well as DNA and RNA isolation from FFPE (formalin fixed and paraffin embedded) samples. Proficiency Testing schemes on liquid biopsies previously developed by IBBL under the project CANCER-ID – namely isolation of circulating cell-free DNA, circulating cell-free RNA and circulating tumour cells from whole blood – will be used 'as is' by SPIDIA4P.

"We are honoured that the efforts we put in conceiving, deploying and refining our PT schemes have been recognised at the EU level and that our work will be able to feed the activities of SPIDIA4P", states Olga Kofanova, Biospecimen Quality Team Leader at IBBL.



“We are honoured that the efforts we put in conceiving, deploying and refining our PT schemes have been recognised at the EU level.”

SCIENTIFIC PUBLICATIONS

Biospecimens and biobanking in global health

Mendy M, Lawlor RT, van Kappel AL, Riegman PHJ, Betsou F, Cohen OD, Henderson MK.
Clinics in Laboratory Medicine, Volume 38, Issue 1, Pages 183-207

IL8 and IL16 levels indicate serum and plasma quality

Kofanova O, Henry E, Quesada RA, Bulla A, Linares HN, Lescuyer P, Shea K, Stone M, Tybring G, Bellora C, Betsou F.
Clinics in Laboratory Medicine, doi: 10.1515/cclm-2017-1047

Random and independent sampling of endogenous tryptic peptides from normal human EDTA plasma by liquid chromatography micro electrospray ionization and tandem mass spectrometry

Dufresne J, Florentinus-Mefailoski A, Ajambo J, Ferwa A, Bowden P, Marshall J.
Clinical Proteomics, Volume 14, Issue 41 (IBBL acknowledgement)

The proteins cleaved by endogenous tryptic proteases in normal EDTA plasma by C18 collection of peptides for liquid chromatography micro electrospray ionization and tandem mass spectrometry

Dufresne J, Florentinus-Mefailoski A, Ajambo J, Ferwa A, Bowden P, Marshall J.
Clinical Proteomics, Volume 14, Issue 39 (IBBL acknowledgement)

Loss of Myosin Vb in colorectal cancer is a strong prognostic factor for disease recurrence

Letellier E, Schmitz M, Ginolhac A, Rodriguez F, Ullmann P, Qureshi-Baig K, Frásquilho S, Antunes L, Haan S.
British Journal of Cancer, Volume 117, Issue 11, Pages 1689-1701

Freeze-dried plasma proteins are stable at room temperature for at least 1 year

Dufresne J, Hoang T, Ajambo J, Florentinus-Mefailoski A, Bowden P, Marshall J.
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Distinct metabolomic signature in cerebrospinal fluid in early Parkinson's disease

Trezzi JP, Galozzi S, Jaeger C, Barkovits K, Brockmann K, Maetzler W, Berg D, Marcus K, Betsou F, Hiller K, Mollenhauer B.
Movement Disorders, Volume 32, Issue 10, Pages 1401-1408

Multidisciplinary quality assurance and control in oncological trials: Perspectives from European Organisation for Research and Treatment of Cancer (EORTC)

Members of EORTC QAC, Working Groups of Scientific Experts (Betsou F. as collaborator for Luxembourg)
European Journal of Cancer, Volume 86 (Supplement C), Pages 91-100

High-Throughput Processing to Preserve Viable Cells: A Precision Medicine Initiative Cohort Program Workshop

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Betsou F.
Biobanking of Human Biospecimens: Principles and Practice. Springer, Pages 23-49

Biobanks as producers of reference materials

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RNA sequencing and transcriptome arrays analyses show opposing results for alternative splicing in patient derived samples

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Colonization and succession within the human gut microbiome by archaea, bacteria and microeukaryotes during the first year of life

