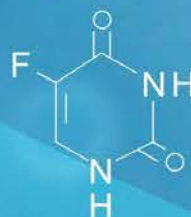


Technology Department

C2RT - C2RA - C2RI - CRBIP Core facilities

March 2023



GENERAL INTRODUCTION

The Department of Technology is one of the components of the Department of Scientific Affairs. Its aim is to develop a technological environment at the most advanced level to further enhance the Institut Pasteur's excellence in research. It provides access to outstanding shared resources, including a unique continuum of expertise, facilities, key technologies and biological resources, and it continuously invests in its development.

These strategic resources are organized in four centers:

- The C2RT: the Center for Technological Resources and Research (C2RT) is composed of several UTechS (Technology and Service Units) and Technological Platforms. Fields as varied as omics; design and production of biomolecules and their structural analysis; imaging; cell sorting and phenotyping; phenotypic screening; microfluidics and 3D cell culture are covered.
- The C2RA: Support in animal research and animal models is provided through the Center for Animal Resources and Research (C2RA), allowing animal experiments to be performed in the best ethical and regulatory conditions.
- The C2RI: The Center for Informatic Resources and Research (C2RI) offers support in computational biology, informatics and scientific computing, data analysis and management to Institut Pasteur's research Units and platforms.
- The CRBIP: Access to a large panel of biological resources and associated expertise is provided by the Biological Resource Centre (CRBIP), which is a multidisciplinary biobank harbouring collections of both microbial and human origin.

These centers, as shared resources, aim to support all the research teams of the institute in a cost-effective manner and achieve higher usage and impact of cutting-edge technologies and tools requiring high-level expertise for their operation. They are also open to external users from national or international research organizations or private institutions.

They work in close connection with the scientific departments at several levels to ensure that their activities, developments, and strategy are aligned with the needs of the Institut Pasteur community:

- Organizational level: core facilities have the possibility to be affiliated to a scientific department with matching research activities.
- Research team support level: user committees and general assemblies are regularly organized.
- Strategic level: scientific departments are represented in each core facility steering committee. They help define a strategic vision in terms of developments, acquisition of large equipment, recruitment of personnel, and the associated funding strategies..

This brochure provides you with an overview of the expertise, equipment, products and services accessible for the advancement of your scientific projects along with information on how to obtain expert information, to file an application or to initiate a joint work.

“

The teams in the four centers of the Institut Pasteur Technology Department provide expertise, equipment and resources in a wide range of domains. They do not simply provide service on demand but are usually integral part of scientific projects. Together with the scientific departments, we employ an ambitious strategy to further develop the institute's capacity to respond to today's and tomorrow's challenges in basic science related to human health.

Michael Nilges,

Vice-president for technology of Institut Pasteur

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C2RT

Technological core facilities

INTRODUCTION

Diverse cutting-edge technologies

The Center for Technological Research and Resources (C2RT) is integral to the Department of Technology, comprising one of the three main technology centers. In this context organized as some twenty technological platforms (a.k.a. core facilities, and described in the following pages) we aim to provision and develop the latest technologies to answer the needs of researchers at the Institut Pasteur, and beyond into the wider international scientific community.

Mission of the Center for Technological Resources and Research

The vision of C2RT is founded in science-as-a-service, with technology research leading the way to new insights on the biology of life and its usurpation by disease. Developing research technologies, methods and modalities, our expertise helps assure the pipeline of production for new therapeutics, diagnostics, environmental health and biotechnologies. It is in this context our mission is to support Institut Pasteur researchers by addressing their need for advanced robust research technologies.

C2RT achieves its mission goals serving the scientific community by assuring our facilities provide the necessary resources to facilitate our experts:

- open access to advanced research technologies for life sciences
- provide researchers with state-of-the-art equipment, services, and technical expertise
- guarantee fair and open access to STEM teaching, training and education in advanced life science technologies and methods
- develop, and optimize R&D approaches to invent and improve technologies for life sciences, proposing methodological enhancements
- anticipate and inform on emerging life science technology trends and providing a forum for their dissemination
- ensure facilities have all the support to establish the highest standards of performance, quantitative rigor and reproducibility for experimental data acquisition and analyses
- have capacity to build comprehensive archives of scientific protocols, laboratory records and standard operating procedures satisfying professional criteria
- guarantee facility users safe, compliant biocontainment laboratory space with standards matching and surpassing those required for protection for health, safety and protection of the environment

A technology driven scientific vision based on close interactions among talented scientists across Institut Pasteur and its international network

On the Paris campus the C2RT comprises around two dozen core facilities, and over one hundred and fifty scientists covering a large range of technological areas. The C2RT is a part of Institut Pasteur's critical research infrastructure and is a key component to our global research capacity serving and participating to most every aspect of scientific activities from basic to translational and clinical research at all levels.

“

The vision of C2RT is founded in science-as-a-service, with technology research leading the way to new insights on the biology of life and its usurpation by disease. Developing research technologies, methods and modalities, our expertise helps assure the pipeline of production for new therapeutics, diagnostics, environmental health and biotechnologies.

Pr Spencer L. Shorte,

Director of the center for technological resources and research

OMICS, PROTEOMICS, METABOLOMICS AND SINGLE CELL

Biomics Core facility

A structure dedicated to the sequencing of second (short-reads) and third (long-reads) generation

Head of Core Facility: Marc Monot

Contact

Mail: biomics@pasteur.fr

Website: <https://biomics.pasteur.fr>

Mission

The mission of the Biomics core facility is to facilitate scientific discovery through high-throughput sequencing technologies.

To this end, it offers personalised support per project, ranging from training in the various sequencing methods, including the use of autonomous sequencers, to complete management, from sampling to data analysis, for the most complex projects.

On the other hand, Biomics carries out internal development projects to be able to continue to offer the latest advances in sequencing.

What we do

Biomics is a structure dedicated to the high-throughput sequencing of second (short-reads) and third (long-reads) generation. The short-reads sequencing is centered on the Illumina technology for which we are equipped with ISeq, MiSeq and NextSeq instruments. We have acquired a Pacific Bioscience Sequel instrument for long-reads sequencing and also have access to Oxford nanopore technologies.

Our team provides training on the autonomous use of equipment (BioAnalyzer, QuBit, Covaris, ISeq, NextSeq) for the realization of stand-alone sequencing.

We are constantly optimizing and adapting new protocols. This includes the automation of workflows and working with degraded or low-concentration samples. For data analysis, our dry-lab offers many standard pipelines as well as the development of dedicated pipelines.



Our expertise includes

- Technology: Short-Reads (Illumina), Long-Reads (PacBio & Nanopore)
- DNA-Seq: Sequencing de novo and targeted
- RNA-Seq: Transcriptomic Analysis
- Metagenomic: Targeted sequencing studies (16S, 18S, ITS) or random (Shotgun)
- Bioinformatics: NGS data analysis (Variant, Assembly, Methylation study...)

Some examples of success stories

Biomics involvement in Sequana, a Python framework designed to provide pipelines to analyse NGS data sets, has led to the publication of a dynamic graphical interface (Sequanix) and a stand-alone application to decipher genomic variation (sequana_coverage).

How to work with us/how to apply for support

A request for support starts by asking a question or submitting a new project via our project manager: <https://biomics.pasteur.fr>. Then you will be put in contact with a Biomics project manager who will explain the next steps of your sequencing project (kickoff, libraries, sequencing, data analysis...).



Certifications and Networks

We are IBISA labeled and ISO9001 certified.
We are cofounder of the France Génomique Consortium.



Mass Spectrometry for Biology (MSBio UTechS)

Towards a deeper exploration of proteomes

Proteins are the chief actors in cells, carrying out the activity specified by the information encoded in genes. The large-scale analysis of proteins can therefore provide significant insight into many cellular processes and their dysregulation. The last decade has seen amazing advances in mass spectrometry-based proteomics and the technology is now used for large variety of biological applications. The objective of the MSBio UTechS is to develop innovative mass spectrometry-based proteomics approaches for applications in biology and human health with a particular emphasis in infectious diseases.

Head of UTechS: Julia Chamot-Rooke
Head of Core Facility: Mariette Matondo

Contact

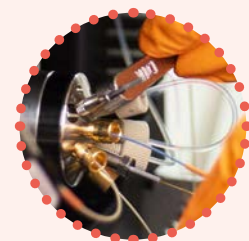
Mail: msbio@pasteur.fr
Website: <https://research.pasteur.fr/fr/team/mass-spectrometry-for-biology/>

Mission

The Mass Spectrometry for Biology (MSBio) Unit aims at developing service and research activities in mass spectrometry for the analysis of proteins.

It comprises a facility, providing mainly service in bottom-up proteomics (large scale analysis of peptides after protein enzymatic digestion) and a research group with two main technological research axes: top-down proteomics (analysis of intact proteins) and structural proteomics (analysis of protein complexes).

MSBio is equipped with the latest generation of high-resolution mass spectrometers: Orbitrap Q-Exactive Plus, Orbitrap Q-Exactive HF, Orbitrap Fusion Lumos and Eclipse (Thermo Fisher Scientific). The MSBio UtechS is also a Unit of Support and Research "Unité d'Appui à la recherche" UAR 2024.



What we do

Our Unit provides custom-tailored and innovative analytical solutions to meet the challenging demands of both academic laboratories and private companies. Our highly-trained staff offers expertise and counseling from sample preparation to data analysis in:

- Identification of low abundant proteins in complex biological matrices
- Advanced relative and absolute quantitative proteomic strategies
- Characterization of post-translational modifications (PTMs)
- Analysis of proteoforms (intact proteins) using top-down MS approaches
- Large-scale analysis of protein-protein interactions (*in vivo* cross-linking MS)
- Structural analysis of proteins and protein complexes (Hydrogen/Deuterium Exchange MS, Native MS).

Some examples of success stories

- Unique French partner of the European Proteomics Infrastructure providing Access, EPIC-XS; <https://epic-xs.eu>
- De novo sequencing of antibody light chains from patients with multiple myeloma. Dupré M *et al*, *Anal. Chem.*, 2021.
- Proteomic characterization of the human midbodies. Addi C *et al.*, *Nat.Comm.*, 2020.
- Identification of candidate vaccine (Rizzo J, *JEV*, 2021.



How to work with us/how to apply for support

A request for support starts by sending a mail to msbio@pasteur.fr

For the proteomics facility, a request form is available online. To contact platform members directly: proteomics@pasteur.fr

Certifications and Networks

We are IBSA labeled and ISO 9001 certified.

We are part of Core for Life, CTLS, Labex IBEID, EPIC-XS European Infrastructure.



Metabolomics Core facility

For a large-scale biochemical characterization of the phenotype

Metabolomic analyses allow the identification and quantification of small biochemical molecules <1500 Da (metabolites) which reflect a biological activity. These metabolites have been transformed during metabolism as substrates, products or effectors in a system and at a given time. Also considered as metabolites are xenobiotics (drugs, pesticides, environmental chemicals, ...) and molecules produced by the bacterial flora constituting the intestinal microbiota which can be partially metabolized by the host.

All of these metabolites (metabolome) therefore serve as direct signatures of the dynamic biochemical activity of the cell and are easily correlated with the phenotype without any direct link strictly with gene expression. Metabolomics then enables a better understanding of systems biology by highlighting metabolic interactions that could not be detected with traditional biochemical approaches.

Head of Core Facility: Sandrine Aros

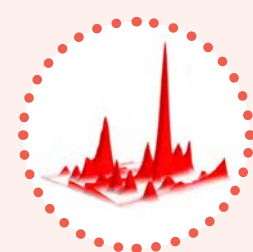
Contact

Mail: metabolomics@pasteur.fr
Website: <https://research.pasteur.fr/en/team/metabolomics-core-facility/>

Mission

The Metabolomics platform will aim to provide to Pasteur's research departments a pipeline of analyses (Mass Spectrometry and Mass Spectrometry Imaging) for both metabolic phenotyping and the absolute and relative quantification of biochemical molecules (metabolites and lipids) in biological systems.

The platform will also develop new analytical approaches adapted to specific requests compatible with the platform's fields of expertise. On the other hand, particular attention will be paid to the development of new analytical and computational methods in order to increase the performance of non-targeted metabolomics in terms of detection, identification of metabolites and interpretation of metabolic signatures.



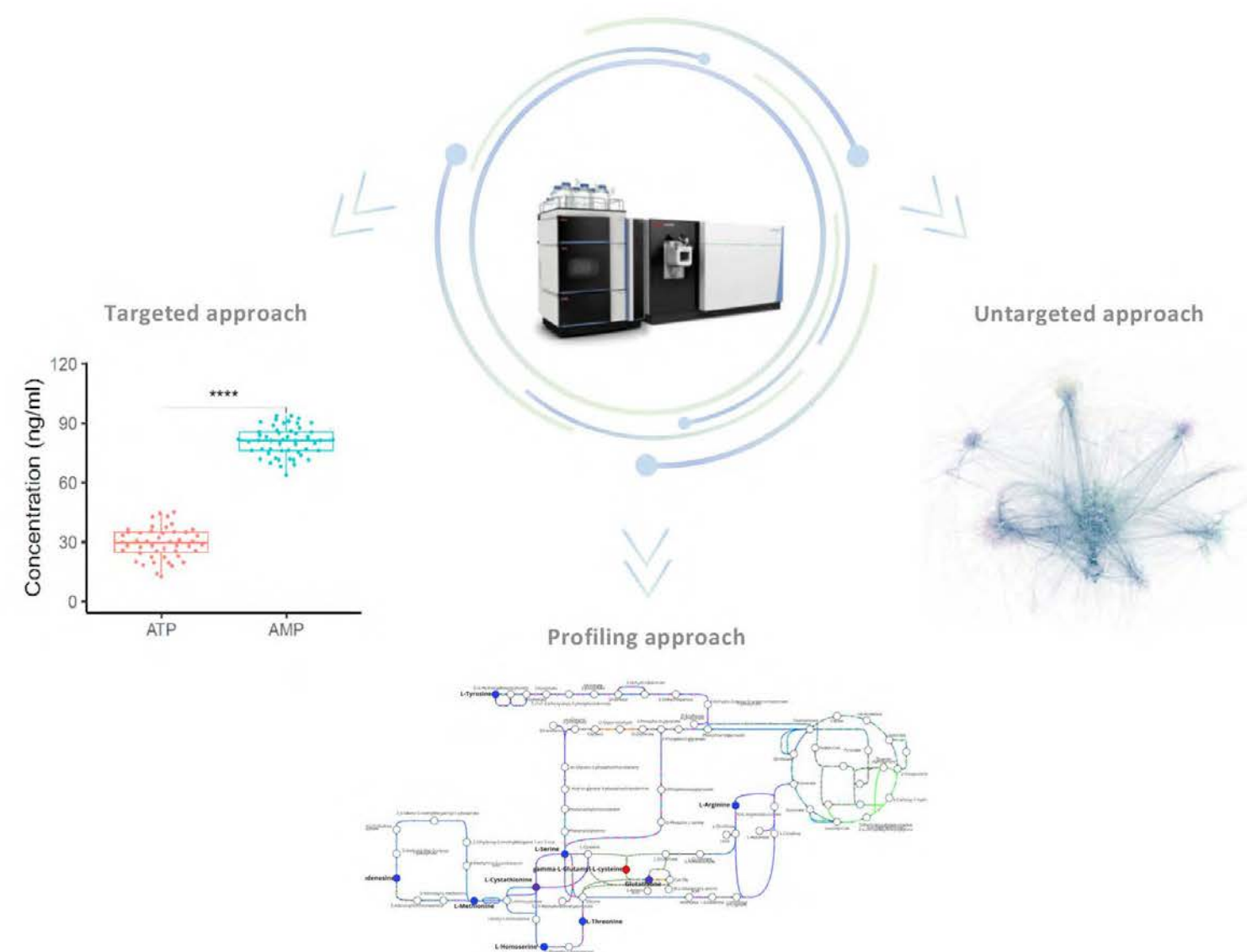
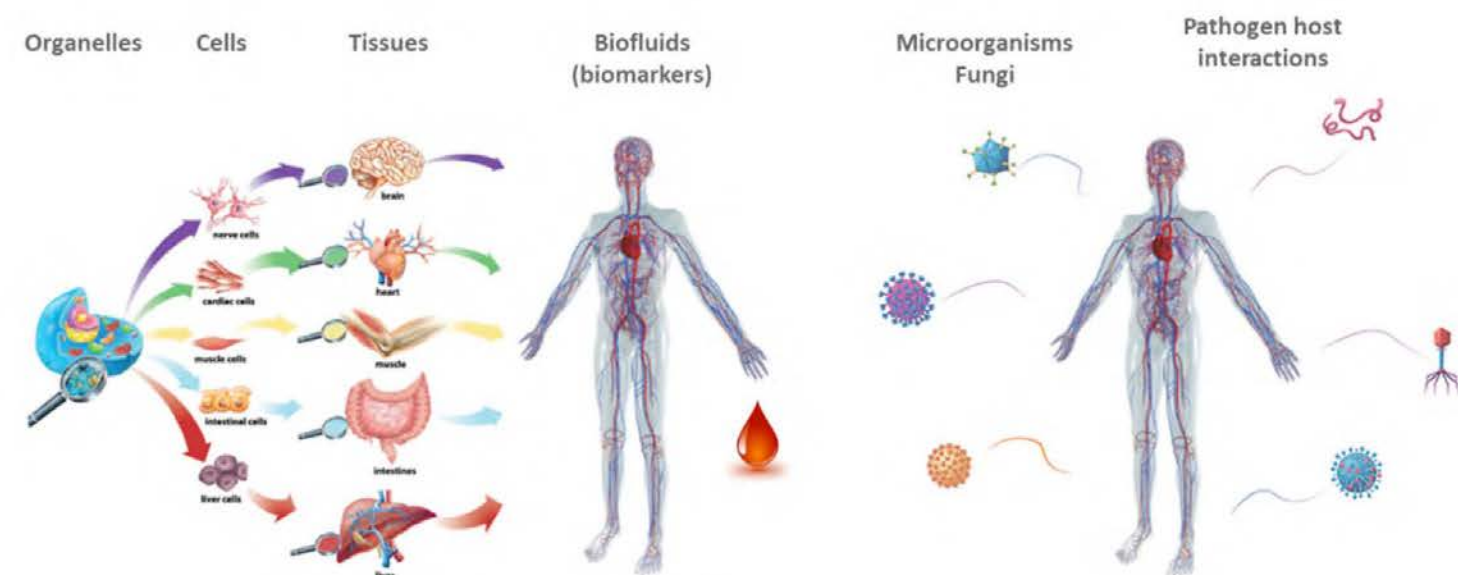
What will we do ?

Large-scale metabolomic analyses can provide us with important information about many cellular processes and their disturbances.

- Comparison of metabolomes between two biological systems under study allows genotypes and phenotypes to be linked.
- On the other hand, the comparison of metabolomes within the same group of biological systems under different conditions makes it possible to elucidate the influence of the environment on the expressed phenotype.

One of the main challenges of these analyses is to be able to measure metabolites with extremely diverse physico-chemical properties and to date we do not have an exhaustive knowledge of all existing metabolites.

One of the specificities of this platform will be to elucidate on a large scale these unknown compounds for a fine understanding of cellular physiological mechanisms.



Cytometry and Biomarker (CB UTechS)

Full support to a biomedical project within a single technological unit

Through its unique configuration, the CB UTechS provides project-tailored solutions for fundamental, translational and clinical research, from sample processing to data analysis.



Head of CB UTechS: Milena Hasan
Head of the CB UTechS's platforms:
Cytometry: Sophie Novault
Single Cell: Milena Hasa
Immunomonitoring: Milena Hasan
Biomarkers: Milena Hasan

Contact

Mail: CB_UTechS@pasteur.fr
Website: <https://research.pasteur.fr/en/team/technical-core/>

Mission

The CB UTechS has the mission of facilitating biomedical research through state-of-the-art technologies. Our 33 instruments have been selected to allow cell phenotyping and sorting, protein and RNA profiling and single cell OMICS. A significant part of the equipment is installed within fully equipped Bsl2+ cell culture laboratories to permit manipulation of human and infectious material.

What we do

Our team provides high-quality service and training. Expert advice is available for experimental design and data analysis. We develop and apply project-tailored bioinformatic tools to analyze complex data generated by our technologies. We collaborate with researchers on application of our technologies and pipelines in the context of various studies.

Our expertise includes

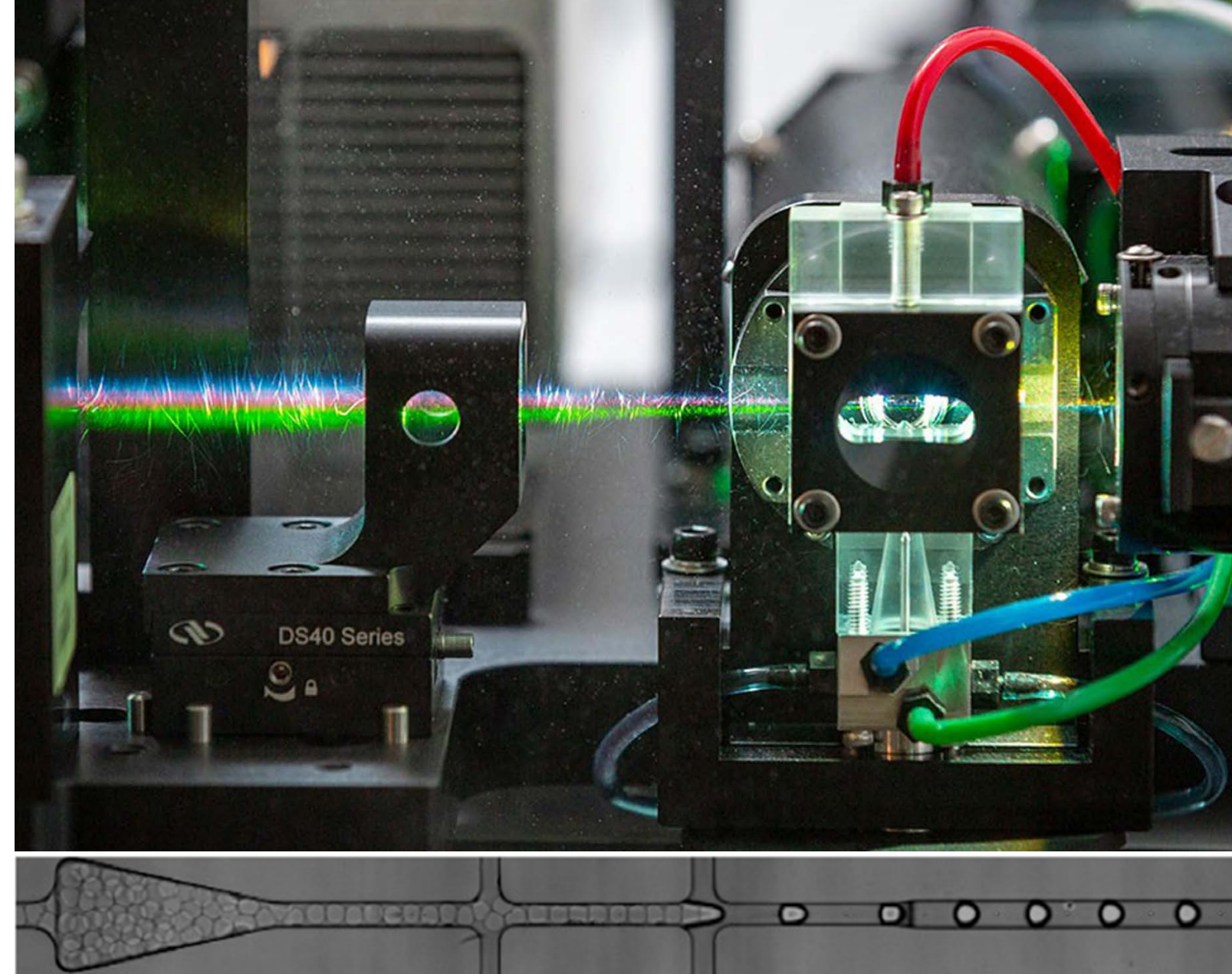
- 1) Cell phenotyping, sorting, functional cellular assays:
 - Flow cytometry: conventional, spectral, imaging
 - Image - fluorescence-based single cell sorting
 - Live-content imaging
 - Cellular metabolism
 - High-throughput 3D-spheroid analysis
 - Experimentation under hypoxia
- 2) Single-cell OMICS
- 3) Molecular profiling:
 - RNA
 - Protein: multiplex, ultrasensitive, single cell
- 4) Bioinformatics
- 5) Immunomonitoring

Some examples of success stories

In collaboration with the Microbiology Department, we have established the "NanoFlow" pipeline for detection, quantification, size estimation and nanoparticles purification.

The newly created Single Cell platform of the CB UTechS, supports a growing number of scientific projects through the most recent single cell pipelines (single_cell@pasteur.fr).

In collaboration with two scientific units, we have implemented pipelines for high-throughput 3D-spheroid analysis and for image-based single-microbe sorting.



How to work with us/how to apply for support

The CB UTechS is an open-access facility that welcomes projects and users from the Institut Pasteur and its International Network, from academia, clinics and industry.

The access is per-project based, upon submission through our web-based tool <https://utechscb.pasteur.fr/v3/main/blue/login.html>

Training request and instrument booking are available through PPMS.

Certifications and Networks

10xGenomics-certified since 2022.

ISO 9001 certified since 2011.

The CB UTechS is a highly collaborative core facility, both nationally and internationally:

- FOCIS Center of Excellence
- core facility of the LabEx project "Milieu Intérieur"
- Afribiota and the "Milieu Intérieur" consortia
- Core for Life and CTLS
- IBISA-labeled



MULTISCALE IMAGING

Photonic Bio-Imaging (PBI UTechS)

Providing optical imaging expertise in life sciences and especially their application in studies on infectious biology

Head of UTechS: Spencer L. Shorte
Head of Core Facility: Nathalie Aulner

Contact

Mail: pbi.contact@pasteur.fr
Website: <https://research.pasteur.fr/en/team/photonic-bioimaging-utechs-pbi/>

Mission

Our vision is highly multi-disciplined, and collaborative, with the mission goal focused on the use of quantitative imaging and analysis to understand the processes of cell/tissue-biology, and their usurpation by infection and disease.

What we do

Our team carries out support tasks and develops new protocols for optical imaging, including service rendering, training, technology-driven research and technology development. The R&D is founded upon the need to develop optical imaging methods that bring new understanding of host-pathogen interactions and *in situ* high-content imaging techniques and their application to infection, cell biology, and cellular microbiology. We work on novel techniques extrapolating quantitative information on spatiotemporal dynamics *in situ* and we push the limits of existing approaches aiming to enhance their performance thereby broadening their experimental utility.

Our expertise includes

- Intravital imaging
- *In vivo* technologies
- Super resolution technologies including sample preparation
- Molecular dynamics (SPT/FCS/FRAP/FLIM)
- High Content Imaging and Analysis
- Bioluminescence in cells, tissues and whole organism
- Technological development and implementation (optics, probes, data analysis)



Some examples of success stories

Contribution to studies on SARS-Cov2

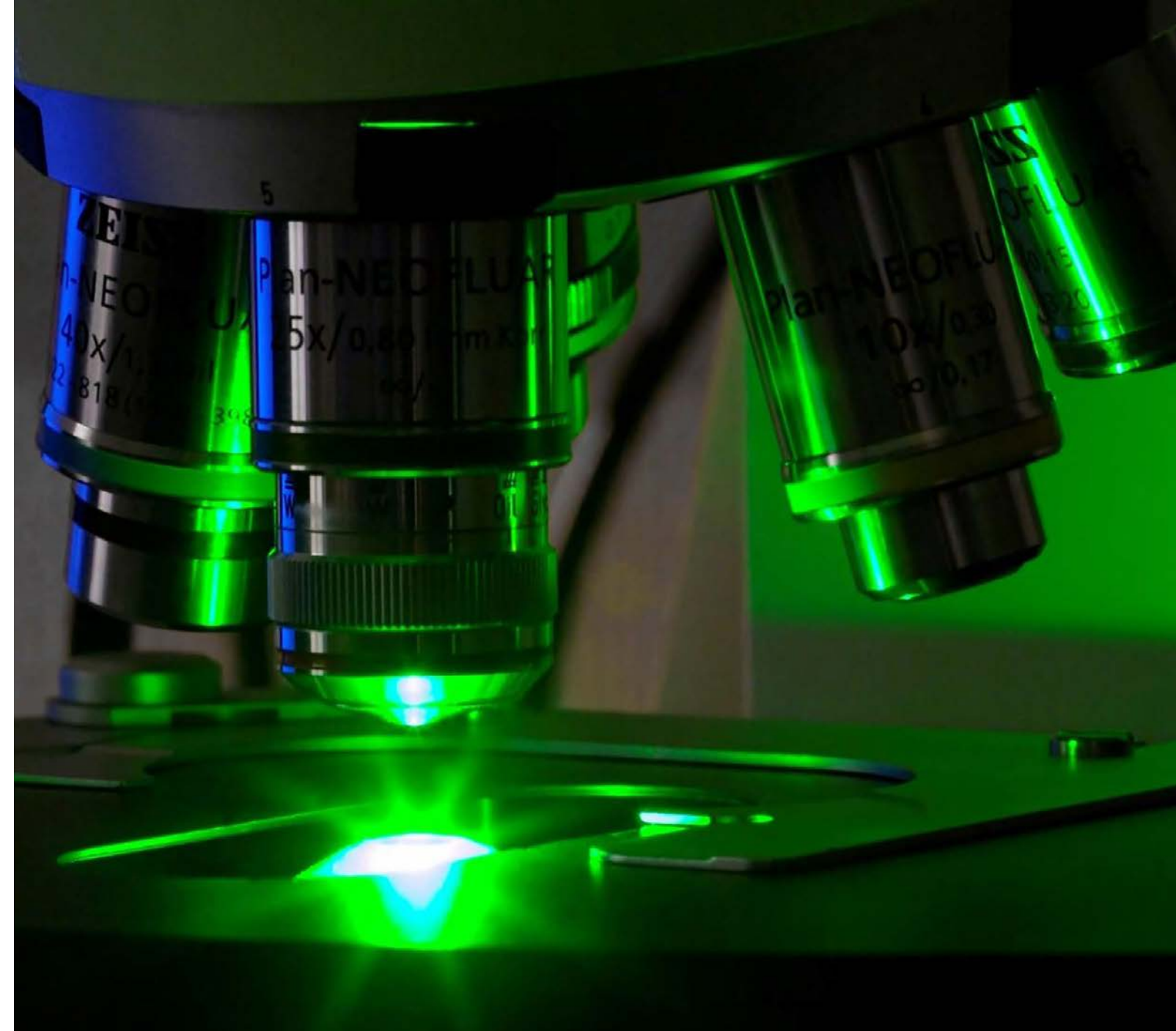
- SARS-CoV-2 infection induces the dedifferentiation of multiciliated cells and impairs mucociliary clearance. Robinot R *et al*, *Nature Communications*, 2021, 12:4354
- Considerable escape of SARS-CoV-2 Omicron to antibody neutralization. Planas D *et al*, *Nature*, 2021, Dec 23.

Contribution to the understanding of cellular processes by super-resolution imaging

- Redistribution of FLA-gellar Member 8 during the trypanosome life cycle: Consequences for cell fate prediction. Calvo-Álvarez E *et al*, *Cell Microbiol.*, 2021, 23:e13347.
- The viral restriction factor tetherin/BST2 tethers cytokinetic midbody remnants to the cell surface. Presle A *et al*, *Curr Biol.*, 2021, 313:2203-2213.

How to work with us/how to apply for support

Open desks are organized every other Monday afternoon to make a first contact with the team. A request for support starts by filling a form on our PPMS website for training, assisted session or collaboration. Based upon your request, you might be asked to fill additional documents (GMO, live pathogens or primary cells imaging). We aim to promote the vast majority to autonomous use of our instruments.



Certifications and Networks

We are IBISA labeled and ISO9001 certified.

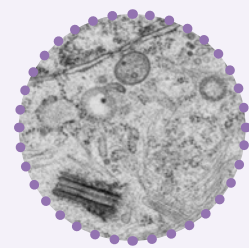
We are part of the following networks: CTLS (core technologies for life sciences, cofounder), C4L (core for life), FBI (France Biolmaging), FLI (France Life Imaging), ELMI European Light Microscopy Initiative, cofounder), RTmfm (Réseau de Microscopie de Fluorescence Multidimensionnelle), EuroBiolmaging, Global-Biolmaging, EuCAI (European Cell-based Assay Interest group, Cofounders).



Ultrastructural Bio-Imaging Core facility (UBI)

Seeing is believing

Electron microscopy (EM) is the method of choice to see fine details of cells and pathogens and to study how pathogens interact with their host in the most direct way. You feel your project would benefit from EM approaches? Come and talk to us: we will help you find the best solution to address your biological question.



Head of Core Facility: Adeline Mallet

Contact

Mail: ubi.all@pasteur.fr

Website: <https://research.pasteur.fr/en/team/ultrastructural-bioimaging-core-facility/>

Mission

We provide scientific and technical support in Scanning and Transmission Electron Microscopy to research groups of Institut Pasteur and external institutes. We routinely perform a wide range of sample preparations and imaging techniques at room temperature, in cryo or in 3D. The ultrastructural characterization of pathogens and host-pathogen interactions is an important focus but a large array of samples is analyzed. We also develop new sample preparations and imaging pipelines that can be applied in the projects of our users.

What we do

- Samples preparation
- Scanning Electron microscopy
- Transmission Electron microscopy
- Cryo-methods
- Immunolabelling
- Correlative Approaches
- 3D Electron Microscopy : Electron tomography, FIB-SEM
- Implementation of new methods

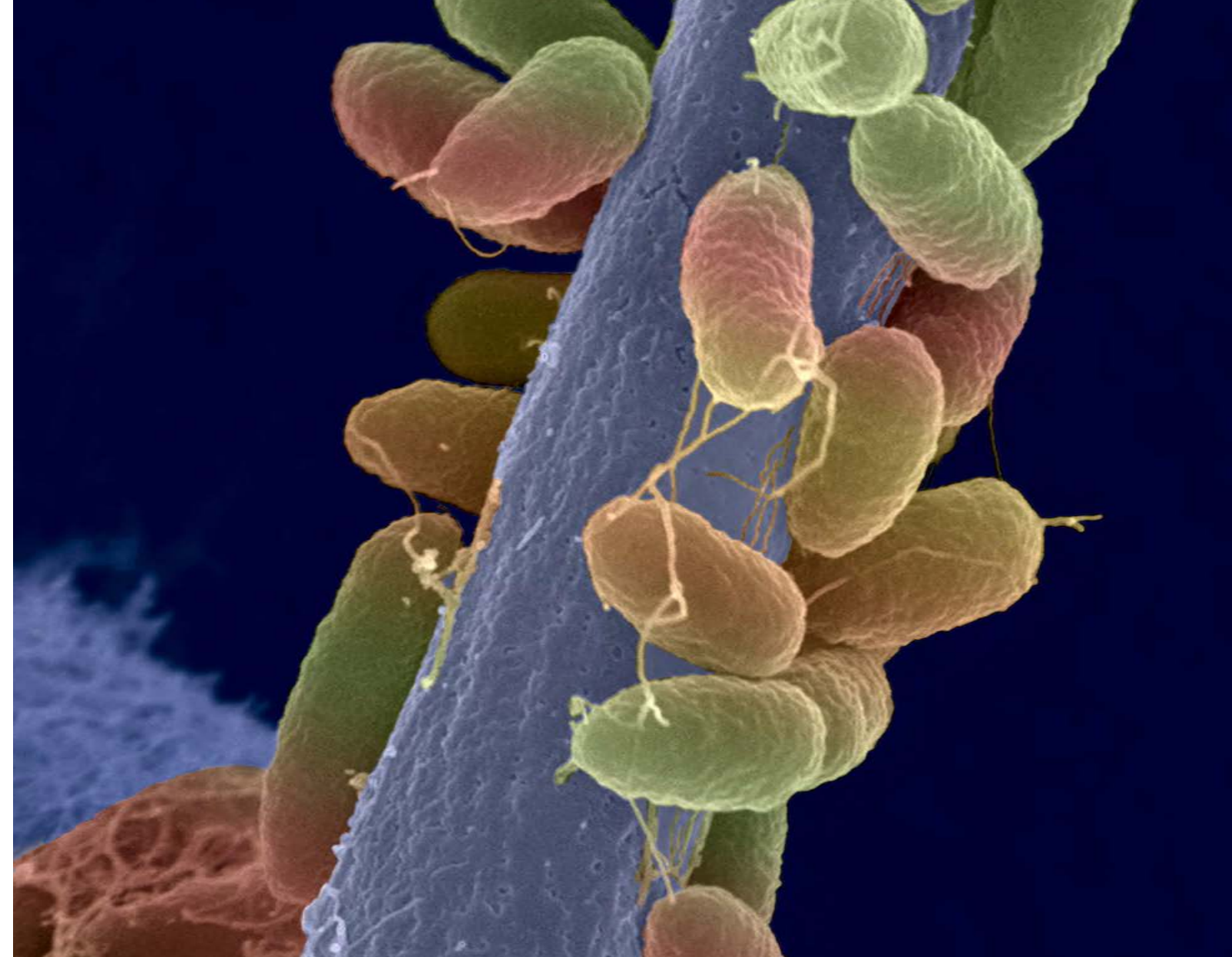
Some examples of success stories

- Ultrastructural morphology by scanning (SEM) and transmission electron microscopy (TEM)

SARS-CoV-2 infection induces the dedifferentiation of multiciliated cells and impairs mucociliary clearance. Robinot R *et al*, *Nat Commun*. 2021, 12:4354. doi: 10.1038/s41467-021-24521-x. PMID: 34272374.

Tetanus Toxin Synthesis is Under the Control of A Complex Network of Regulatory Genes in *Clostridium tetani*. Chapeton-Montes D *et al*, *J. PLoS Pathog*. 2021, 17:e1009550. doi: 10.1371/journal.ppat.1009550. eCollection 2021 Apr. PMID: 33930101.

- Serial sectioning transmission electron microscopy
Salmonella enters a dormant state within human epithelial cells for persistent infection. Luk CH *et al*, *PLoS Pathog*, 2021,17:e1009550. doi: 10.1371/journal.ppat.1009550. eCollection 2021 Apr. PMID: 33930101.
- Negative staining transmission electron microscopy
Translocated *Legionella pneumophila* small RNAs mimic eukaryotic microRNAs targeting the host immune response. Sahr T *et al*, 2022, *Nat Commun*. 13:762. 10.1038/s41467-022-28454-x, PMCID: PMC8828724.



- FIB-SEM (Focused Ion Beam – Scanning Electron Microscopy)

Ultrastructural Changes of the Mitochondrion During the Life Cycle of *Trypanosoma brucei*. Bílý T *et al*, 2021. *J Eukaryot Microbiol*, 68:e12846. doi: 10.1111/jeu.12846. Epub 2021 Mar 19. PMID: 33624359.

How to work with us/how to apply for support

New projects should be requested via our online system PPMS-UBI (<https://www.pasteur.fr/ppms/login/?pf=5>). You will be asked to briefly present your project in our weekly team meeting. You can describe here the global philosophy of how you work (e.g. promoting autonomous users) and what you value.

Certifications and Networks

We are IBISA labeled and ISO9001 certified. We are part of FBI (France BioImaging), CTLS (Core Technologies for Life Science), C4L (Core For Life), COST COMULIS (Correlated Multimodal Imaging in Life Sciences), RIME (Réseau d'Imagerie en Microscopie Electronique), Labex IBEID.



Nano-Imaging Core facility (NCF)

Cryo-Electron Microscopy for all who need it, or never thought they needed it

Head of Core Facility: Dr. Matthijn Vos

Contact

Mail: nanoimaging@pasteur.fr

Website: <https://research.pasteur.fr/en/team/nanoimaging/>

Mission

To make the technology of cryo-electron microscopy in all its forms accessible and available for all working at, or collaborating with Institut Pasteur.