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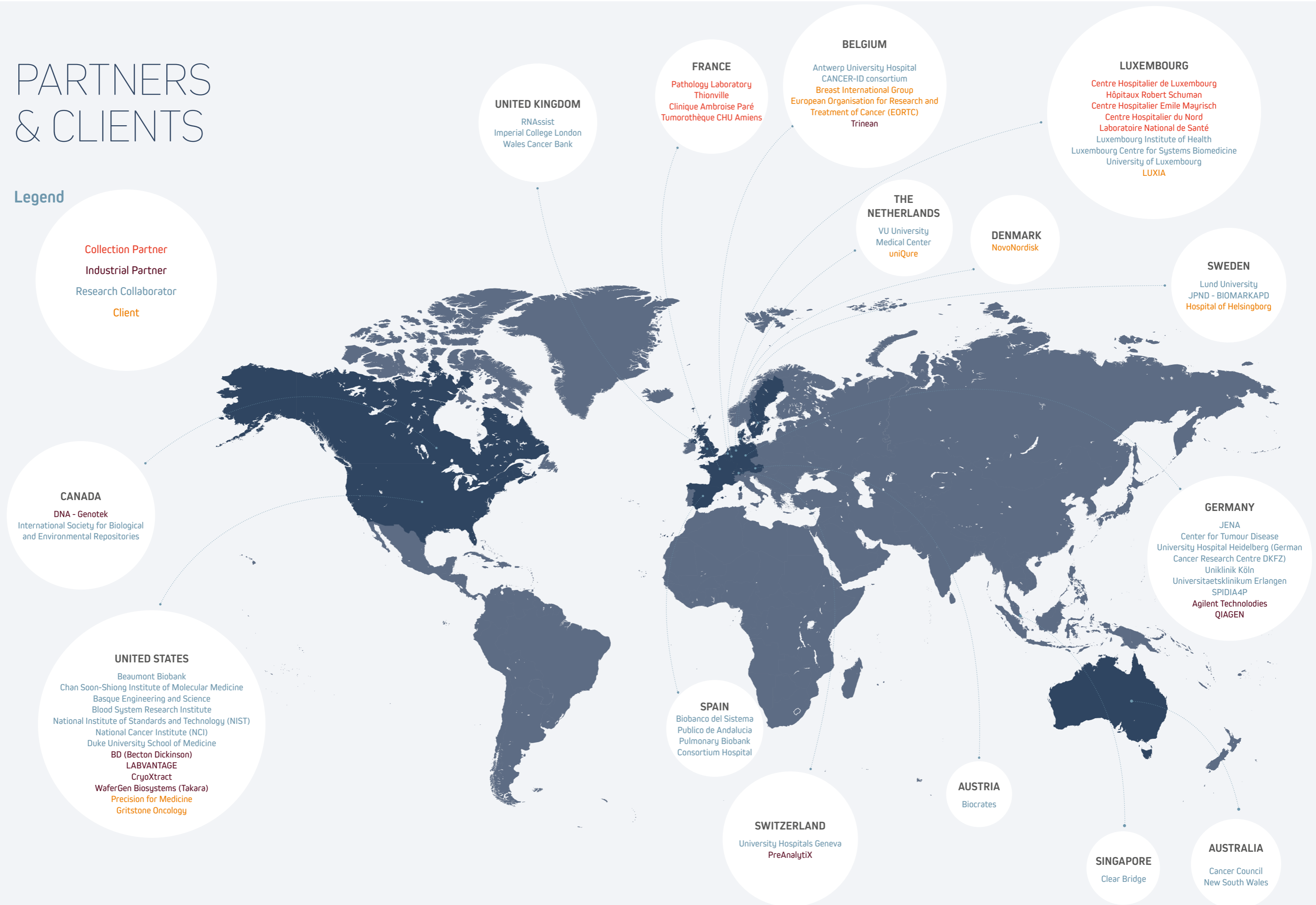
Trezzi JP, Jager C, Galozzi S, Barkovits K, Marcus K, Mollenhauer B, Hiller K.
MethodsX, Volume 4, Pages 95-103