What we do

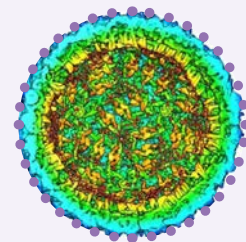
The Nanoimaging core facility provides high throughput cryo-electron microscopy aimed at resolving the structure of isolated proteins in solution as well as imaging at the nanometer scale inside the cellular environment.

Our expertise includes

- High-throughput sample preparation and screening
- High-throughput single particle analysis data collection
- Focused Ion beam milling under cryogenic conditions
- High-throughput cryo-electron tomography
- Cryo-electron microscopy and sample preparation training and scientific consultancy

Some examples of success stories

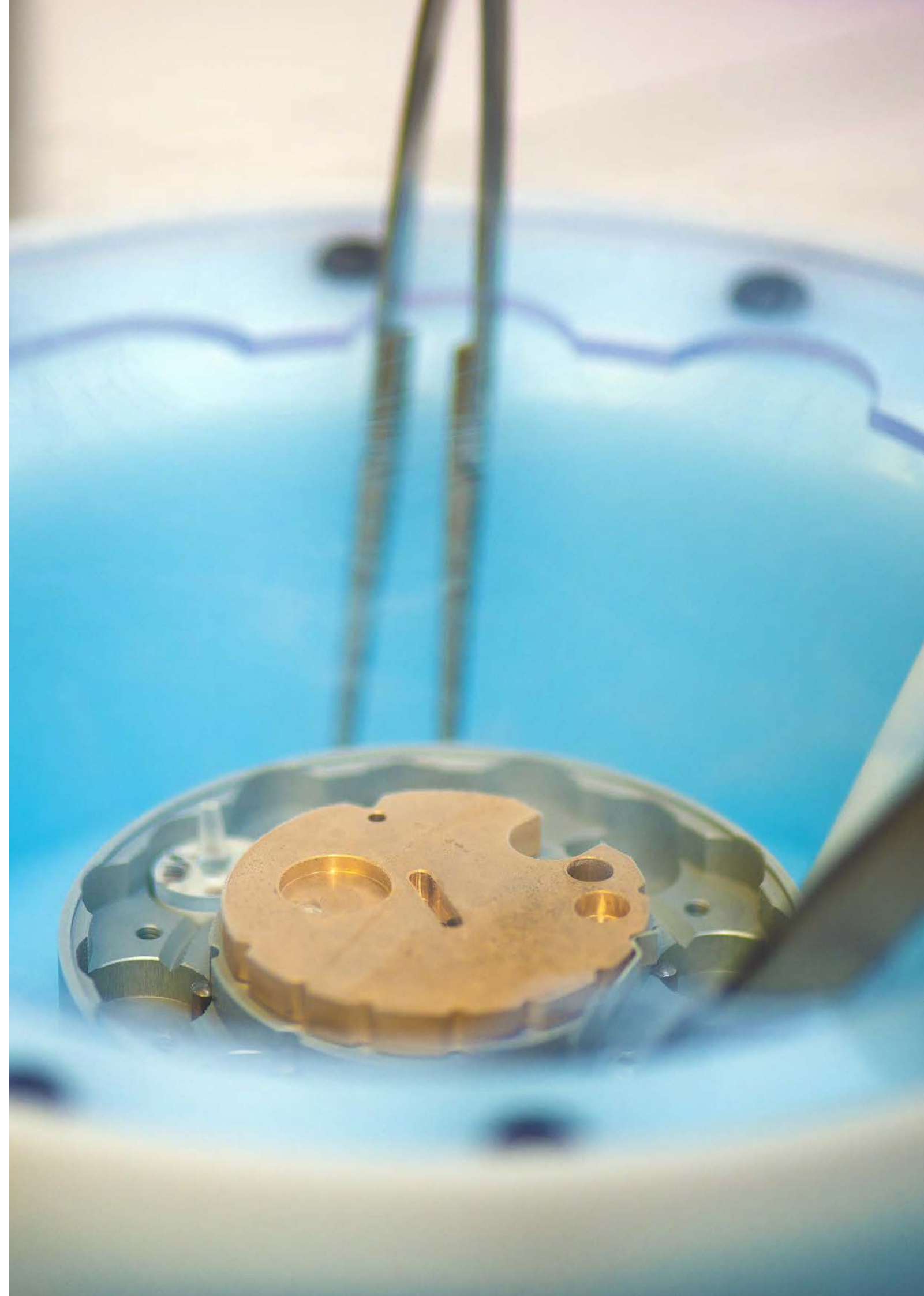
The core facility started full operation on October 7, 2019. As of now, the core has over 80 users of which over 20 user external. We organize 3 annual hands-on microscopy course and have delivered over 40 autonomous users. The microscopes will be upgraded in 2022 to the latest standard of detectors and cameras to keep up with the developments in cryo-EM.



The core has received funding from several successful grant applications to upgrade the microscopes as well as received funding from Institut Pasteur. The core had an outstanding rating on the HCERES review in 2021.

How to work with us/how to apply for support

Applications for access are online through the submission form on PPMS. After successful submission user are given access to the microscope agenda on PPMS where they can book a time slot. Before the day of imaging, we advise to meet with the core staff to discuss the different projects and how to best approach the sample preparation and imaging, this is, however, not mandatory. It is up to the unit head to decide the order of imaging if a unit has multiple projects from different group leaders within the unit. We strive to apply a "fair-use-policy". Users can use the microscope without supervision only after sufficient training and proven ability to operate the microscope as well as approval from the core staff. Details on how to apply can be found on our website.



Hearing Institute Bioimaging Core facility (Imag-IdA)

Making audition visible

Hearing loss is the most frequent sensory deficit and is constantly on the rise as a result of higher life expectancy and increasing over-exposure to noise – whether caused by ever denser urbanization or headphone use, especially in young people. WHO estimates that there are nearly 500 million people worldwide currently living with hearing loss, a figure that is likely to rise to 900 million by 2050, and hearing impairments will be the seventh leading cause of burden of disease by 2030. In France, there are currently 6 million people with hearing loss.

Regardless of the degree of severity and the age at which hearing loss occurs, it can have a significant negative impact on social interaction, leading to isolation often accompanied by depressive symptoms.

The aim of the Hearing Institute is to improve understanding of the principles and mechanisms that underpin the development and workings of the auditory system. Its research fields particularly include auditory perception and cognition, audio communication, multisensory integration, and interactions between the genome and the acoustic environment.

The hearing Institute is a satellite of Pasteur Institute in the 12th arrondissement.

Head of Core Facility: Maia Brunstein

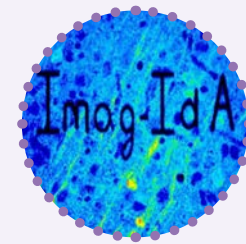
Contact

Mail: maia.brunstein@pasteur.fr

Website: <https://research.pasteur.fr/fr/team/hearing-institute-bioimaging-core-facility/>

Mission

Our mission is to provide the equipment and the expertise for scientific imaging. The several systems available at Imag-IdA allow observing the sample at different levels, from the entire organoid to the details of intracellular structures (~150nm of lateral resolution in



optical microscopy and ~10nm resolution in electronic microscopy). In collaboration with the Photonic BioImaging facility (PBI) and the imaging analysis Hub of Pasteur Institute, we offer support in the imaging acquiring process as well as the treatment, analysis and interpretation of images.

What we do

We provide to the user the guidance through the whole imaging processes:

- sample preparation
- choosing the most appropriate technology to answer the biological question
- assistance in the use of the systems
- imaging acquisition
- imaging analysis and treatment.

Our expertise includes

- Fluorescence microscopy,
- Electronic microscopy,
- In vivo imaging,
- Super-resolution imaging,
- Image analysis,
- Optical development.



How to work with us/how to apply for support

You can contact us by mail:

maia.brunstein@pasteur.fr or through the PPMS page: <https://ppms.eu/pasteur/?BIIdA> and tell us how we can help you with your project.



BIOMOLECULAR SCIENCE

Production and Purification of Recombinant Proteins Technological Core facility (PF3PR)

A versatile protein production and purification core facility for your projects

Head of Core Facility: Stéphane Pêtres

Contact

Mail: PF3PR@pasteur.fr

Website: <https://research.pasteur.fr/en/team/production-and-purification-of-recombinant-proteins/>

Mission

The PF3PR facility was created to provide large amounts of high-quality purified proteins for the researchers from Institut Pasteur and external users.

What we do

Our team provides high-quality recombinant proteins produced in baculovirus, mammalian cells, *E. coli* or yeast, mainly for structural (X-ray, NMR or Cryo-EM) or functional studies. PF3PR has the expertise staff and large-scale range equipment to deliver proteins through a standardized “pipeline”: automated screening of host-vector expression systems in micro-plates (Tecan platform), optimization of processes in low scale micro-bioreactors, culture scale-up in large volume conventional bioreactors, and chromatographic protein purifications using AKTA systems.

Our core facility is widening the automated processes of culture screening, purification and analyses to a larger number of eukaryotic and prokaryotic expression systems through the implementation of new equipment and new methodologies.



Our expertise includes

- Providing high quality purified proteins in large quantities in the context of services or scientific collaborations, taking into consideration the requirements of delivery in times and costs.
- Optimization and scale-up of protein production using eukaryotic and prokaryotic multiple expression systems.
- Technological and methodological developments to diversify expression systems and biotechnological tools to overcome the expression of difficult proteins.
- Providing to the users of our core facility, scientific and technical training and expert advice concerning the choice of expression systems, culture processes and protein purification
- Training of assisted or autonomous users on our equipment



Some examples of success stories

- Recognition determinants of broadly neutralizing human antibodies against dengue viruses. Rouvinski A *et al*, 2015. *Nature*. 520:109-13.
- The stress sigma factor of RNA polymerase RpoS/ σ^s is a solvent-exposed open molecule in solution. Cavaliere P, *et al*, 2018. *Biochem J*. 2018, 475:341-354.
- The biosynthesis of flavin cofactors in *Listeria monocytogenes*. Sebastián M *et al*, 2019. *J Mol Biol*. 431:2762-2776.
- A comparison of four serological assays for detecting anti-SARS-CoV-2 antibodies in human serum samples from different populations. Grzelak L *et al*, 2020. *Sci Transl Med*. 12:559.
- Prevalence of SARS-CoV-2 antibodies in France: results from nationwide serological surveillance. Le Vu Set *al*, 2021 May 21. *Nat Commun*. 12, 559:3025.

How to work with us/how to apply for support

In order to check the adequacy between our proposed services and your project, please send us a few lines to PF3PR@pasteur.fr.

Complete also our project forms (autonomous or service) and book equipment in PPMS (<https://ppms.eu/pasteur/?PF3PR>).

Regular open desks are organized with other core facilities involved in protein science (from production to structure, dynamics and biophysics) to make a first contact with the team and to discuss your project.

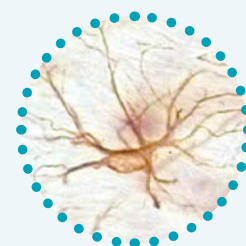
Certifications and Networks

We are IBISA labeled and member of CTLS (Core Technologies for Life Sciences) and P4EU (Protein Production and Purification in Europe).

Antibody Engineering Core facility (PFIA)

To raise nanobodies for basic science support, in vivo imaging and diagnosis

Nanobodies or VHHs are variable antibody fragments isolated from Heavy chain antibodies that are naturally occurring in only Camelidae (camel, dromedaries, llamas, alpacas). These molecules behave like full antibodies in term of antigen binding but they possess some very interesting features allowing them to be potent biotechnological tools: they are small, they diffuse extensively in body tissues, they penetrate into the brain and they bind intracellular antigens. VHHs are useful for basic science, brain imaging, viral diagnosis / neutralization, etc.



Head of Core Facility: Pierre Lafaye

Contact

Mail: anticorps@pasteur.fr

Website: <https://research.pasteur.fr/fr/team/antibody-engineering/>

Mission

Our core facility provides support in developing and characterizing VHH/nanobodies against the desired antigens. The main goal of this collaboration is to provide the right nanobodies that suit to the need of the user. We try not only to provide nanobodies but we can modify them: for example, according to the need, the nanobodies can be engineered to add a fluorochrome, to perform imaging; in this way, bispecific molecules can be created.

What we do

We immunize alpacas with the antigen. After immunization, we recover lymphocytes to isolate RNA. By RT-PCR we obtain cDNA encoding for nanobodies genes. These genes are then cloned in a phagemid vector to obtain phage displayed nanobody libraries. Pannings with the antigen are performed to isolate the specific VHHs. The selected VHHs are then expressed and characterized.

Our team carries out support tasks and develops new protocols for immunization (cell-based immunization), site-specific labeling of nano-bodies and expression in different formats.

We have been deeply involved in the Covid-19 pandemia. We have raised VHHs against nucleoprotein, spike protein, RNA polymerase and ACE2. The VHHs directed against the nucleoprotein are being used to develop rapid diagnostic tests (antigenic tests). Some of these VHHs are able to neutralize the virus by blocking the interaction between the spike and the human receptor ACE2.

Our expertise includes

- Phage display of phage VHH libraries
- Expression and characterization of VHH/nanobodies
- Site specific labeling with fluorochromes
- Droplet based microfluidic
- Automatization of the process
- Rapid diagnostic tests

Some examples of success stories

- A novel Nanobody precisely visualizes phosphorylated histone H2AX in living cancer cells. Moeglin E *et al*, *Cancers*, 2021, 13, 3317.
- Development of a highly specific and sensitive VHH based immuno-assay for the detection of the SARS-CoV-2 Nucleoprotein. Gransagne M *et al*, *Jo Biol Chem*, 2022, 298, 101290.
- Neutralizing Single Domain antibodies directed to SARS-CoV-2 spike protein. Gransagne M *et al*, *US patent* 63/236, 603.



How to work with us/how to apply for support

Regular open desks are organized with other core facilities involved in protein science (from production to structure, dynamics and biophysics) to make a first contact with the team.

Alternatively, a request for support starts by sending a mail (anticorps@pasteur.fr).

A meeting is organized to analyze the feasibility of the project and the needs of the applicant. Then a form has to be filled and submitted as a project.

We are IBISA labeled.

We are part of the EuroMabnet Network and CTLS (Core technologies for life sciences).

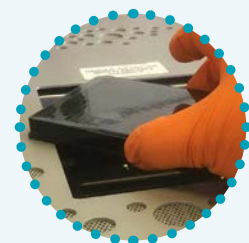


Certifications and Networks

Molecular Biophysics Core facility (PFBMI)

All you need to master your biological system at the molecular level

The PFBMI brings together a large panel of complementary technologies that allow to dissect the molecular processes involved in life and disease, and to design efficient therapies and prophylaxes. The PFBMI experts will help you to obtain meaningful insights into the physicochemical properties of the biological macromolecules and assemblies of YOUR project. You will also be able to receive high- quality training and to develop new skills under our guidance.



Head of Core Facility: Patrick England

Contact

Mail: biophysique@pasteur.fr
Website: www.pasteur.fr/biophysics/

Mission

At the PFBMI, you will find the largest panel of molecular-scale characterization approaches available in France, enabling you to gather precise quantitative data about your proteins (or other macromolecules) and the interactions in which they are involved.

The PFBMI provides cutting-edge instrumentation and expertise to support the campus and the scientific community in general (both in academic and industrial contexts).

For each technology, expert support is available and users can be trained to gain operational autonomy. Turnkey solutions for quality control of purified protein samples are also provided.

PFBMI also develops innovative approaches, in particular regarding the analysis of membrane proteins, large multi-molecular complexes and lipid-protein interactions.

What we do

The following biophysical technologies are available on campus:

Analytical ultracentrifugation (AUC), Circular dichroism (CD), Fluorescence spectroscopy (including anisotropy and DSF), Light scattering (DLS and MALS), Mass Photometry (MP),

Microcalorimetry (ITC and DSC), Microscale thermophoresis (MST), Real-time biosensing (SPR and BLI) and Taylor dispersion/viscometry. PFBMI also provides access to synchrotron facilities for small-angle X-ray scattering (SAXS) measurements.

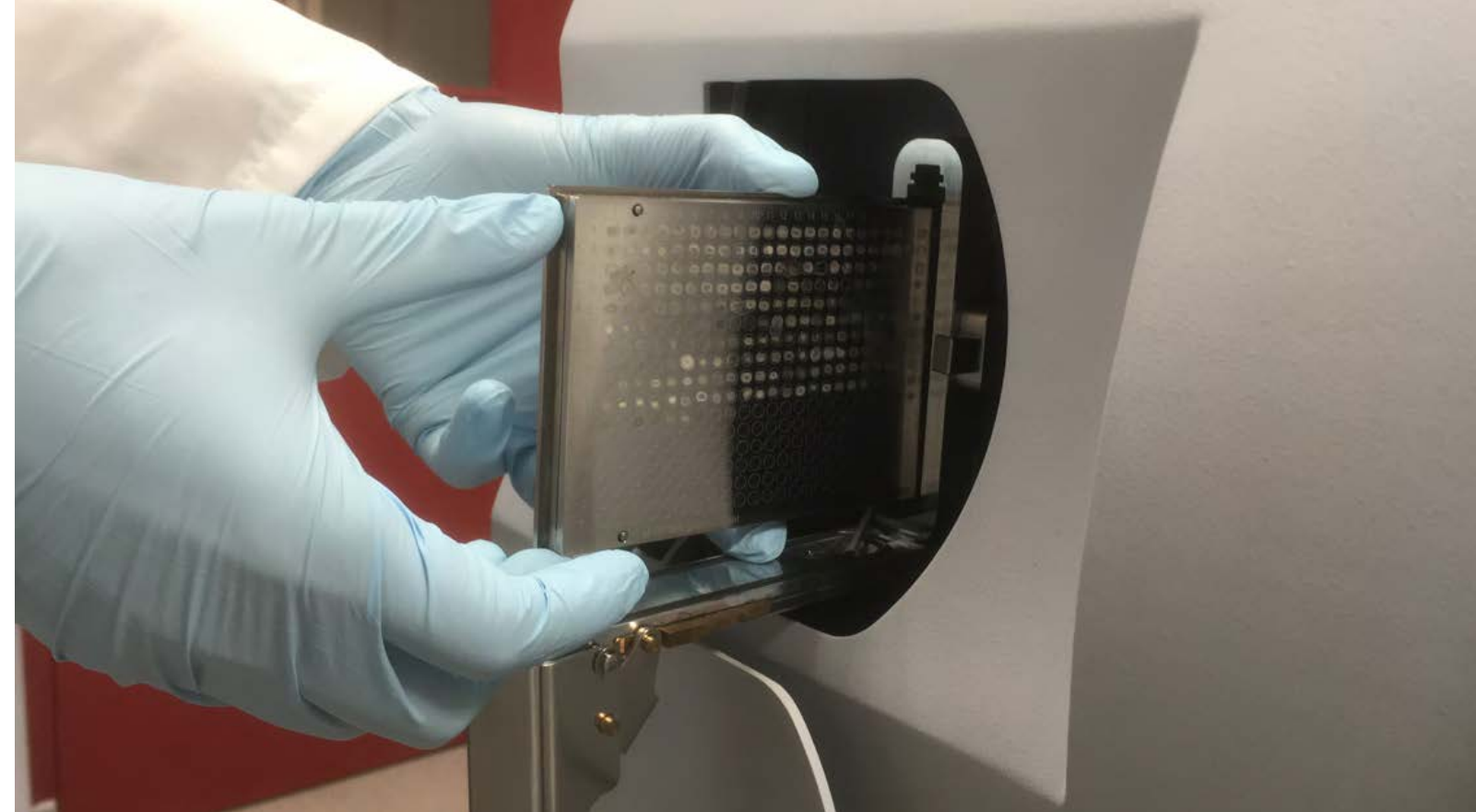
You feel lost among all these technologies and acronyms? Don't worry: we are here to help you through and make sure you go back home with more than what you expected!

Our expertise includes

- Molecular interactions
- Hydrodynamics
- Spectroscopy
- Kinetics
- Thermodynamics
- Purified protein quality control

Some examples of success stories

- The PFBMI plays an essential role in the development of novel therapeutic antibodies against a variety of targets, involved notably in viral and autoimmune diseases. Fruitful collaborations have been developed over the years, for instance with the teams of Felix Rey and Pierre Bruhns, leading to several high profile publications (Cell, Nature, Science, Nature Biotechnology).



- Efficient international networking is necessary for a core facility to remain at the forefront. The PFBMI coordinates a large pan European network in molecular-scale biophysics, which was lacking until 2014. MOSBRI (see below) currently brings together 15 institutions from 11 European countries, with many more closely linked to it through the ARBRE association. By working with us, you will be in touch with all the expert stakeholders in the field, wherever they are situated.

How to work with us/how to apply for support

Requests should be submitted by e-mail to biophysique@pasteur.fr

An initial face-to-face or virtual meeting allows to design a tailored experimental strategy and to agree together on an implementation procedure (most frequently involving both the PFBMI personnel and that of the requesting lab, at least in the initial phases).

You can also meet with the PFBMI team at open desks that are organized jointly with the other C2RT core facilities involved in the field of protein science.

The PFBMI always tries to ensure that it provides a significant and relevant added value to each project it is involved in. After initial proof-of-concept experiments, partnerships are strongly valued and encouraged (for instance joint grant applications, student co-tutorship...).

Furthermore, the PFBMI encourages the users to become autonomous and trains them accordingly.

Certifications and Networks

We are labeled by IBIISA as a core facility of national relevance since 2008.

We initiated in 2014 a network of molecular-scale biophysics core facilities, infrastructures and resource laboratories: ARBRE (Association of Resources for Biophysical Research in Europe. This network,

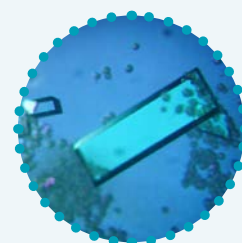
coordinated by Patrick England and widely recognized as the European reference in the field, was a large pan European COST Action between 2016 and 2020, and is now funded by the European Commission as a European Research Infrastructure called MOSBRI (MOlecular-Scale Biophysics Research Infrastructure).



Crystallography Core facility (PFX)

High-throughput crystallization screening and 3D structure determination of biological macromolecules

X-ray crystallography is the most widely used technique to reveal the three-dimensional structure of biological macromolecules at atomic resolution. These structures are essential to understand the molecular details of protein function, protein-protein interactions and overall mechanistic reactions. The biological macromolecules studied by research groups at Institut Pasteur are of major concern in the field of life sciences related to human health. With this powerful technique, our goal is to solve the three-dimensional structures of biological macromolecules for therapeutic, diagnostics and vaccine development.



Head of Core Facility: Ahmed Haouz

Contact

Mail: pf6@pasteur.fr

Website: <https://research.pasteur.fr/fr/team/crystallography/>

Mission

The crystallography core facility provides research groups working in the field of macromolecular crystallography with the expertise and technology required for high-throughput crystallization screening, X-ray diffraction measurements, and crystallographic computing.

We offer expertise in crystallography, from the crystallization of selected protein targets to the resolution of crystal structures of biological macromolecules. We ensure this mission by participating as a partner in scientific research projects (ANR, PTR, and individual collaborations) involving studies of single proteins and protein complexes.

We have recently expanded our portfolio of service provision to the resolution of structures by cryo-EM single particle analysis.

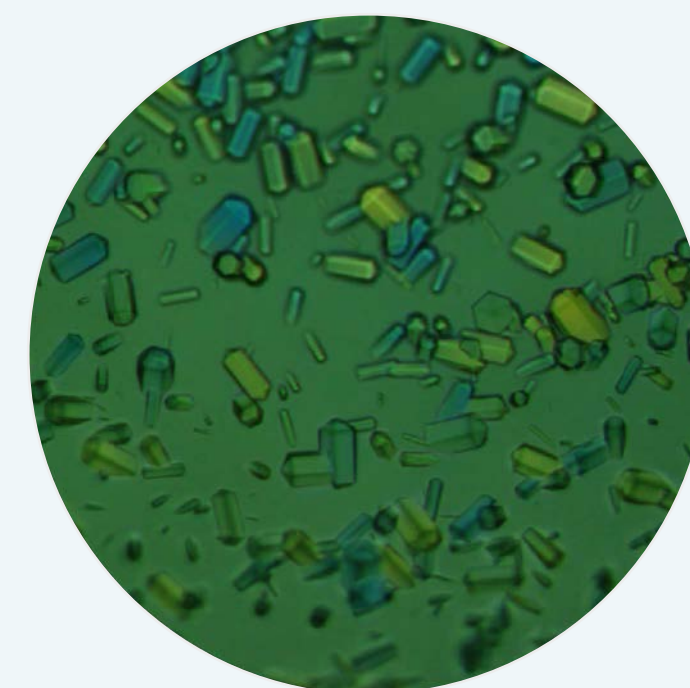
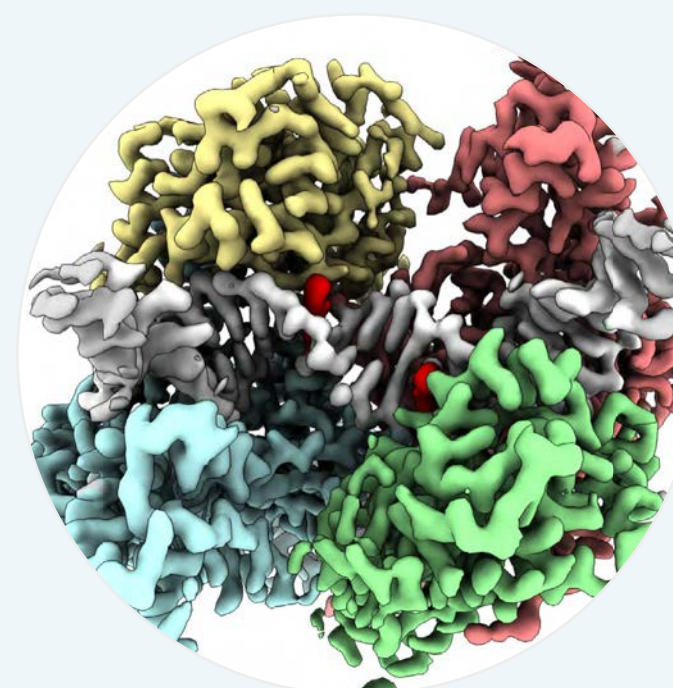
What we do

Protein samples submitted to our facility are subjected to high-throughput crystallization for X-ray studies, and depending on the size of the macromolecule, an aliquot of the sample can be used to prepare cryo-EM grids for imaging at the Institut Pasteur Nanoimaging facility.

For X-ray data collection, the core facility is a member of the Block Allocation Group (BAG) of Institut Pasteur for regular access to synchrotrons ESRF (Grenoble) and SOLEIL (St Aubin).

Our expertise includes

- Protein Biochemistry
- Liquid handling automation
- Crystallization of biological macromolecules
- X-Ray Diffraction
- 3D Structure determination and refinement (X-ray crystallography and CryoEM-SPA)
- Computing for molecular structural biology



Some examples of success stories

- 1 Sleiman D *et al*, A third purine biosynthetic pathway encoded by aminoadenine-based viral DNA genomes. *Science*. 2021 Apr 30, 372:516-520.
- 2 Sharma A *et al*, The epitope arrangement on flavivirus particles contributes to Mab C10's extraordinary neutralization breadth across Zika and dengue viruses. *Cell*. 2021 Dec 9, 184:6052-6066.
- 3 Bruch EM *et al*, Actinobacteria challenge the paradigm: A unique protein architecture for a well-known, central metabolic complex. *Proc Natl Acad Sci U S A*. 2021 Nov 30, 118:e2112107118. doi: 10.1073/pnas.2112107118. PMID: 34819376
- 4 Madru C, et al., Structural basis for the increased processivity of D-family DNA polymerases in complex with PCNA. *Nat Commun*. 2020 Mar 27;11:1591.
- 5 Weber et al., High-Throughput Crystallization Pipeline at the Crystallography Core Facility of the Institut Pasteur. *Molecules*. 2019 Dec 5, 24:4451.

How to work with us/how to apply for support

For crystallography projects, depending on the expertise of the users, three options are offered: service provision, instrument allocation, and scientific collaboration.

Apply by e-mail to: pf6@pasteur.fr

You can meet with the PFX team at regular open desk meetings organized jointly with the other C2RT core facilities involved in the field of protein science.

Certifications and Networks

We are GIS-IBiSA labeled and ISO-9001 certified.



Biological NMR and HDX-MS Core facility (PF BioNMR-HDX)

NMR and HDX-MS technologies for your structural biology needs

Nuclear Magnetic Resonance (NMR) and Hydrogen/Deuterium eXchange followed by Mass Spectrometry (HDX-MS) are powerful and versatile techniques to tackle challenging biological questions and offer complementary information to X-ray and cryo electron microscopy.

Head of Core Facility: Iñaki Guijarro

Contact

Mail: bionmr@pasteur.fr
Website: wwwBioNMR-HDX

Mission

We provide state of the art solution NMR and HDX-MS techniques to study at an atomic or molecular level protein interactions, dynamics, structure, fragment and ligand screening, post-translational modifications, real-time kinetics, chemical structure of carbohydrates and small compounds.

What we do

We are equipped with three NMR spectrometers: an 800 MHz and a 600 MHz (Bruker) dedicated to biological NMR. Both are equipped with high sensitivity cryogenic probes and automated sample changers. Our 500 MHz (Agilent) is dedicated to routine QC for chemists. HDX-MS is performed on a SynaptG2-Si HDMS (Waters) with ETD, an ACQUITY UPLC M-Class system, and a LEAP-Pal robot for automated sample handling and data acquisition.

Our team carries out support tasks, provides analyzed data and develops innovative methods in HDX-MS to aid in the rapid statistical validation and visualization of large HDX-MS datasets (MEMHDX software), to study membrane proteins and proteins in complex environments.



Our expertise includes

- Molecular interactions of proteins (proteins, nucleic acids, carbohydrates, compounds...)
- Fragment/Ligand screening, hit validation and characterization
- Protein and protein-complex dynamics over a large time-scale (picoseconds – hours)
- Intrinsically disordered proteins and protein folding
- Post-translational modifications (phosphorylations, acetylations...)
- 3D solution structure of small proteins

Some examples of success stories

- The structural analysis of *B. pertussis* CyaA toxin led to a publication in *FASEB J.* 2019 (3:10065-10076) on the role of acylation in the control of the function and folding of the toxin – collaboration with A. Chenal.
- NMR and HDX-MS used with cryoEM to unravel the dynamics of a type 2 secretion system pseudopilus – collaboration with Izadi N and Nilges M, *J Biol NMR*, 2019,73:293-303.



How to work with us/how to apply for support

You can meet with the BioNMR-HDX core facility team at regular open desks that are jointly organized with the other C2RT core facilities involved in the field of protein science.

A request for support starts by sending an email to bionmr@pasteur.fr, contacting us by phone or personally, prior to submit an application and a sample description form available on our website. We will shortly organize a meeting to define with you the feasibility, the experimental strategy and the schedule.

In most instances, we will perform experiments and analyze the data. For relatively long studies (> 1.5 years), we will provide hands-on training and technically support PhD students or postdocs throughout their project to become autonomous. In addition, we provide spectrometer time for NMR experts or we record data to be analyzed by the users.



SCREENING, MICROFLUIDICS AND ORGAN ON CHIPS

Chemogenomic and Biological Screening Core facility (CCB)

Exploring the world of small molecules and biologics for new medicines and deciphering biological networks

Chemogenomic and biological screening are important steps in precision medicine and for the discovery of new medicines, as well as in dissecting molecular pathways and biological networks.

Head of Core Facility: Fabrice Agou

Contact

Mail: pfccb@pasteur.fr

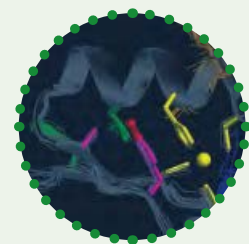
Website: <https://research.pasteur.fr/fr/team/fabrice-agou-team/>

Mission

We support researchers in improving the efficiency of their target-based (HTS) and phenotypic (HCS) screening bioassays, in identifying genetic modulator of function, in assessing target engagement, in isolating high quality chemical or biological substances of therapeutic, diagnostic or mechanistic interest, as well as in using core technologies typically applied to miniaturization and automation of bioassays.

What we do

We assist research teams with the development of robust target-based (HTS) and phenotypic (HCS) assays, and provide high quality hits. For HCS, phenotypic analysis can be carried out either with a conventional automated microscope (IX83, Olympus) or the new microscope StellarVision (Optical Biosystems, USA) that uses structured illumination and Synthetic Aperture Optics (SAO). For HTS screening, we have the ability to support cellular and biochemical assays using a wide variety of HTS readouts (absorbance, fluorescence anisotropy, AlphaScreen, HTRF, luminescence and TSA). We also make available the Octet HTX instrument, which enables high throughput label-free detection via biolayer interferometry (BLI) technology (FortéBio, Molecular Devices).



With our acoustic nl dispenser (Echo550, Labcyte) and the Freedom EVO® 200 workstation (TECAN), we can very easily reformat multiwell plates for you (96, 384 and 1536 format), offer cherry-picking service and prepare any daughter plates from our biological and chemical collections. Finally, we also provide strong supports for developing chemical probes as well as drug candidates (hit to lead and lead optimization), especially for some promising projects with a high therapeutic index.

Our expertise includes

Assay development for HCS and HTS screening bioassay; protein-protein and RNA-protein interaction inhibitors; medicinal chemistry; target deconvolution following phenotypic screen; various functional and chemical libraries including small molecules, cyclic peptidomimetics, antibody-like protein and siRNA/gRNA (ubiquitome and personalized siRNA libraries).

Some examples of success stories

- Nhabane Said Halidi K *et al* (2019). *IScience*, 20:292- 309.
- Borkowski O *et al*, 2020. *Nat Commun*, 11:1872.



- Savulescu A *et al*, 2021, *Cell Rep Methods*, 1:100068.
- Zahradník J *et al*, 2021. *Nat Microbiol.*, 6:1188-1198.
- Lavigne, M *et al*, 2021, *Nucleic Acids Res.*, 49:7695-7712.

How to work with us/how to apply for support

A request for support starts by sending a mail to pfccb@pasteur.fr. You will be asked to give us an overview of your project at first, submit your project to our steering committee, and then meet in person to give us any details so we can figure out together the best way to develop and miniaturize your HTS or HCS bioassay. We can also assist and train you to become autonomous on some automated equipment, help you during every step of the screening process, and can perform for you a small, medium and large screening campaign for you.

Certifications and Networks

France: Société Française de Biochimie et Biologie Moléculaire (SFBBM), Société de Chimie Thérapeutique (SCT) and ELRIG (European Laboratory Research & Innovation Group).

Europe: alliances of Life Sciences for Core facilities; HTSRC Rockefeller, NY (High Throughput & Spectroscopy Research Center).



Biomaterials and Microfluidics Core facility (BMcf)

Designing and producing your MicroPhysiological System

Today's biomedical research heavily relies on fast-paced innovation. The use of state-of-the-art technologies offers an important competitive advantage. Both microfluidics and 3D cell culture technologies have opened new venues for the development of innovative cellular assays as they allow a better recapitulation of the biophysical and biochemical microenvironment.

Head of Core Facility: Samy Gobaa

Contact

Mail: bmcf@pasteur.fr, samy.gobaa@pasteur.fr
Website: <https://research.pasteur.fr/fr/team/biomaterials-and-microfluidics/>

Mission

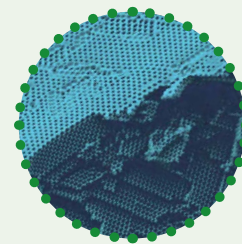
Our objective is to bridge biology and engineering to help with the development of biomedical projects with a strong technological focus. To this end, we provide a set of tools targeted for the better understanding of complex cell-pathogen and or cell-microenvironment interactions.

What we do

We provide the campus with microfluidic chip design and production capabilities, a library of synthetic hydrogels dedicated to 3D cell culture. We are also investigating multiple organoid protocols. Finally, we are operating an Organ-on-Chip Center that offers microfluidic systems capable of recapitulating *in vitro* organ/tissue function.

Our expertise includes

- Microfabrication
- Microfluidics
- Hydrogels
- Micro-patterns
- 3D cell culture
- Organ-on-Chip

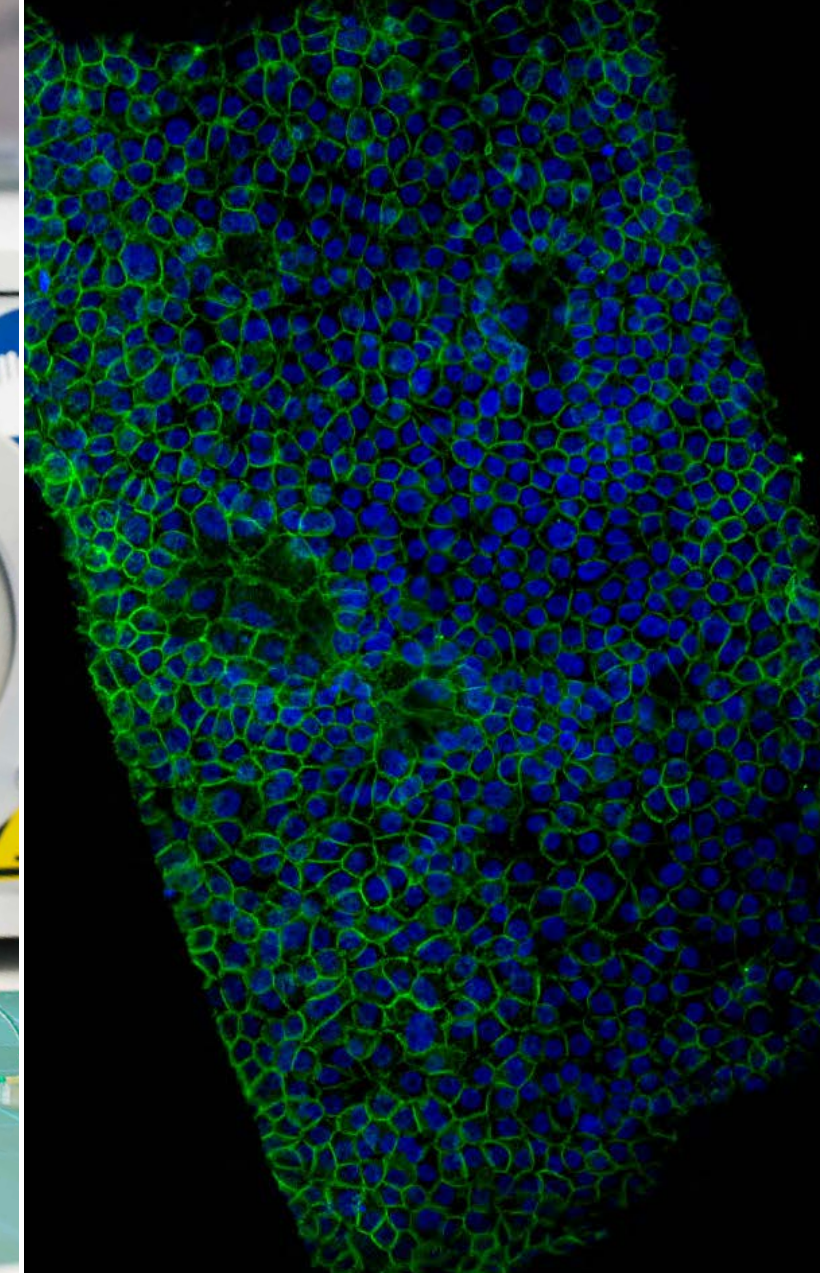


Some examples of success stories

- In collaboration with the team of Nathalie Sauvonnet we have developed a new model of intestinal infection based on a microfluidic Organ-on-Chip device. This tool showed that *Shigella* infection can be faithfully recapitulated in by mimicking the mechanical forces of the intestinal microenvironment (including shear stress and peristaltic motion) on-chip.
- Bioengineered Human Organ-on-Chip Reveals Intestinal Microenvironment and Mechanical Forces Impacting *Shigella* Infection. Grassart A, Malardé V, Gobaa S, Sartori-Rupp A, Kerns J, Karalis K, Marteyn B, Sansonetti P, Sauvonnet N.