PARTNERS & CLIENTS

Legend

Collection Partner
Industrial Partner
Research Collaborator
Client



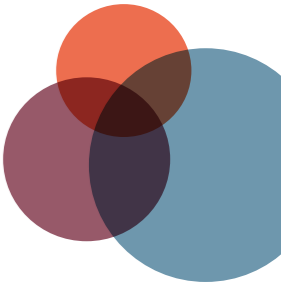
PROJECTS

BIOSPECIMEN RESEARCH	
TOPIC	PARTNERS
Cell counting method comparison	National Institute of Standards and Technology (NIST)
Impact of slide waxing on extracted nucleic acids	Breast International Group (BIG), Imperial College London (ICL)
CSF freeze drying and fitness-for-purpose for metabolomics and proteomics	Luxembourg Centre for Systems Biomedicine (LCSB)
DNA extraction from FFPE tissue and fitness-for-purpose for NGS	Private pathology laboratory in Thionville
Evaluation of a new blood collection tube	Becton Dickinson
Urine stability study	Internal project
Impact of vacuum drying on extracted nucleic acids	Internal project
Evaluation of fully automated method for DNA extraction from FFPE tissue	ICL
CSF processing and inter-laboratory reproducibility	Erlangen University Hospital
CSF qualification	VU University Medical Center
Impact of cold ischemia time on tissue mRNA	International Society for Biological and Environmental Repositories (ISBER) Biospecimen Science Working Group, National Cancer Institute (NCI)
RNA and miRNA stability in FFPE tissue	ICL, Wales Cancer Bank
Impact of physicochemical factors on tissue miRNA	Denator, Wafergen Biosystems (Takara)
Interactive protocol project for simultaneous DNA, RNA and protein extraction from tissue	ICL, Beaumont Biobank
Impact of Proteinase K digestion on DNA extraction from FFPE tissue	ICL
Formalin contamination of tissue processors	Internal project
Research and validation of micro- and macro-molecular biomarkers for the quality of preservation of biological samples, and the validation of the related methods	International Society for Biological and Environmental Repositories (ISBER) Biospecimen Science Working Group
Stool metabolite stability	Biocrates
Microbiome reference materials	Internal project
Stool collection tube comparison	LUXIA

DIABETES	
TOPIC	PARTNERS
Colonisation, Succession and Evolution of Human Gastrointestinal MICrobiome from Birth to Infancy (COSMIC)	LCSB : Eco-Systems Biology, Science for Life Laboratory, Centre Hospitalier de Luxembourg (CHL)
Innovative approach towards understanding and arresting type 1 diabetes (INNODIA)	Innovative Medicines Initiative 2 (IMI2)

CANCER	
TOPIC	PARTNERS
Lung Cancer Study (LCS)	Luxembourg Institute of Health (LIH), Partnership for Personalised Medicine, CHL
Biomarker discovery & validation in lung cancer	LIH, Personalised Medicine Consortium (PMC)
Collection of skin biopsies for establishment of melanoma cell lines	University of Luxembourg (Uni.lu)
Discovery of new therapeutic targets for colorectal cancer (SOCS)	Laboratoire National de Santé (LNS), Uni.lu, LIH, Hôpitaux Robert-Schuman (HRS), Centre Hospitalier Emile Mayrisch (CHEM), CHL
Cancer treatment and monitoring through identification of circulating tumour cells and tumour related nucleic acids (Cancer-ID)	Bayer AG, University Hospital Hamburg-Eppendorf, University of Twente, Menarini Silicon Biosystems
Tumorothèque Thionville (THION2)	Private pathology laboratory in Thionville
Plan Cancer Collection (PKC)	CHEM, CHL, Centre Hospitalier du Nord (CHdN), HRS, LNS
Non-invasive microbiome derived multiomic biomarkers for early stage colorectal cancer detection (MiCa)	CHEM, CHL, European Molecular Biology Laboratory (EMBL), German National Center for Tumor Diseases Heidelberg (NCT), LCSB, University Hospital Heidelberg (UHH), Uni.lu
Adoption of personalised medicine and molecular diagnostics in Luxembourg (MDLUX2)	Institut National du Cancer (INC)
The implementation of a personalized screening tool for pre- and probiotic interventions in colorectal cancer patients (PerPreProBioCRC)	LCSB, PMC
Role of MiR-371-373 cluster in tumor initiation and metastatic colonization (MiRMet)	Uni.lu
Biobanking of blood, breast tissue and tumour in Luxembourg: a pilot study (3B)	CHL