How to work with us/how to apply for support

Classically we run 4 types of projects: Do-It-Yourself, Proof-of-Concept, Co-Development or Organ-on-Chip. If you have an idea you think (bio)engineering can help with, please feel free to contact the BMcf team for a joint brainstorming, consulting or even for outlining a future collaboration.



1. Do it Yourself. Benefits from the full set of bookable equipment at the facility. Users must undergo training sessions in order to be able to work as s autonomous users.
2. Proof of Concept. These aim at investigating whether the envisioned bioengineering approach can help with the biological question at hand. First round of investigation is directly performed by our team (chip design and fabrication, cell encapsulation assay...). In a later stage, users are requested to take over the data generation process after the first proof-of-concept.
3. Co-Development. Involvement of the Biomaterials and Microfluidics core facility will be larger and will span over a longer period of time.

4. Organ-on-Chip. The Organ-on-Chip center hosted by the Biomaterials & Microfluidics core facility is geared towards the production fully matured Emulate recapitulating different types of organs. We provide dedicated personnel and chip actuation machines in a BSL2 and BSL3 environment.

You can either email us, call or simply drop by the core anytime. Our philosophy is to accept all the (technologically feasible) requests. We commit to providing you with a first answer on feasibility within a few days.



Diagnostic Test Innovation & Development Core facility (CF Diag)

Imagine and design tomorrow's bioassays for health

The COVID-19 pandemic has shown the importance of *in vitro* diagnostic assays to evaluate the prevalence of the infection in local or world-wide populations. New generations of prognostic, diagnostic and therapy follow-up bioassays blossom from science and technology innovation supporting and improving our health care systems from point-of-care to high-throughput laboratories.

Head of Core Facility: Thierry Rose

Contact

Mail: diag@pasteur.fr

Website: <https://research.pasteur.fr/en/team/diagnostic-test-innovation-and-development-core-facility/>

Mission

This new core facility aims to be a precursor of tomorrow's diagnostic tests for a better care of each patient from the corner of the street to the end of the world. Along collaborative projects, we design, develop, assess and run innovative technologies, methods or reagents up to pre-industrial maturity for assaying specific biomarkers in samples for diagnostic purposes.

What we do

We develop *in vitro* assays for specific biomarkers at high-throughput on multi-well plates, highly multiplexed on slides, rapid tests on lateral flow devices (LFIA) and instant tests in tubes with standard or innovative detection modes: absorbance, fluorescence, FRET, fluorescence polarization, time-resolved fluorescence, time-resolved FRET, luminescence, BRET, AlphaScreen®, AlphaLISA®, plasmonic resonance intensity or phase. Biomarkers can be proteins or nucleic acids of scientific, clinic, veterinarian, epidemiologic or environmental interest and samples are human or animal body fluids, cell biopsy or tissue lysates, culture media,

smears or environmental water or waste. Assays are mainly based on constructs involving a probe and a reporter. We design or screen probes for their binding properties such as antibodies, single-chain variable domain antibody fragments and nanobodies (VHH) which can be displayed in libraries of phages (M13/P11) or *Escherichia coli* (intimin). For the reporting component, we design and develop high-performance luciferases for bioluminescence, protein domains for fluorescence, FRET or BRET, nanogold binding tails as well as streptavidin binding tags.

The high-sensitivity and high-throughput plate reading is achieved using multi-mode apparatus (Mithras 2 or Centro from Berthold Technologies) or, single tube monitoring apparatus (LSC from Hydrex, Lumat from Berthold). Our plate washer/loader (Zoom, Berthold) also insures reproducible and high-performance operations. We design and develop lateral flow device prototypes in our dedicated workshop. Our programmable liquid handling automates (EVO, Tecan) can be used for loading or reformatting samples in tubes, multi-well plates (from 6 to 1536 wells), membrane as well as slides, and running large series of samples (up to 20,000 LuLISA assays/day) for scientific, clinic or epidemiologic collaborative studies using new or gold standard methods.



We also develop mechanic force assays on cells or protein-coated beads using acoustic (Lumicks), laminar flow, centrifugation or optical tweezers (ISIR). Cell-cell interactions, cell adhesions to coated beads or surface can be measured at the single cell level from one to several thousand of cells to detect alteration and/or decipher activation or recognition mechanism in order to diagnose cellular alterations associated with infection, cancer and immune pathologies from blood drops.

We collaborate with internal and external research and technical teams (start-ups, companies, institutions) for methodological or technological development of their assays, their automation and their evaluation using gold standard methods and reference samples.

Our expertise includes

Multi-mode immunoassay development, bioluminescence applications in imaging and bioassay, mechanobiology method development for cell adhesion and cell-cell interaction assay.

Some examples of success stories

- Le Vu S *et al*, *Nat Commun*. 2021, 12:3025.
- Roederer T *et al*, *The lancet Public Health* 2021, 6:e202-e209.
- Anna F *et al*, *O. Eur J Immunol*. 2021, 51: 180–190.

- Goyard S *et al*, *Allergy*. 2020, 75:2952-2956.
- Kamsma Det *al*, *Cell Reports*. 2018, 24:3008-3016.

How to work with us/how to apply for support

Send us (at diag@pasteur.fr) a very short description of your project and your expectations. We will provide you with a feedback shortly including a planning of the next steps. For assay development missions requiring more 5 consecutive days of work, your project will be submitted to our steering committee.

Certifications and Networks

We have an incentive networking action in the field of bioassays and diagnostics. We are affiliated to the innovation accelerator of the Institut Pasteur benefiting of its business development and intellectual property supports.





C2RA

Animal core facilities

INTRODUCTION

Mission of the Center for Animal Resources and Research

The mission of the C2RA is to support the Institut Pasteur research teams and scientific departments in achieving their research objectives by addressing their present and future needs for animal research.

C2RA aims at:

- Providing researchers with state-of-the-art equipment, services, and technical expertise to enable the success of their projects
- Providing training and education on advanced technologies and methods
- Sourcing new and emerging technologies through technological surveillance and proposing methodological developments
- Identifying in close connection with the scientific departments the strategic needs for laboratory animal science expertise
- Meeting high standards for animal welfare
- Ensuring compliance with ethical principles and regulation

“

At the Institut Pasteur, we have always combined cellular and animal models as complementary approaches to obtain a precise understanding of diseases and develop relevant preventive and therapeutic strategies, for the benefit of human health. We care about laboratory animals and are committed to reducing and refining their usage in particular through the improvement of experimental design, the implementation of alternative experimental models and new technologies as well as by improving the skills of personnel through training.

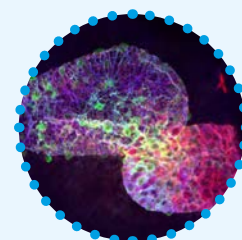
Jean Jaubert,

Director of the center for animal resources and research
and head of Institut Pasteur central animal facility

Central Animal Facility (CAF)

Providing access to a wide range of animal models and experimental settings in accordance with animal welfare and ethical rules

Studying biological mechanisms in whole organisms remains essential in many areas of research investigated at Institut Pasteur. The use of animals must comply with strict regulatory, ethical, and biosafety rules. The quality of data produced using animal models critically depends on the physical and microbiological environment provided to the animals. Animal research requires all personnel to be adequately trained and projects to be authorized.



Head of Core Facility: Jean Jaubert

Contact

Mail (administrative issues):

sec-anim@pasteur.fr

In case of emergency or for non-administrative questions, contact the head managers of the different poles by phone.

Website: https://webcampus.pasteur.fr/jcms/c_87159/portail-animalerie

Mission

Our core facility provides the necessary biological resources, technological support, and expertise to access to animal models.

What we do

The CAF is divided into five poles with different managers and missions:

- Animal Welfare, Regulatory follow-up (training, skills, drugs...) – Myriam Mattei
- Equipment washing, Maintenance, Logistics – François Rimlinger
- CFJ facility and related activities (breeding zone), Embryology – Franck Bourgade
- Lwoff facility and related activities, Center for Gnotobiology of the Institut Pasteur, Technical-Assistance – Marion Bérard
- A3, Metchnikoff, Monod/Fernbach facilities and related activities – Laëtitia Breton

On top of the activities specific to these poles, we also offer different transversal services:

- Quality control: a team is in charge of the microbiological and genetic quality control of the rodents, rabbits, and quails housed in the animal facilities. The team also controls the efficacy of disinfection processes used at the CAF (autoclave, chemical disinfection in locks or isolators). They can be contacted at sentinelle-anim@pasteur.fr or genotypage-anim@pasteur.fr
- Evaluation of the risks associated to protocols (biological, chemical, or physical) performed on animals, in partnership with Service Prevention des Risques. Submit your protocol at risk-anim@pasteur.fr
- Importation and Exportation of animals either as live animals or frozen material, organized in partnership with the Import-Export service on campus. Contact us at anim-impex@pasteur.fr
- Help in designing and prototyping customized equipment to carry out animal experiments in the best conditions and in compliance with the 3Rs. Contact the head of the corresponding pole.



- Specific Training related to animal experimentation, organized in close collaboration with the Education Center (contact: ae-mouse@pasteur.fr)
 - Regulatory course for project designers (rodents and lagomorphs): 2 sessions per year, in English
 - Specific training to design and perform surgical procedures on rodents: 2-3 sessions per year, in French or English

How to work with us/how to apply for support

The different support forms to fill are available on the CAF website on webcampus (internal access only): http://webcampus.pasteur.fr/jcms/c_87140/fr/accueil-animalerie

You can also access each pole's specific webpage or our FAQ.



CAF / Animal Welfare Body and Regulatory Monitoring

Facility accreditation, Animal Welfare body (AWB), Designated veterinarian, Training, Competence monitoring, Pharmacy

The use of animals for experimental purposes must comply with regulatory and ethical rules. The quality of the data produced using animal models and the reproducibility of the results depend greatly on the respect of animal welfare and the competence of the personnel.

Head of Pole: Myriam Mattei

Contact

Email (designated veterinarian):

myriam.mattei@pasteur.fr

Email (animal welfare body):

sbea-anim@pasteur.fr

Web: internal access only, on webcampus

https://webcampus.pasteur.fr/jcms/c_442205/fr/structure-chargee-du-bien-etre-des-animaux-sbea

Mission

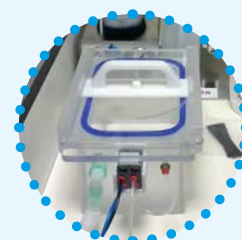
Our mission is to ensure that the Institut Pasteur's animal facilities obtain and/or renew their accreditation, monitor the animals in breeding and in experimentation, assist researchers in the design and implementation of their experimental projects, train personnel involved in animal experimentation, and monitor their skills. We also provide drug management services.

What we do

We provide support and regulatory expertise in animal experimentation for the Institut Pasteur.

Each animal facility must be accredited. We ensure that the design of facilities, the procedures, and the laboratories and equipment for working on animals comply with the regulations. We accompany the legal authorities (DDPP) during site visit inspections for accreditation.

Each person must be trained, both initially and regularly. We organize training in relation to animal experimentation and keep track of



the skills of every user in accordance with the regulation.

Each project involving animals must be approved. We provide veterinary and animal welfare advice for each project application prior to its evaluation by the ethics committee (CETEA).

Each animal in experimentation must be followed. We ensure the care and welfare of animals at all times through the Animal Welfare Body (SBEA in french), in compliance with the 3Rs (Replace, Reduce, Refine). We help researchers in the study and prototyping of customized equipment to carry out animal experiments in the best conditions and in compliance with the 3Rs.

Each drug used must be traced. We ensure the supply and control of drugs used on animals.

Our expertise

- Animal experimentation regulation, facility accreditation
- Laboratory animal veterinary science
- Animal welfare and ethics
- Training



Some examples of success stories

- La chirurgie aseptique et l'importance des soins post-opératoires chez la souris dans les conditions des animaleries de la recherche. M. Mattei, *STAL*, 2021
- Bread Feeding Is a Robust and More Physiological Enteropathogen Administration Method Compared to Oral Gavage. Derbise *et al*, *Infect. Immun.*, 2020
- Mise en place de structure en charge du bien-être animal en situation complexe. Joubert *et al*, *Colloque OPAL*, 2018

How to work with us/how to apply for support

Contact us at our generic e-mail address: sbea-anim@pasteur.fr

Or through our website on webcampus (internal access only) https://webcampus.pasteur.fr/jcms/c_442205/fr/structure-chargee-du-bien-etre-des-animaux-sbea



CAF / Equipment Washing - Maintenance - Logistics

A support team acting transversally for the animal facilities across campus and Hearing Institute

The implementation of animal experimentation within the animal facilities of the Institut Pasteur relies on a support team that takes care of equipment washing, maintenance, and logistics.

Head of Pole: François Rimlinger

Contact

Email (washing): laverie-anim@pasteur.fr

Email (maintenance):

maintenance-anim@pasteur.fr

Email (logistics): log-anim@pasteur.fr

Web: internal access through webcampus only

[https://webcampus.pasteur.fr/jcms/](https://webcampus.pasteur.fr/jcms/wcp_1000450/fr/pole-laverie-maintenance-logistique)

[wcp_1000450/fr/pole-laverie-maintenance-logistique](https://webcampus.pasteur.fr/jcms/wcp_1000450/fr/pole-laverie-maintenance-logistique)

Mission

Equipment washing, maintenance, and related logistics for most of the Institut Pasteur's animal facilities, including facilities that do not depend directly on the CAF (C2RA, Hearing Institute, CNR...). We provide expertise and support to all these structures in the maintenance, modification, and installation of equipment.

What we do

The washing section ensures the washing, reconditioning, and sterilization of the small equipment used on a daily basis within the animal facilities. Whenever possible we use state-of-the-art robotic equipment.

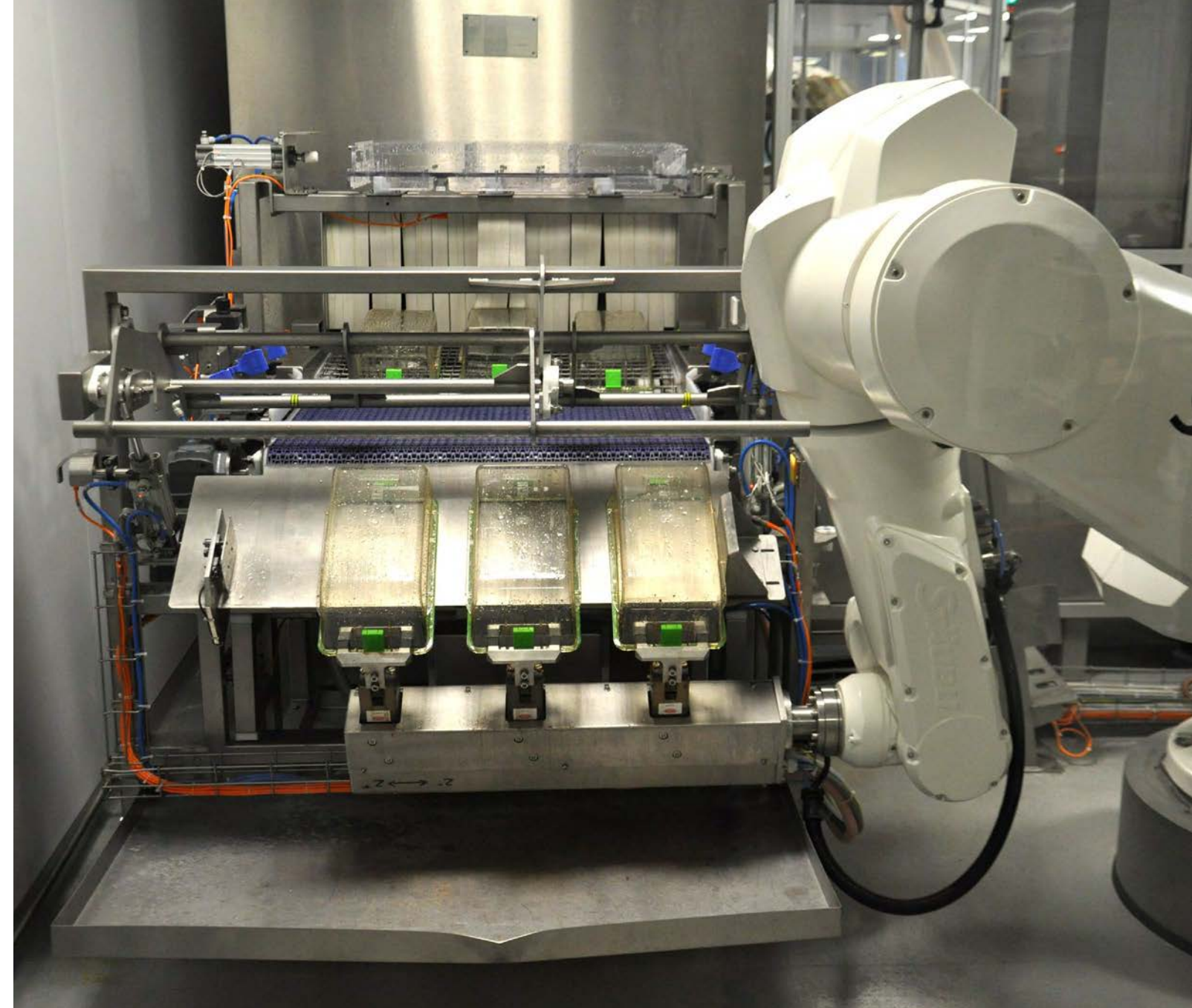
The maintenance section ensures both preventive and curative maintenance for all equipment used in the different animal facilities, in accordance with regulatory requirements (Risk Prevention Department, SBEA, ANSM, DDP, HCB). We specifically:

- Accompany external service providers within controlled areas for specific interventions
- Work in strong collaboration with the Institut Pasteur internal technical services for small interventions and the establishment of preventive planning
- Perform most interventions within controlled areas

The logistics section manages orders, traces stock, and organizes the dispatching of the various consumables required for operating within the animal facilities. We also manage, in conjunction with the purchasing department, calls for tender specific to our activity (food, bedding, protective clothes...).

Our expertise includes

- Robotic, mechanic, electricity, and automation
- Logistic and supplies
- Biosafety and risk assessment



How to work with us/how to apply for support

Contact us at our generic e-mail addresses.

Or through our website on webcampus (internal access only):

https://webcampus.pasteur.fr/jcms/wcp_1000447/fr/pole-bien-et-re-animal-suivi-reglementaire



CAF / Center François Jacob facility and related activities, Embryology

Rodent Breeding Services, Rederivation through embryo transfer, Cryopreservation

The CFJ animal facility houses centralized breeding of genetically modified mouse and/or rat strains, at the highest sanitary level, to meet researchers' experimental needs in respect of the 3Rs. The breeding zone works in conjunction with the Embryology team. The CFJ animal facility also houses the animal component of other C2RA core facilities: CIGM, and HDM.



Head of Pole: Franck Bourgade

Contact

Email (breeding coordination):

elevage-anim@pasteur.fr

Email (whole EOPS-CFJ team):

bimeeops-anim@pasteur.fr

Email (embryology):

cryodeconta-anim@pasteur.fr

Web: internal access through webcampus only

[https://webcampus.pasteur.fr/jcms/](https://webcampus.pasteur.fr/jcms/wcp_1000451/fr/pole-cfj-et-activites-liees-embryologie)

[wcp_1000451/fr/pole-cfj-et-activites-liees-embryologie](https://webcampus.pasteur.fr/jcms/wcp_1000451/fr/pole-cfj-et-activites-liees-embryologie)

Mission

The breeding zone in the CFJ animal facility (BIME-EOPS) aims to maintain and produce high-value transgenic lines under SOPF (Specific and Opportunistic Pathogen Free) sanitary conditions. The breeding zone offers tailored breeding levels that meet the needs of the Institut Pasteur researchers, in respect of the principles of the 3Rs rules (Replace, Reduce, Refine) driving animal experimentation. This work is performed in close conjunction with the embryology team.

What we do

Contact the breeding coordination people in advance to discuss your project and your needs and set up tailored breedings to meet your experimental needs. We maintain and

breed your strain of interest at SOPF sanitary status and exit animals for your experimentation purposes at your request (exits occur twice weekly, on Tuesdays and Thursdays). You can visualize your produced animals and create specific requests through the dedicated software (Mayakind-EL) and/or the CAF own database system (BDAC).

The Embryology team performs the redervation of all transgenic lines to enter the breeding zone. We also propose cryopreservation services for all these transgenic strains, by freezing either sperm or embryos. This allows safeguarding the researcher's most valuable transgenic lines and can be used to revitalize the line in case of any microbiological contamination, a drop in fertility, a change in the expression of a transgene over time, or genetic contamination.

Embryology team members also participate in different Pasteur courses (IP-Mouse Genetics, IP-Regulatory Training in Mouse Experimentation).

Our expertise includes

- Breeding services (Mice and Rat)
- Rederivation by embryo transfer (after In-vitro Fertilization-IVF, or spontaneous plugs)
- Mouse and Rat Cryopreservation (sperm or embryos)
- Rapid Colony Expansion (through IVF)
- Working in SOPF and SPF sanitary conditions



Some examples of success stories

- A human immune system mouse model with robust lymph node development. Li *et al*, *Nature methods*, 2018
- Identification of new loci involved in the host susceptibility to Salmonella Typhimurium in collaborative cross mice. Zhang *et al*, *BMC Genomics*, 2018

How to work with us/how to apply for support

Contact us at our generic e-mail addresses:

i) breeding coordination:

elevage-anim@pasteur.fr;

ii) whole BIME-EOPS team:

bimeeops-anim@pasteur.fr

iii) embryology team:

cryodeconta-anim@pasteur.fr

Or through our website on webcampus (internal access only):

https://webcampus.pasteur.fr/jcms/wcp_1000451/fr/pole-cfj-et-activites-liees-embryologie



CAF / Centre for Gnotobiology of the Institut Pasteur, Technical Assistance

Producing axenic and gnotoxenic rodents and associated services. Providing technical assistance to implement experimental procedures on animals.

Head of Pole: Marion Bérard

Head of the animal technician team of the
Centre for Gnotobiology: Eddie Maranghi

Assistant to the head/coordinator of the
Technical-Assistance: Déborah Groussard

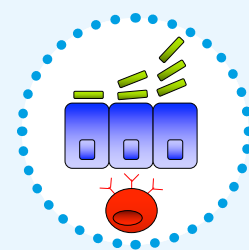
The Centre for Gnotobiology of the Institut Pasteur (CGIP)

Contact

Email: axenie-anim@pasteur.fr

Procedures to follow to access CGIP services are available at:

https://webcampus.pasteur.fr/jcms/c_516275/fr/centre-de-gnotobiologie



Mission, What we do, Our expertise

The CGIP was created in 2009 to answer to new needs expressed by the Institut Pasteur scientific community. Transfer of technology from the INRAe and the CNAM allowed implementation of the production of axenic lines by cesarean section, which could then be further bred and used in different facilities across the campus. In 2015, all the activities developed at the CGIP were centralized in Lwoff renovated animal facility. The CGIP is now a partner for the Institut Pasteur research units and one of the technological bases for the development of scientific projects involving the study of Host-Microorganism interactions. This service is also open to external collaborators.

The CGIP includes specialized staff, equipment and a dedicated facility (Lwoff), which are part of the CAF and C2RA.

The CGIP provides the services that are necessary to carry out the experimental protocols on axenic and gnotoxenic mice:

- Production of axenic mice from non-axenic mice, breeding, weekly quality controls by aerobic and anaerobic culture (in addition to the annual FELASA health tests).
- Production of gnotoxenic mice (by gavage of axenic mice with isolated bacteria, carried out by the CGIP and/or the research groups) and breeding of the C57BL/6 gnotoxenic mouse line carrying the oligoMM12 microbiota.
- Experimental protocols whether or not involving infectious agents. The CGIP provides the technical assistance, equipment, and materials necessary for the research groups and carries out the protocols transmitted by the research groups.
- Production of tissues collected from axenic mice (C57BL/6J and C3H) raised at the CGIP. Available tissues include blood, urine, duodenum, jejunum, ileum, caecum, spleen, kidneys, liver, brain.



Technical Assistance

Contact

Email for rodents:
at-anim@pasteur.fr

Email for rabbits: lapins-anim@pasteur.fr

Procedures to follow to access the technical assistance services are available at:
https://webcampus.pasteur.fr/jcms/wcp_984325/fr/aide-technique/-/technical-assistance



Mission, What we do, Our expertise

Technical-Assistance is a service proposed to all scientists working at the Institut Pasteur and the Institut de l'Audition to implement for them (and sometimes with them) experimental procedures on animals, in the different animal facilities of the Institut Pasteur (main campus and Hearing Institute campus).

The staff implementing the experimental procedures on-demand, are partners for the Institut Pasteur research units and constitute one of the technological bases for the development of scientific projects involving live animals.

We coordinate responses to the research units requests and the implementation of experimental procedures on rodents and rabbits, which can involve for instance administration (s.c., i.m., i.v., i.p., i.n., oral gavage), sampling (blood, urine, feces), surgeries, behavioral testing, or training of animals for 2P-microscope imaging. This assistance can be punctual or on the long run. We can implement already developed procedures on existing animal models (rodents and rabbits), or develop new techniques/animal models, whether or not involving infectious agents. We provide technical assistance and carry out the protocols transmitted by the research groups.



Some examples of success stories

- Development of gnotobiotic mouse models:
 - to improve the efficiency of cancer therapy: *Science*, 2015, **350**:1079;
 - to study the impact of gut microbiota on the postnatal development of the immune system: *Immunity* 2019, **50**:1276
 - to study phagotherapy: *Cell Host Microbe*, 2020, 28:390
 - to study the interactions of gut microbiota and the brain *Nat. Commun*, 2020, **12**:6363
- Contribution to the implementation of a hamster model of SARS-CoV-2 for therapeutics screening together with the Chemogenomic and Biological Screening Platform (PF-CCB) (BSL-3 facilities / infectious animal models).
- Contribution to the implementation and in vivo study of the phenotype of several mouse models for the Neurosciences department (to explore: Alzheimer Disease; Hearing; Gut-Brain axis).

Certifications and Networks

The CGIP is one of the co-founder of the European Consortium for Gnotobiology and one of the partner of the INFRAFRONTIER 2020: <https://www.infrafrontier.eu/infrafrontier-research-infrastructure/international-collaborations-and-projects/infrafrontier2020>.

AFSTAL (Association Française des Sciences et Techniques de l'Animal de Laboratoire); FELASA (Federation of European Laboratory Animal Science Associations); AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care); CTLS (Core Technologies for Life Science).

CAF / A3, Metchnikoff, Monod/Fernbach facilities and related activities

Teams and experts at your disposal to support research in life sciences

Our different teams act in support of investigators and are always ready to accompany them in their projects.

Head of Pole: Laëtitia Breton

Contact

Email for A3 facilities: a3-anim@pasteur.fr

Email for Monod/Fernbach facilities:

monod-anim@pasteur.fr

Email for Metchnikoff facility:

metchnikoff-anim@pasteur.fr

Web: internal access through webcampus only

[https://webcampus.pasteur.fr/jcms/](https://webcampus.pasteur.fr/jcms/wcp_1011382/fr/pole-a3-metchnikoff-monod/fernback)

[wcp_1011382/fr/pole-a3-metchnikoff-monod/](https://webcampus.pasteur.fr/jcms/wcp_1011382/fr/pole-a3-metchnikoff-monod/fernback)

[fernback](https://webcampus.pasteur.fr/jcms/wcp_1011382/fr/pole-a3-metchnikoff-monod/fernback)



Mission

Our main mission is to meet the needs of the Institut Pasteur investigators using animals for scientific purposes, in compliance with the different regulations (Animal Experimentation, GMO, Biosafety and Biohazards...). We work in close collaboration with the Risk Prevention Service (SPR on many subjects).

What we do

We offer a wide-range of housing options and confinement in the different structures: filtered-top cages, individually ventilated cages, isolators, disposable cages ... to adapt to the specific needs of animals and experimental projects.

We offer access to different experimental spaces and setup: surgery, behaviour setup, in-vivo imaging lab in BSL3 – managed by UtechS BPI.

We are in charge of the husbandry of different animal species: mice, rats, hamsters, guinea-pigs, gerbils, rabbits and quails. We take care

of the comfort of these animals, with feeding adapted to the different animal species, and the maintenance of their accommodations.

We also control all the environmental factors of our structures in order to maintain containment, hygiene, safety of people and treatment of animals. We also ensure a daily observation in accordance with the regulation and in close collaboration with the animal welfare body (AWB).

We support investigators with technical assistance in the realization of their research protocols within our structures and in any new project. For technical assistance with rabbits, contact us at lapins-anim@pasteur.fr. For technical assistance with other species, contact us at at-anim@pasteur.fr (see a more detailed description of this activity in the dedicated pole).

Our expertise includes

- Accommodation, care, control and follow-up
- Animal welfare, animal handling
- Regulations and procedures
- Hygiene and safety rules



Some examples of success stories

- Attenuation of clinical and immunological outcomes during SARS-CoV-2 infection by ivermectin (Dias de Melho *et al*, *EMBO Mol. Med.*, 2021).
- COVID-19-related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters (Dias de Melho *et al*, *Sci Transl Med.*, 2021).
- Intranasal vaccination with a lentiviral vector protects against SARS-CoV-2 in preclinical animal models (Ku *et al*, *Cell Host Microbe.*, 2021).

How to work with us/how to apply for support

Contact us at one of our generic e-mail addresses, or Laëtitia Breton by phone at extension 9551, or through our website on webcampus (internal access only): https://webcampus.pasteur.fr/jcms/wcp_1011382/fr/pole-a3-metchnikoff-monod/fernback



Center for Production and Infection of Anopheles (CEPIA)

Mosquitoes and Plasmodium parasites for Malaria Research

Malaria, a major worldwide public health problem, is caused by the infection of humans with *Plasmodium* parasites. These parasites are transmitted to people by the bite of infected female *Anopheles* mosquitoes. CEPIA provides the infrastructure, scientific and technical expertise for studying the complete life cycle of *Plasmodium* parasites.



Our expertise includes

- *Anopheles* breeding.
- Scientific and technical expertise in the complete life cycle of rodent (*P. berghei*) and human (*P. falciparum*) parasites

Some examples of success stories

- Partner of Infravec2 consortium funded by the European Commission Horizon 2020 Research Infrastructure Program (INFRAIA).
- Costa DM *et al*, TRSP is dispensable for the *Plasmodium* pre-erythrocytic phase. *Sci Rep*. 2018, **8**, 15101. doi: 10.1038/s41598-018-33398-8.
- Aliprandini E *et al*, Cytotoxic anti-circumsporozoite antibodies target malaria sporozoites in the host skin. *Nat Microbiol*. 2018, **3**, 1224-1233. doi: 10.1038/s41564-018-0254-z. Epub 2018 Oct 22. PMID: 30349082.
- Singh P *et al*, Role of a patatin-like phospholipase in *Plasmodium falciparum* gametogenesis and malaria transmission. *PNAS*. 2019, **116**, 17498-17508.

Contact

Mail: cepia@pasteur.fr

Website: <https://research.pasteur.fr/fr/team/center-for-production-and-infection-of-anopheles/>

Mission

Our core facility provides the necessary biological resources (parasite/vector/host) and expertise for malaria research projects.

What we do

We continuously mass breed *Anopheles coluzzi* and *A. stephensi* mosquitoes.

We routinely perform in vitro culture of *P. falciparum* asexual and sexual (gametocyte) stages.

Infections of *Anopheles* mosquitoes with human (*Plasmodium falciparum*) and rodent (*P. berghei*) parasites are undertaken weekly.

Upon request, dissections can be performed to obtain samples of infected mosquitoes such as hemolymph sporozoites, midguts and salivary gland sporozoites.

Existing protocols are improved and new ones developed.

Training is provided for users to become autonomous in the facility.



How to work with us/how to apply for support

A request for support starts by sending a mail to cepia@pasteur.fr with an outline of project.

A meeting will be organized with CEPIA team to assess its feasibility.

You will be asked to provide additional information concerning risk prevention, animal experimentation etc.

<https://research.pasteur.fr/fr/team/center-for-production-and-infection-of-anopheles/>



Mouse Genetics Engineering Center (CIGM)

Murine Transgenesis and Gene Editing

Transgenesis and, more recently, Gene Editing by specific nucleases allow the introduction/modification/expression of genes of interest and have become an indispensable tool to modern biology for the generation of an endless number of new murine models for medical and basic research.



Head of Core Facility: Francina Langa Vives

Contact

Mail: francina.langa-vives@pasteur.fr
Website: <https://research.pasteur.fr/en/team/mouse-genetics-engineering/>

Mission

CIGM provides the main steps and expertise for the generation of genetically modified murine models by all types of transgenesis, additive and targeted. We use our broad expertise in molecular and cellular biology to render the best quality services in transgenesis techniques and we provide a tailor-made service while encouraging the development of project-driven technologies in tight collaboration with our partners.

What we do

CIGM creates new models of genetically modified mice/rats by additive transgenesis by microinjection of embryos with DNA fragments, BACs, YACs or lentiviral transgenes.

We also generate Knock-Out (KO) and Knock-In (KI) new murine models by targeted transgenesis using Homologous Recombination in Embryonic Stem-ES cells or, more recently and increasingly, microinjecting / electroporating specific nucleases, specially gene editing with new CRISPR/Cas9 systems.

In addition, we also provide molecular biology services, related to the generation (CRISPR/Cas9 strategy design) and genotyping of genetically engineered mice.

Our expertise includes

- Preimplantation murine embryo Micromanipulation,
- Zygote/Morula/Blastocyst Microinjection,
- Embryonic Stem (ES) Cell Culture,
- Zygote and ES Cell Electroporation,
- Gene editing by CRISPR/Cas9, TALE, ZFN Technologies in mouse/rat zygotes.

CIGM members also participate to different Pasteur Courses (*IP-Mouse Genetics*, *REVIVE-Advances in Stem Cell Biology*, *IP-Regulatory Training in Mouse Experimentation*).

Some examples of success stories

- Brain cross-protection against SARS-CoV-2 variants by a lentiviral vaccin in new transgenic mice (Ku *et al*, *EMBO Mol Med*, 2021)
- Generation of modified mouse embryos by CRISPR/Cas9 systems for studying the *Fgf8* regulatory landscape (Hornblad *et al*, *Nature Comm.*, 2021)
- Rat KO & KI models for nicotine addiction by Zinc Finger Nucleases (Forget *et al*, *Curr. Biol*, 2018)
- Mouse KI model for *Ataxia Telangiectasia* disease by CRISPR/Cas9 (Lesport *et al*, *Oncotarget*, 2018)
- Mejo KO mice by homologous recombination in ES cells (Abby *et al*, *Nature Comm.*, 2016)



- *Tmem176a/Tmem176b* double KO mouse by CRISPR/Cas9 (Lemoine *et al*, *J. Genet & Genomics*, 2016).

How to work with us/how to apply for support

You can contact us by e-mail: francina.langa-vives@pasteur.fr in order to define your needs and choose the best transgenesis approach for your project (customized collaborations).

Certifications and Networks

FLV is a cofounder of the International Society for Transgenesis Technologies (ISTT, 2006).

Member of CELPHEDIA (Creation, ELevage, PHEnotyping, DIstribution and Archiving of model organisms) network since 2016.

Member of ARRIGE (Association for Responsible Research and Innovation in Genome Editing) network since 2019.



Hearing Institute Animal and Phenotyping Core facility (AIDA)

Characteristics of auditory and vestibular profiles of mouse models

In France, according to the WHO, six million people are affected by some form of deafness or hearing loss and globally by 2050 one in four people will have hearing problems. In order to address this public health major problem, the aim of the Hearing Institute is to improve understanding of the principles and mechanisms that underpin the development and workings of the auditory system. Its research fields particularly include auditory perception and cognition, audio communication, multisensory integration, and interactions between the genome and the acoustic environment.

The use of animals is essential to approach the auditory organ as a whole and animal research requires a highly controlled technical and administrative environment.

Head of Core Facility: Marta Lindner

Contact

Mail: marta.lindner@pasteur.fr

Website: <https://research.pasteur.fr/fr/team/hearing-institute-animal-phenotyping-core-facility/>

Mission

The main mission of AIDA is to provide housing services for mice mostly, maintenance of mouse strains, animal care, and welfare in compliance with animal experimentation regulations. AIDA is also in charge of applying the procedures for the maintenance of sanitary status and of maintaining experimental rooms in good working order.

The Auditory Phenotyping platform, which is a part of AIDA, provides infrastructure and technical background to **characterize the auditory and vestibular profiles** of mouse models and to evaluate the effectiveness of innovative therapies and treatments on animal models of audio-vestibular dysfunction.



What we do

The Auditory Phenotyping platform provides electrophysiology and behavior setups that allow determining the auditory and vestibular profile of various mouse models in order to understand the functioning of the auditory system.

PF offers access to equipment, assistance, and training for:

- measurements of auditory brainstem response,
- measurements of cochlear microphonic potentials and otoacoustic emissions,
- noise exposures of different levels,
- analysis of startle response,
- animal tracking in a free or constrained environment,
- analysis of oculovestibular reflex (coming soon),
- analysis of the kinetic or dynamic distribution of mice weight (coming soon),
- rotarod performance test (coming soon),
- balance test: forced swimming test, balance beam.

The development of the Auditory Phenotyping platform is based essentially on close collaboration with the Center for Research and Innovation in Human Audiology (CERIAH) developing and realizing research protocols involving humans to characterize auditory and vestibular functions. This collaboration allows the simultaneous development of approaches, tools, and methods in humans and in animal models to obtain perfectly comparable data and conclusions.



AIDA offers also access to other experimental spaces like a surgery room with stereotaxic instruments or a perfusion system.

Our expertise includes

- Electrophysiological exploration of hearing,
- Behavioral hearing tests,
- Animal care and welfare; advice in animal ethics.

How to work with us/how to apply for support

You can contact us by e-mail: marta.lindner@pasteur.fr in order to define your needs and specify if/how AIDA can contribute to the success of your project.

<https://research.pasteur.fr/fr/team/hearing-institute-animal-phenotyping-core-facility/>



Histopathology Platform (HistoPath)

Offers a state-of-the-art histotechnological laboratory with a specialized team

Our platform is available for histotechnological collaborative research. Many projects are currently ongoing on animal models of infectious diseases, cancer, immunotherapy or inflammation with internal or external research teams. Individuals wishing to develop collaborative research efforts are encouraged to contact us when developing research projects. Optimal results are obtained when the staff is contacted as early as possible in the conception of the *in vivo* part of the project; this allows us to help determine how the histological approach can best support the research aim.

Head of Core Facility: David Hardy

Contact

Mail (general): historequest@pasteur.fr

Website: <https://research.pasteur.fr/en/team/histopathology/>

Mission

Our Histopathology platform offers a state-of-the-art large histotechnological laboratory with a specialized team for your histopathological study.

What we do

A variety of histology services is available to research investigators:.