POPULATION STUDIES	
TOPIC	PARTNERS
Collection of control biological samples from the population	Zitha Gesondheetszenter (ZithaKlinik, HRS)
Applying systems immunology to the search for personalised biomarkers of clinical efficacy	LIH
European Health Examination Survey (EHES) extended with local component	EHES, LIH, Ministry of Health
Second observational study of cardiovascular risk factors in the general population in Luxembourg (ORISCAV II)	Ketterthill Laboratories, LIH

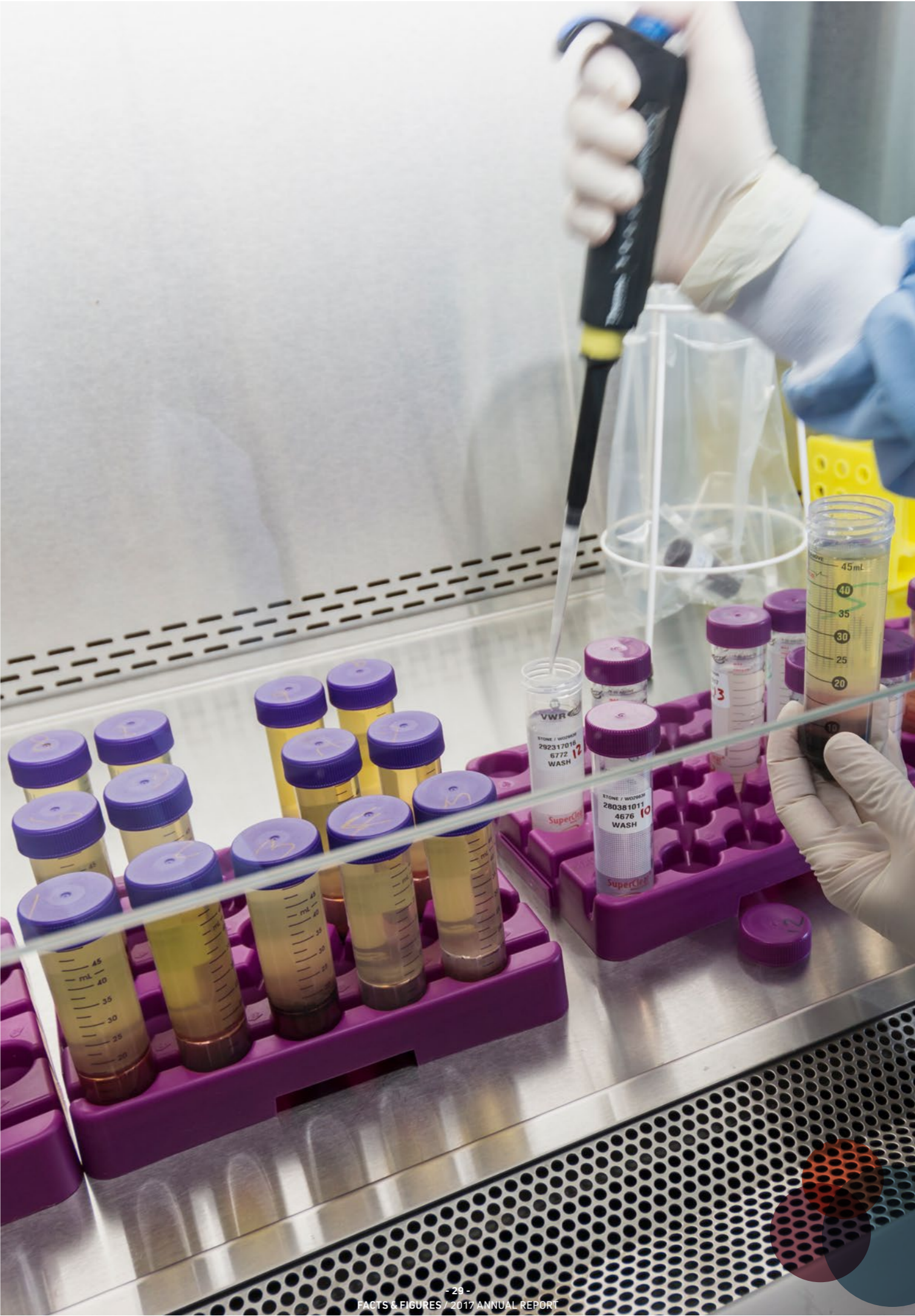


PARKINSON’S DISEASE

TOPIC	PARTNERS
BIOMARKAPD - Biomarkers for Alzheimer’s and Parkinson’s disease. A project within the EU Joint Programme for Neurodegenerative Diseases (JPND)	European Joint Programme for Neurodegenerative Disease Research (JPND) consortium members
Advanced modelling of Parkinson’s disease with three-dimensional human midbrain organoids	LCSB
Metabolomics & neuronal imaging in PD (METIMAGPD)	LCSB, Uniklinik Köln
Biomaterial collection for neurodegenerative disease research (ND Collection) in the framework of the National Centre for Excellence in Research on Parkinson’s Disease (NCER-PD) programme	CHL, Fonds National de la Recherche (FNR), LCSB, LIH
Development of a multifactorial biomarker signature for the diagnosis of motor- phase and prodromal Parkinson’s disease (DIAGNOSIS) in the framework of the National Centre for Excellence in Research on Parkinson’s Disease (NCER-PD) programme	CHL, FNR, LCSB, LIH
A deep phenotyping approach for comprehensive genetic stratification of therapy out- comes for deep brain stimulation in Parkinson’s disease (Earlystim Subproject Genetic Stratification)	LCSB, EARLYSTIM partners