- Necropsy & gross examination of animal tissues
- Design of the protocol
- Methodology advice on proper tissue collection
- Choice of morphological approaches (fixation, embedding, slide preparation, slide treatments)
- Evaluation of the slides
- Histological and morphometric analysis
- Fine-tuning of Histopathology protocols



- Discussion of the results
- Recommendations for further experiments

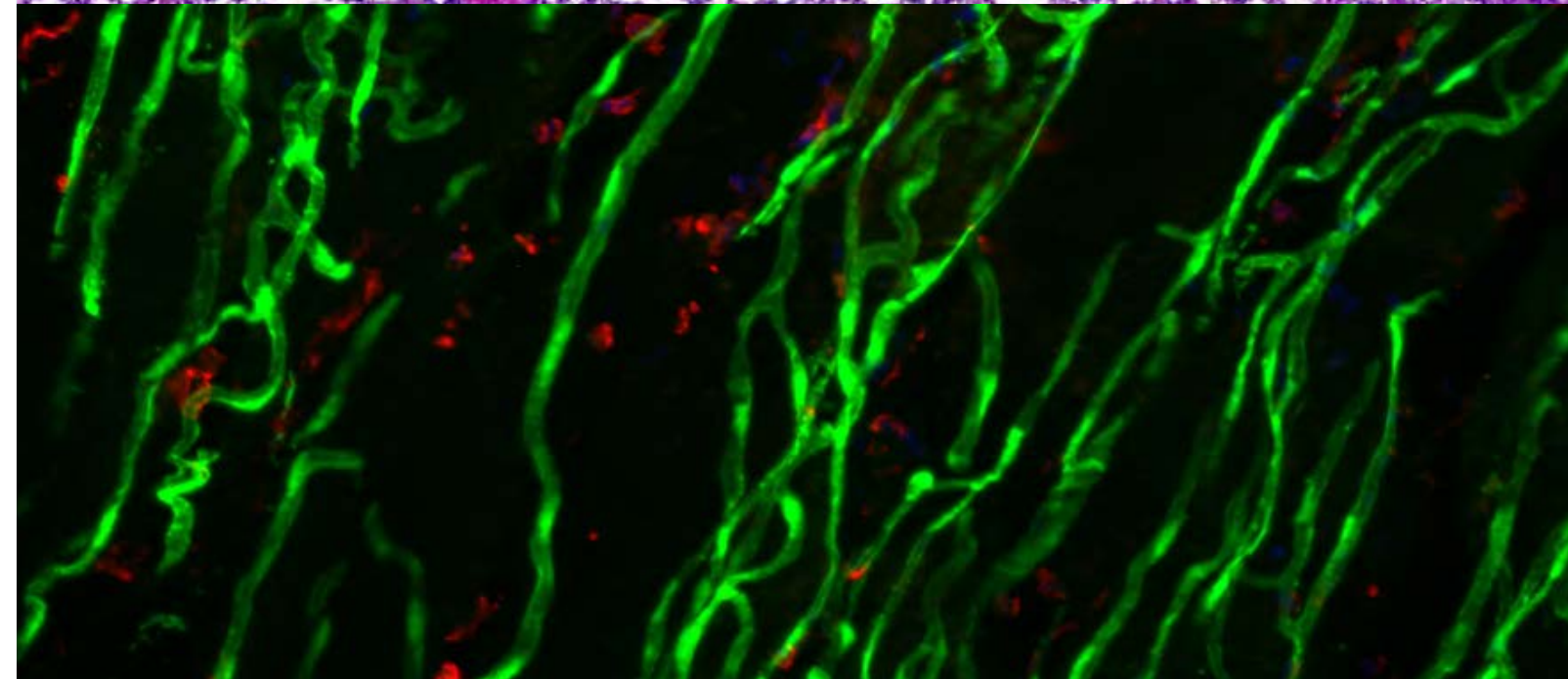
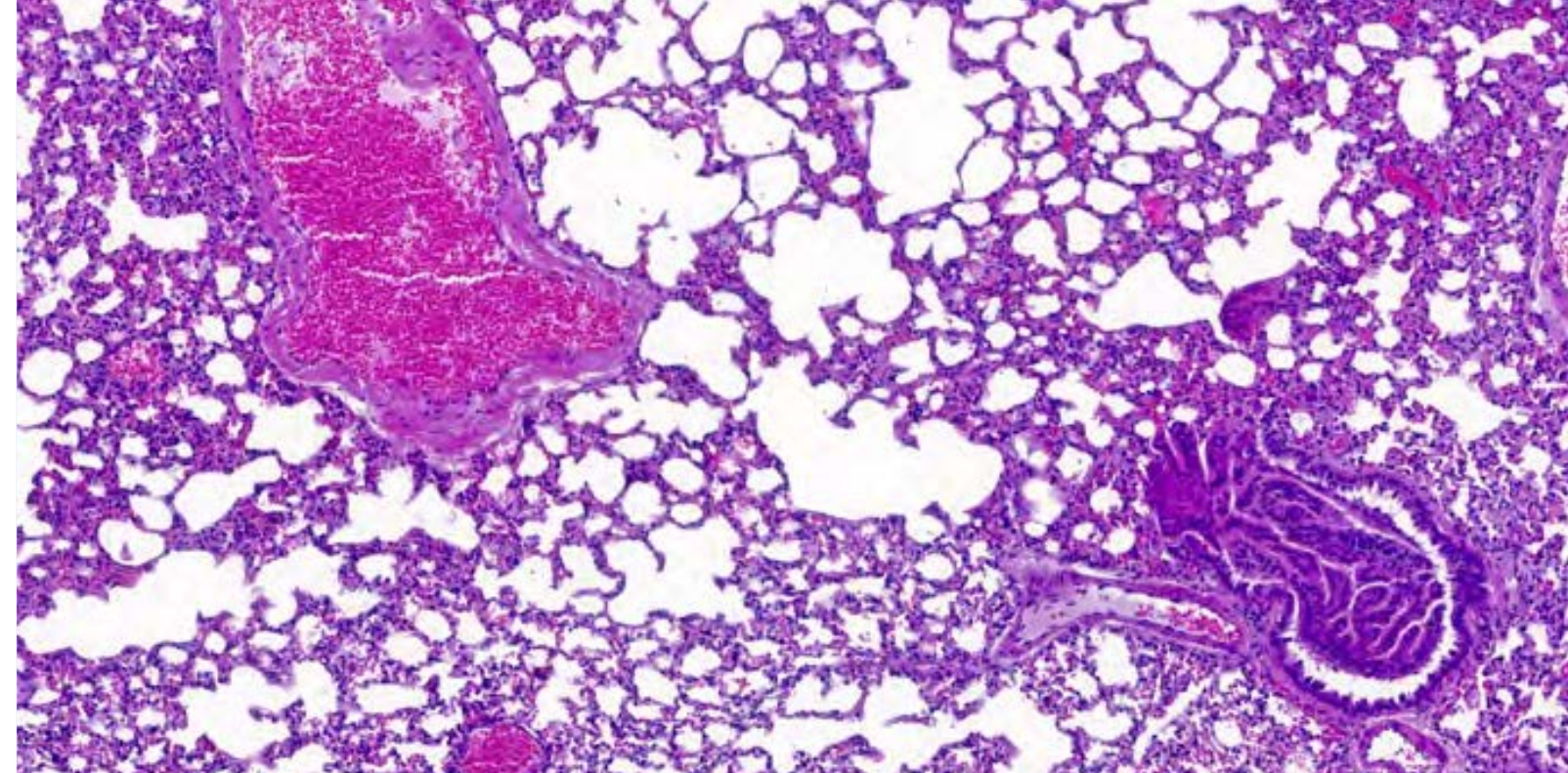
Technics

Our Histology platform prepares slides and a wide variety of quality, flexible histopathological and immunohistochemical stains for investigative staff. We also develop new technical tools for animal tissue analysis:

- **Embedding:** Low-melting point paraffin (P37), Classical paraffin (P60), Acrylic resin, frozen tissues, fresh tissue.
- **Cutting:** Microtome (3µm), Cryostat (7µm), Vibratome (50-100µm)
- **Staining:** Classical (Haematoxylin & Eosine) or specific staining like: Red Sirius, Perls, Oil Red'O, Alcian blue, PAS, Grocott etc.
- **Immunohistochemistry:** Customization and fine-tuning of immunochemistry and immunofluorescence.
- We also have access to **Safety level 3** facility for frozen sectioning of infected human or animal tissues.

Some examples of success stories

- Brain cross-protection against SARS-CoV-2 variants by a lentiviral vaccine in new transgenic mice (Ku *et al*, *EMBO Mol. Med.*, 2021)
- A live measles-vectored COVID-19 vaccine induces strong immunity and protection from SARS-CoV-2 challenge in mice and hamsters (Frantz PN *et al*, *Nature Comm.*, 2021)



- Attenuation of clinical and immunological outcomes during SARS-CoV-2 infection (de Melo *et al*, *EMBO Mol. Med.* 2021)
- Hidden Biomass of Intact Malaria Parasites in the Human Spleen (Leonardo *et al*, *N. Engl. J. Med.*, 2021).

How to work with us/how to apply for support

Mail (general): historequest@pasteur.fr

Website: <https://research.pasteur.fr/en/team/histopathology/>



Human Disease Models platform (HDM-PF)

Mouse models harboring a Human Immune System (HIS)

HIS mice are a robust *in vivo* model for studying immuno-biology and for analyzing the safety and effectiveness of potential new drugs modulating the immune system. HIS mice engrafted with Hematopoietic Stem Cells (HSC) are advantageous *in vivo* models for long-term studies in the field of human immune cells biology, immune-oncology and infectious disease.



Head of Core Facility: Mathilde Dusséaux

Contact

Mail: mathilde.dusseaux@pasteur.fr
Website: <https://research.pasteur.fr/en/team/human-disease-models-core-facility/>

Mission

HDM-PF produces HIS-mice and provides expertise for the possible applications of this model. Immuno-deficient mice engrafted with human hematopoietic stem cells (HSC) develop all major human lymphocyte classes (B, T, and NK cells) and their specialized subsets as well as a variety of myeloid cells (dendritic cell, monocytes, and macrophages). They constitute a small animal model in which to interrogate human immune responses against tumors or infections and to analyze the safety and activity of new drugs modulating the immune system.

What we do

HDM-PF provides immune-deficient mice bearing a human immune system (HIS). Different models are available:

- **BRGS (BALB/c Rag2^{-/-} Il2rg^{-/-} SirpaNOD) HIS mice**

These mice harbor all the major human hematopoietic cell subsets, such as B cells, T cells, NK cells, and the myeloid compartment including dendritic cells (DCs), plasmacytoid cells (pDCs), and monocytes/macrophages.

- **BRGSA2DR2 (BRGS expressing HLA-A2 and DR2 transgenes) HIS mice**
BRGS with improved human T-cell development and function after injection of matched HSCs.
- **BRGSF (BRGS Flt3^{-/-}) HIS mice boosted with soluble Flt3L**
BRGS with improved human myeloid and NK lineage
- **BRGST (BRGS expressing mTSLP transgene) HIS mice**
BRGS with improved lymph node development.

PF-HDM provides service levels tailored to the investigator's needs:

- **standard quality controlled HIS mice** to the research team which will perform their own experiments.
- **customized quality controlled HIS mice.** HIS mice engrafted with gene-edited HSCs or HSCs from patients provided by the research team (please contact us for more details).
- **In vivo pharmacology services** including, in close collaboration with the investigator, study design, protocol writing and execution, data analysis and study report.

Our expertise includes

- Maintenance of immune-deficient mice colonies (BRGS, BRGSA2DR2, BRGSF, BRGST).
- CD34⁺ cell isolation from Human Fetal liver.
- Construction of humanized mice by engraftment of human HSCs.



- Confirmation of reconstitution of a human hematopoietic system (T, B, NK, myeloid cells) in peripheral blood 10-14 weeks post-engraftment, by FACS.
- Injection of HIS mice with human pathogens or tumors.
- Evaluation of *in vivo* efficacy and safety of new immunomodulatory drugs.
- Human Immune System mouse tissue harvest.
- Flow cytometry, ELISA.

How to work with us/how to apply for support

You can contact us by sending a project request on PPMS or by e-mail: mathilde.dusseaux@pasteur.fr

A meeting will be organized with HDM-PF team to discuss research project needs, a high-level overview of experimental design and timeline, and associated analyses and services.





C2RI

Informatic core facilities

INTRODUCTION

Mission of the Center for Informatics Resources and Research

Scientific progress depends heavily on expertise in informatics. This has led Institut Pasteur to the creation of a large Bioinformatics and Biostatistics Hub, a unique structure that works closely with research units to analyze data, and to develop tailor-made algorithms and make them available to the scientific community via web interfaces. The computational expertise available on campus related to biomedical research is as extensive as the biological research topics and includes areas such as phylogenetic analysis, genomics, statistics, systems biology, image analysis, data management and high-performance computing. In total, around 80 employees are permanently employed in IT support.

The aim of the newly created Center for Resources and Research in Scientific Informatics is to further integrate the existing strengths in informatics at the institute, within the center, with the other support groups of the Department of Technology as well as with national and international organizations.

“

No scientific research in biology without computers, but not every biologist is a computer scientist... The mission of C2RI is to provide advanced support in computational biology to research groups and platforms. This includes data analysis in a large range of competences, development of tailor-made algorithms and web applications, data management, and high performance computing.

Michael Nilges,
Vice-president for technology of Institut Pasteur,
director of the center for Informatic resources by interim

Image Analysis Hub (IAH)

An open access / equal access core facility dedicated to services in Bioimage Analysis

The recent technological progresses in microscopy and probes fostered tremendous advances in Life Sciences fueled by imaging. They opened the way to unique understanding of the mechanisms of life, in particular investigating the processes and dynamics of single cells and organelles. But these advances left us with a large quantity of image data and a new challenge to address: extracting quantitative information from images to get new insights.

Head of Core Facility: Jean-Yves Tinevez

Contact

Mail: iah@pasteur.fr

Website: <https://research.pasteur.fr/en/team/image-analysis-hub/>

Mission

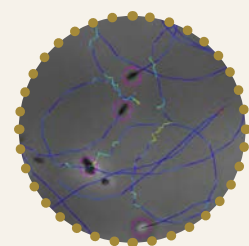
Our mission is to support researchers with the tools of Bioimage Analysis. We are an open access, equal access core facility committed to offering support in image analysis for the Institut Pasteur campus. All requests involving images are considered.

What we do

Our services are organized mainly around 4 activities:

1. Offer walk-in support and trainings for questions involving image analysis.
2. Build and deploy custom analysis tools for projects requiring special developments.
3. Maintain an infrastructure for autonomous image analysis. Deal with complex tool deployments.
4. Develop original and innovative software tools for image analysis, whose scope exceeds user projects.

The IAH was established at the end of 2017 to support researchers with the tools of Bioimage Analysis. We will help you getting quantitative information from images, either by collaborating with you on your project, building new image analysis tools for your research, training you, or by giving you access to commercial software for image analysis.



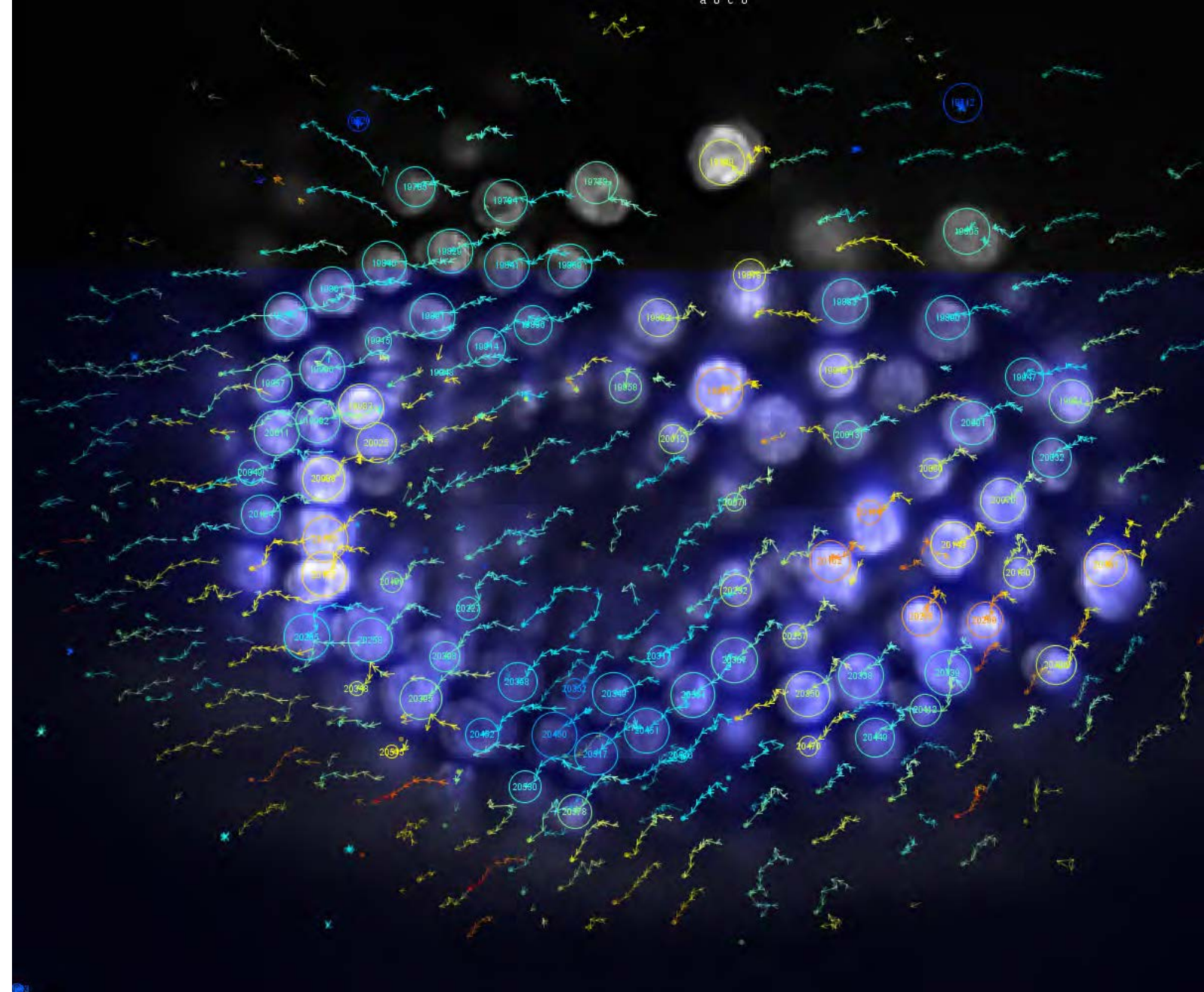
We also lead or contribute to several development projects that aim at building several end-user software tools for image analysis, whose scope exceeds that of a single user project. These tools include Icy, Fiji, TrackMate, Mastodon, etc. These tools give us platforms to answer future requests quicker, and give a competitive advantage to early adopters.

Our expertise includes

- image analysis techniques
- handling large images
- deep-learning
- biophysics
- software development

Some examples of success stories

- SARS-CoV-2 infection induces the dedifferentiation of multiciliated cells and impairs mucociliary clearance. Robinot *et al*, *Nature communications*, 2021.
- LocalZProjector and DeProj: a toolbox for local 2D projection and accurate morphometrics of large 3D microscopy images. Herbert *et al*, *BMC Biology*, 2021.



How to work with us/how to apply for support

Open desks are organized every two weeks on Thursday mornings to make a first contact with the team. You can also submit a project or request a training on our PPMS page: <https://www.pasteur.fr/ppms/?IAH>.

We typically collaborate with our users, contributing scientifically to their projects with image analysis. We also organize trainings and workshops to disseminate know-how to the campus.

Certifications and Networks

We are ISO9001 certified.

We are part of the NEUBIAS (Network of European BioImage Analysts) consortium (<http://neubias.org>) and of France-Bioimaging (<https://france-bioimaging.org/>).



High Performance Computing Core facility (HPC)

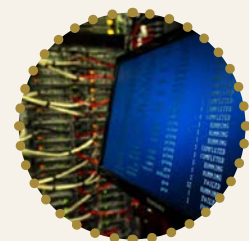
We can help you make your pipelines and workflows run faster!

Head of Core Facility: Youssef Ghorbal

Contact

Mail: hpc@pasteur.fr

Website: <https://research.pasteur.fr/en/team/hpc-core-facility/>



Mission

We provide comprehensive High Performance Computing (HPC) resources and services for Institut Pasteur researchers.