CONTRACTS & OTHERS

TOPIC	PARTNERS
Biospecimen Proficiency Testing	ISBER and other organisations
Epilepsy sample storage	LIH
Logistics, storage and supplies management for an international clinical trial	CHL, LIH, Helsingborg Hospital, Lund University
Long term commercial storage contract for 52,000 samples from a completed European cancer trial	European Organisation for Research and Treatment of Cancer (EORTC), BIG, Institut Bordet
Pathology processing for the Luxembourg arm of the AURORA breast cancer trial LARA	BIG, CHL, LIH
PBMC isolation	Gritstone Oncology
PBMC isolation and shipment services for a clinical trial	UniQure
23 projects for PBMC isolation and shipment services for clinical trials	Precision for Medicine
Sample storage for 2 ongoing European breast cancer trials	BIG
Service agreement for sample storage and DNA extraction among others	Uni.lu
Storage of iPS cell lines	LCSB
Transfer of completed pharmaceutical trial samples to IBBL	EORTC
Liver Investigation: Testing Marker Utility in Steatohepatitis (LITMUS)	47 LITMUS Consortium members including academic and industrial partners
DNA extraction from stool samples, DNA quantification and 16S	Institute of Cardiometabolism And Nutrition (ICAN)
Tissue cassette printing	East West Bio
IHC for ALK protein on Melanoma samples	Uni.lu
Plan national maladies rares Codification Registre Recherche MR	Ministry of Health , LIH, LNS, CNS
Plasma supply to Freenome–CRC and healthy (Freenome)	Freenome



BIOSPECIMEN PROFICIENCY TESTING (PT)



PROCESSING & TESTING
SCHEMES OFFERED

2016
18

2017
19



PROCESSING & TESTING
SCHEMES SUBSCRIBED

2016
354

2017
405



PARTICIPATING
LABORATORIES

2016
94

2017
104



COUNTRIES

2016
26

2017
31

COLLECTION STATISTICS

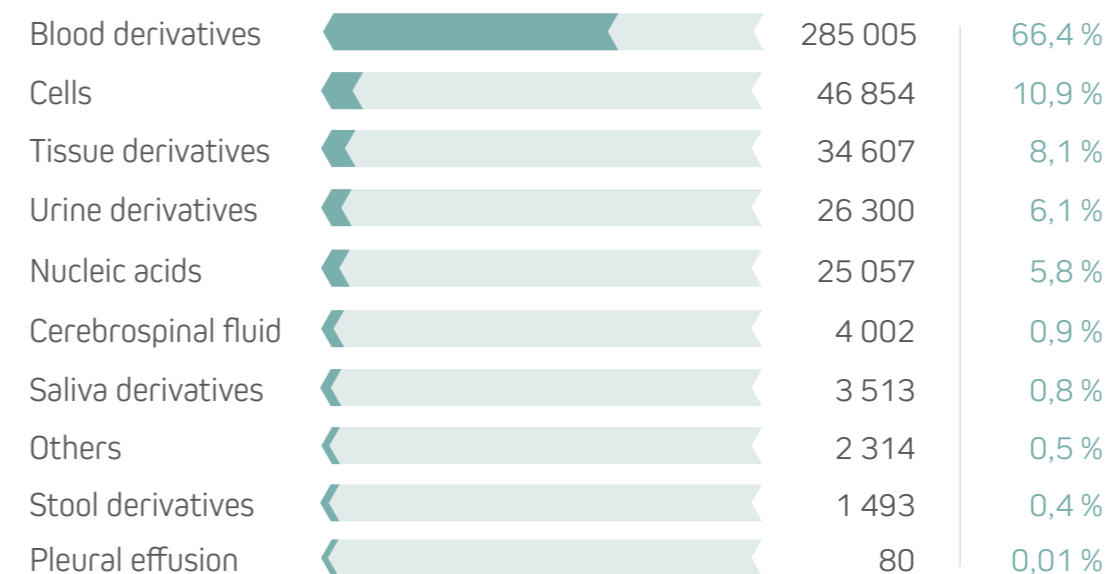
TOTAL SAMPLES COLLECTED



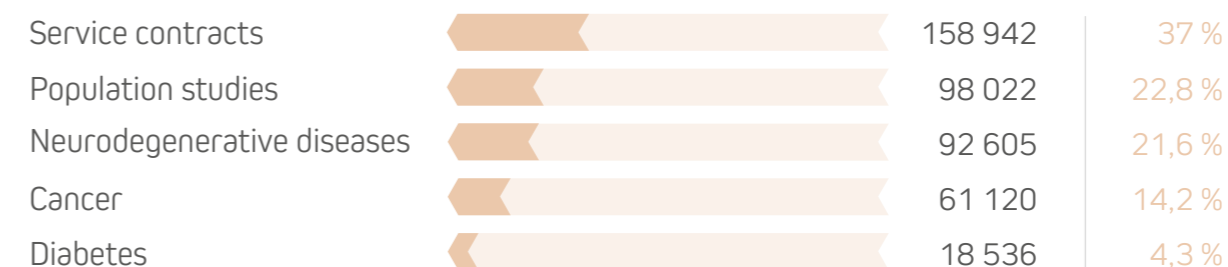
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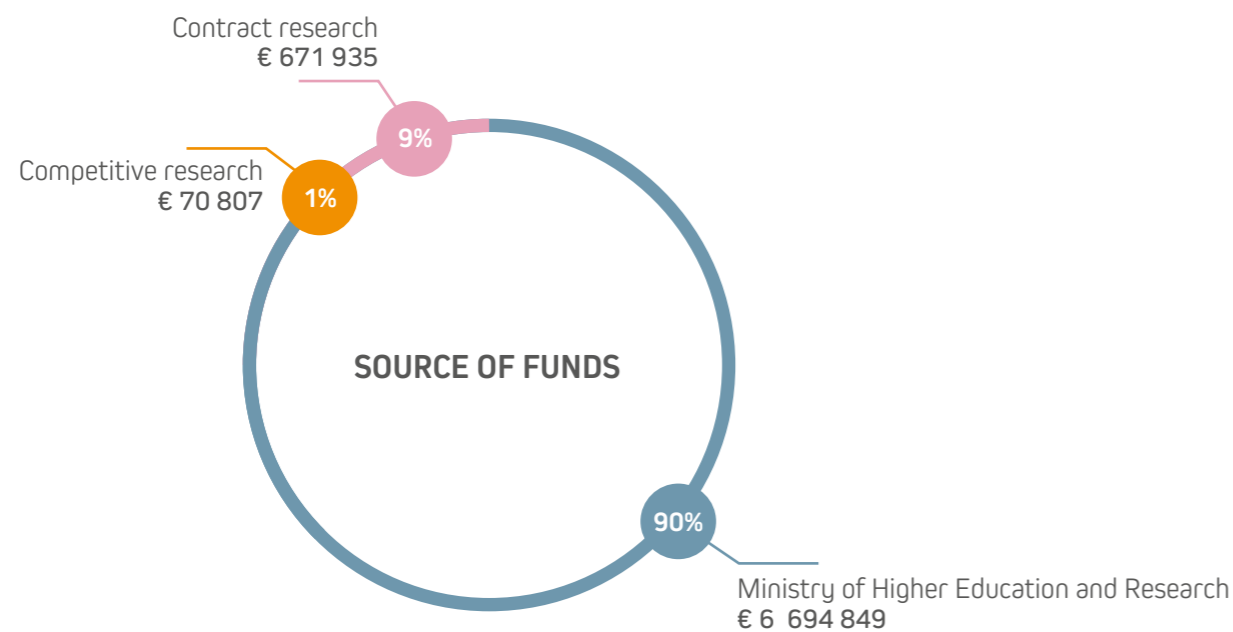
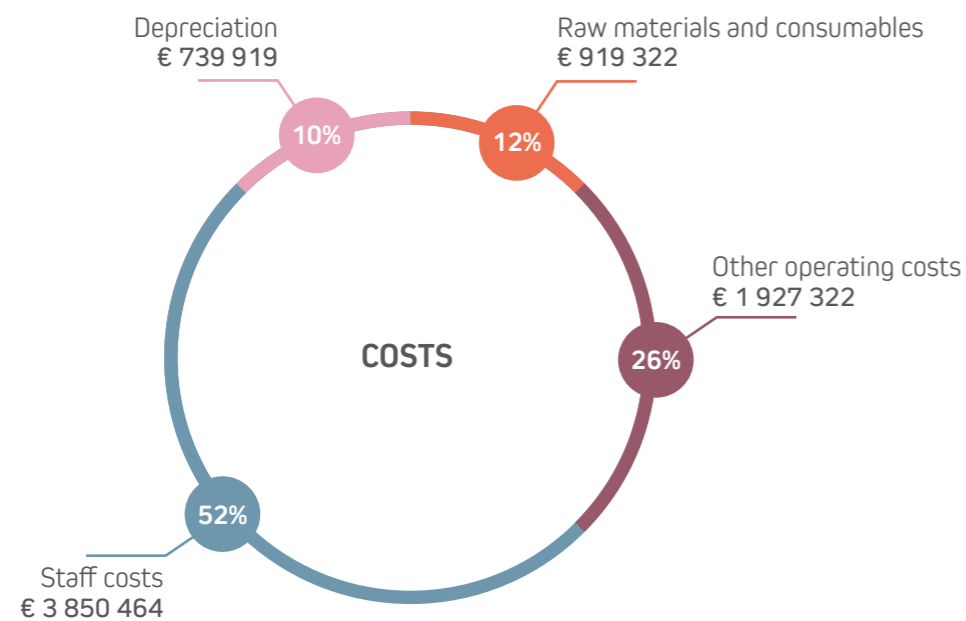
SAMPLES BY TYPE



SAMPLES BY PROGRAMME

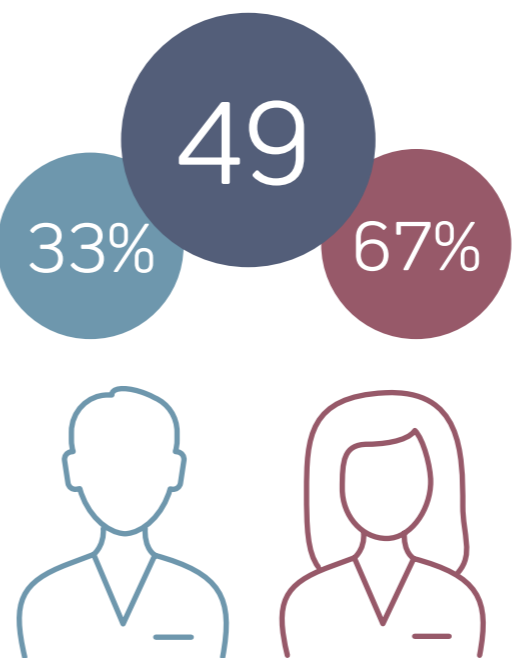


FINANCES



STAFF

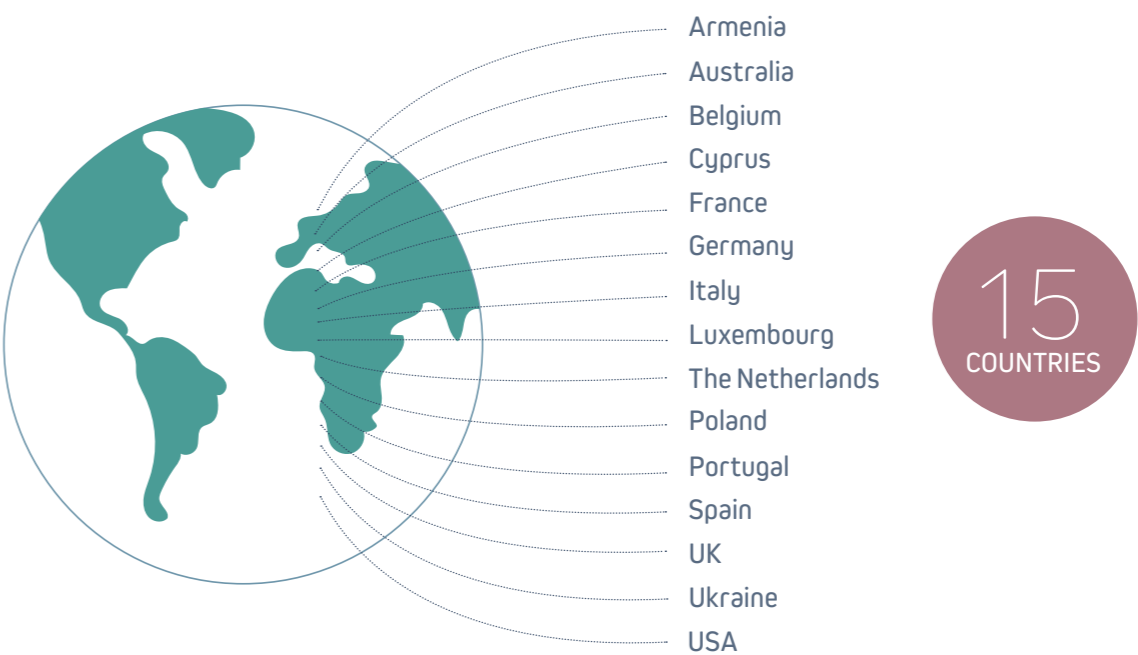
STAFF BY GENDER



SPECIALISTS

- Administrative staff
- (Bio)informaticians
- Laboratory technicians
- Marketing & communication staff
- Pathologists
- Scientists
- Project managers
- Quality manager

STAFF BY NATIONALITY



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Dominic ALLEN
Chief Operating Officer



Marc VANDELAER
Chief Information Officer



Sabine LEHMANN
Quality Manager



Fay BETSOU
Chief Scientific Officer



Karl-Heinz DICK
Chief Financial &
Administrative Officer



Laurent ANTUNES
Chief Clinical Department /
Pathologist



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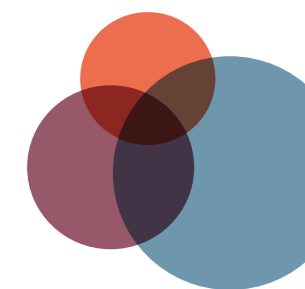
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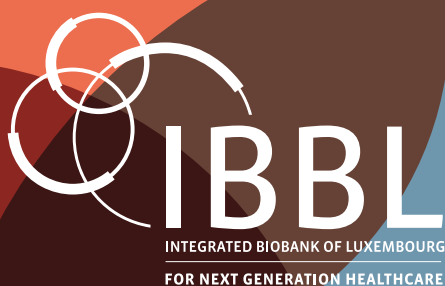
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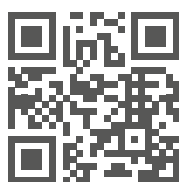




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