What we do

Install and operate HPC clusters: Provide computing resources including cutting edge computing facilities (GPUs, high bandwidth and low latency network, very fast scratch file system).

User assistance: clusters access and on-boarding, jobs monitoring, etc.

Software management and development: install and maintain relevant software collections and reference data catalogues on all HPC clusters

How to work with us/how to apply for support

A request for support starts by sending a mail/request to ask-hpc@pasteur.fr.

We opt for opensource software as much as possible.

Our expertise includes

- Slurm Scheduler System management
- Software development for CPUs and GPUs (CUDA)
- Code Profiling, Optimisation and Parallelisation
- Assistance in third-party software suites cluster integration
- Retrieval and indexing of reference data catalogue (Genomes data banks) automation



Data Management Core facility (DMcf)

Providing access to data management expertise for research data

Head of Core Facility: Anne-Caroline Delétoille

Contact

Mail: datamanagement@pasteur.fr

Website:

<https://research.pasteur.fr/fr/team/data-management-core-facility/>

Webcampus:

https://webcampus.pasteur.fr/jcms/c_915693/fr/plateforme-de-data-management

Our tool: REDCap®

eMail: redcap@pasteur.fr

Website: <https://redcap.pasteur.fr/home/>



Mission

Our main objective is to give support to research units and Core Facilities at Institut Pasteur for the management of their data. We are also involved in transversal projects to structure the organization of research data within the Institute and the integration of the FAIR principles in research projects.

- Implement process in order to ensure the findability, the accessibility, the interoperability and the reusability of the data.
- Help to write a Data Management Plan

The core facility can also provide support for the eCRF tool REDCap® (<https://redcap.pasteur.fr/home/>).

We can help you to set up your eCRFs:

- Advices in eCRF creation
- Trainings
- User Support (The core facility can only provide support for uses of RedCap® in research projects purpose).

What we do

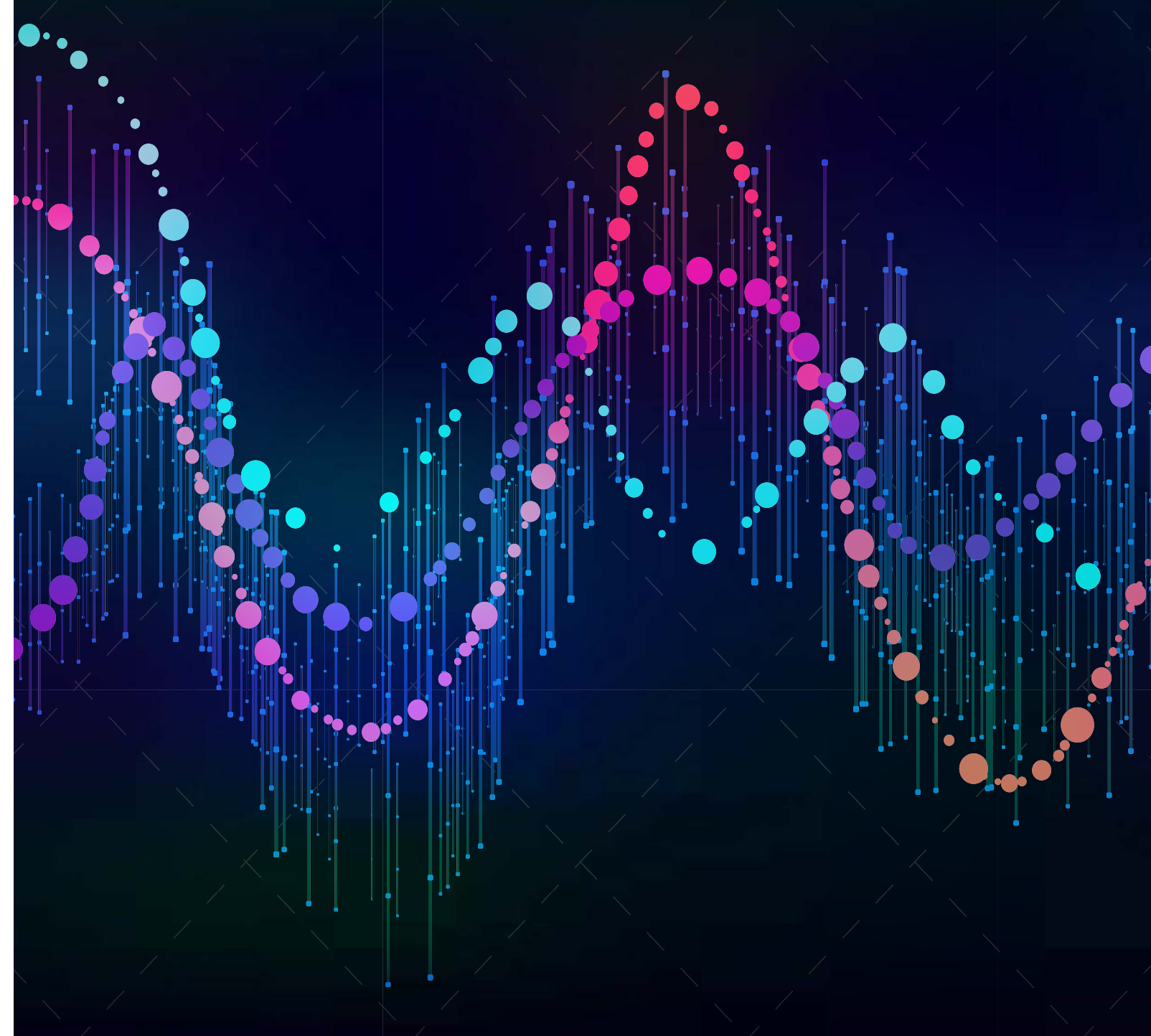
Within the Core Facility, we respond to requests for expertise or we can dedicate a data manager for your project. Our support is provided through the following tasks and responsibilities:

- Plan and anticipate data management needs
- Create, test and validate databases and train users
- Implement consistency checks to validate data and metadata quality and integrity and clean up data
- Ensure data long-term storage (standards, open formats...). Also, we can help on the selection of data to store
- Facilitate data sharing with the scientific community in compliance with regulatory standards
- Write documentation/user guides

Our expertise includes

- Data management of clinical and epidemiological data
- Planning data life cycle
- Checking data quality
- Expertise on data standards

Some examples of success stories: The DM-CF was quickly mobilized for the creation of data collection databases as part of the fight against the SARS-COV-2 virus, mainly for the CORSER, RC-COVID and SocialCov studies. The DM-CF is also involved in the data management of the Milieu Intérieur cohort and AIMS-2-Trial study.



How to work with us/how to apply for support

Applications for access will be accepted on a “first-come-first-served” basis. A request for support starts by sending an email to datamanagement@pasteur.fr. You can ask for expertise or collaboration or for a training. Based upon your request, you might be asked to fill additional documents. Researchers wishing to include our support in grant applications are encouraged to contact us by email.

Certifications and Networks

The Core Facility collaborates with the international REDCap® community and leads the French node of the REDCap® community. The Core Facility is also part of the RDA (Research Data Alliance) and the Ac@DM (groupe des Data Managers académiques).



Bioinformatics and Biostatistics Hub

Get the best of your data!

Head of Core Facility:

Marie-Agnès Dillies and Hervé Ménager

Contact

Mail: hub@pasteur.fr

Website:

<https://research.pasteur.fr/en/team/bioinformatics-and-biostatistics-hub/>

Mission

The Bioinformatics and Biostatistics Hub contributes to the research initiatives in computational biology, provides a strong support to the campus, and disseminates knowledge in bioinformatics and (bio-)statistics. A wide range of expertise is available to meet the needs of scientists, from specific advice on data analysis or experimental planning, to long-term collaborative projects including the development of methods and tools.

Our expertise includes

- **Bioinformatics data analysis:** HTS data analysis, Variant detection, Comparative genomics, Phylogenetics, Genotyping, Epigenomics, Transcriptomics, Single-cell, Metagenomics
- **Biostatistics:** Experimental design, Statistical and mathematical modelling, Machine learning, Multi-variate analysis, Analysis of omics data, Biological networks, GWAS
- **Software development and computing:** Algorithmics, Programming, Databases, UX and data visualization



What we do

- **Direct scientific support to the IP community:** From short questions to long term projects, one of the main objectives of the Hub is to use its pool of expertise to support IP researchers in their scientific projects with dedicated engineers.
- **Maintaining bioinformatics servers:** Among others, the Hub, together with the IT department, is responsible for deploying and maintaining the Galaxy@Pasteur bioinformatics platform.
- **Building bioinformatics and biostatistics capacity within the Institut Pasteur and the Pasteur Network:**
 - Organising and delivering the mandatory courses for IP's PhD students (see link for a complete list).
 - Providing State-of-the-art trainings to the sister institutes in the Pasteur International Network for twining collaborations with IP Paris (e.g. <https://phindaccess.org/>)
 - Supervising activities for M1, M2 and PhD students from different universities
 - Building a network of expertise and spreading a bioinformatics and statistics culture, through the detachment of Hub engineers in platforms and research units from most IP scientific departments.

Networks

We play an active role in several networks, such as the Institut Français de Bioinformatique (member platform), France Génomique (affiliated bioinformatics team), and the SFBI.

Moreover, we are directly involved in the management of the StatOmique group and ELIXIR Europe. Many members of the Hub contributed to the organization of the JOBIM 2021 conference.

The Bioinformatics program for PhD students has been acknowledged by most doctoral schools in Ile de France.



How to work with us/how to apply for support

There are many ways to reach us:

- By direct interaction during the **open-desk sessions**, every Tuesday morning from 10 to 12, in the lobby of Yersin building.
- By submitting **short questions** through our web site
- By collaborating to **research projects**, which you can submit here : <https://c3bi.pasteur.fr/services/submit-project/>

We appreciate working with IP scientists as partner of granted projects. When writing your fundings applications, think of us!



Hearing Institute Data Acquisition and Neural Signal Processing Facility

Signal Processing IDA (SPIDA)

The continuous improvements of technologies to record neuronal activity in larger fields of view, at multiple locations simultaneously, in 3D, with an increased spatiotemporal resolution, for a longer duration of acquisition or for multiple days, brought new insights about neural and behavioral mechanisms. Consequently, the acquisition setups have become more and more complex and multimodal and the amount of data to be processed has expanded. A current challenge is to develop data

acquisition, processing, storage, and standardization methods to collect and extract meaningful information from these systems. In response to these needs, the Hearing Institute, Center of the Pasteur Institute, dedicated to promoting an integrative approach to auditory neuroscience and human audiology, initiated the creation of the platform and hosts it. We provide our services and guidance for the research projects of the IDA research teams mainly and their collaborators.

Head of Core Facility:

Clara Dussaux

Contact

Mail: clara.dussaux@pasteur.fr

Website: <https://research.pasteur.fr/fr/team/hearing-institute-data-acquisition-and-signal-processing-facility/>



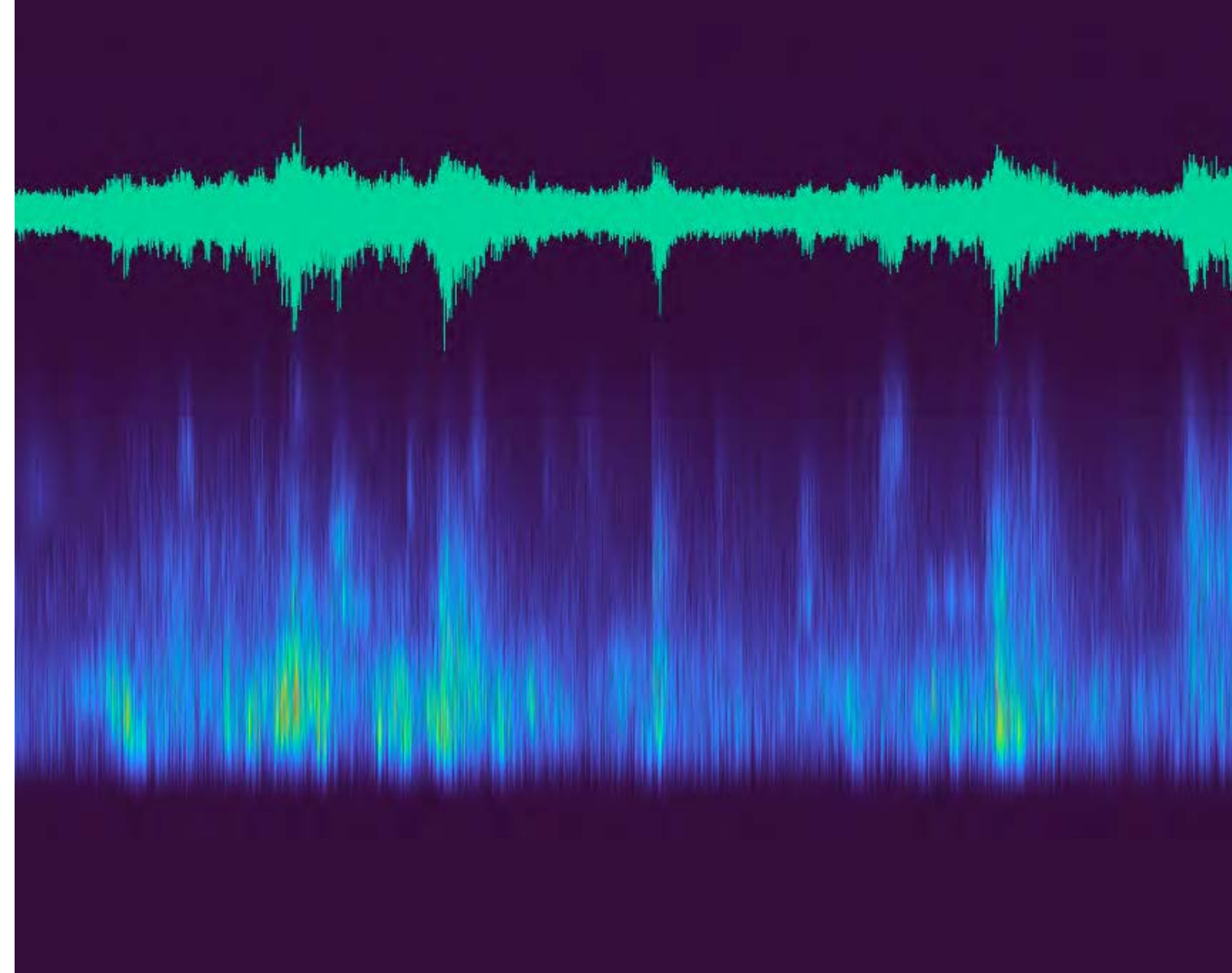
Mission

The mission of the Data Acquisition and Neural Signal Processing platform is to develop methods and tools providing solutions for interfacing, acquiring, and analyzing the multidimensional and multimodal neuronal data generated by the research teams (calcium imaging, electrophysiology, behavior, neurophysiological and auditory signals) both on animal and human.

What we do

- **Data Acquisition and Interfacing:** we develop programming tools for hardware control of custom-designed experimental setups (using National Instrument cards, sound cards, multi I/O processors...). We also offer help for calibration, characterization, and tests of the devices.

- **Signal extraction and processing:** we offer help to establish pipelines for (pre)processing data (segmentation, deconvolution, filtering, denoising) and to find algorithmic solutions to compute quantitative features.
- **Data mining and visualization:** we offer help to explore and visualize your data (classification, clustering, prediction, modeling, simulations).
- **Data sharing:** we aim to gather and know the several tools developed by the scientists of the Hearing Institute to transmit them. We also aim to contribute to the effort for the standardization of data and procedures for reproducible research and open science.
- **Training and assistance:** we offer our help for questions related to signal processing.



Our expertise includes

- Signal/image acquisition and processing in neurosciences and audiology using applied mathematics methods and programming.
- Software and User Interface development.
- The expertise in instrumental and experimental neurosciences (one and two-photon microscopy combined with optogenetics tools, electrophysiology, functional ultrasound imaging) and audiology (Auditory Brainstem Response ABR, OtoAcoustic Emission OAE, Cortical Auditory Evoked Potential CAEP). Knowledge of biological and instrumental possibilities and limitations provides guidance for developing accurate computational tools

How to work with us/how to apply for support

You can send an email at clara.dussaux@pasteur.fr, specifying your needs.





CRBIP

Biobank core facilities

INTRODUCTION

Mission of the Center for Biological Resources

The mission of the CRBIP is to support high quality and reproducible research by the Institut Pasteur teams and the scientific community at large by enabling access to qualified microbial and human-origin samples and associated data.

CRBIP aims at:

- Engaging with scientists to fulfill their needs in terms of biological specimens either from stock or from prospective collections
- Offering secure biorepository facilities
- Advising on fitness for purpose of the biological specimens and raising awareness through seminars
- Adding value to the biological specimens through advanced characterization and quality control
- Operating in compliance with the latest professional biobanking quality standards and applicable regulations
- Expanding its thematic scope with the integration of new microbial collections (fungi, viruses, bacteriophages) and human biological materials of different types
- Developing new tools for the visualization of the biological resources
- Developing services around processing of biological specimens

“

The CRBIP supports research on human diseases by providing project-specific biobanking services and by supplying carefully characterized and fit-for-purpose biological resources. Our long experience makes us a valued partner for our research colleagues, and we are proud to be able to contribute to rigorous research methodologies. We believe that diversity of biospecimens, together with biospecimen science, advanced analytical annotations, and biobanking quality standards, lead to more reproducible research and more innovative applications.

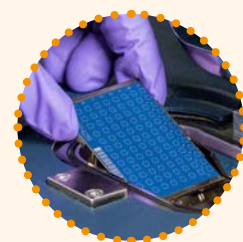
Dr Fay Betsou, Director of the Centre des Ressources Biologiques
of Institut Pasteur (CRBIP)

Biological Resource Center of Institut Pasteur (CRBIP)

An internationally recognized biobank of microbial and human bioresources

The CRBIP is a transversal biobank infrastructure that includes microbial and human specimen collections of Institut Pasteur.

The CRBIP receives, maintains, characterizes and supplies biological resources globally, in compliance with health and environmental safety standards and under applicable laws and regulations.



Head of CRBIP: Fay Betsou

CIP: Dominique Clermont

CNCM: Raquel Hurtado Ortiz

ICAReB-biobank: Emmanuel Roux

PCC: Muriel Gugger

Contacts

Mail: crbip@pasteur.fr

Website:

<https://research.pasteur.fr/en/center/biological-resource-center-of-the-institut-pasteur-crbip/>

Mission

To preserve and make accessible for research, training and quality control purposes, historical and newly collected microbial and human bioresources.

Our expertise includes

- **Collection of Institut Pasteur: CIP**
 - > 25k BACTERIAL STRAINS in one of the oldest collections in the world
cip@pasteur.fr
 - > 200 PATHOGENIC VIRAL STRAINS isolated from humans or animals
cvip@pasteur.fr
 - A GROWING NUMBER OF YEAST AND FILAMENTOUS FUNGAL STRAINS
cfip@pasteur.fr
- **Pasteur Cultures of Cyanobacteria: PCC**
 - > 750 MONOCLONAL STRAIN CULTURES representing the taxonomic and functional diversity of Cyanobacteria
collectionpcc@pasteur.fr

- **National Collection of Cultures of Microorganisms: CNCM**
 - > 4K MICROBIAL STRAINS
 - > 1.5k CELL LINES
cncm@pasteur.fr
- **Integrated Collections for Adaptive Research in Biomedicine: ICAReB-biobank**
 - > 150k SAMPLES AND CLINICAL DATA from patients and healthy volunteers
icareb-biobank@pasteur.fr

What we do

- accept deposits of microbiological materials
- lyophilize strains
- receive and process human fluid biological materials
- characterize the biological materials phenotypically, genotypically, and functionally
- preserve and distribute microbial and human bioresources
- offer training and expertise

Networks

- Microbial Resource Research Infrastructure (MIRRI)
- European Virus Archive - global (EVAg)
- World Data Centre for Microorganisms (WDCM)
- World Federation of Culture Collections (WFCC)



How to work with us/how to apply for support

CRBIP Website



CIP Website



PCC Website



CNCM Website



ICAReB Website



ANNEXES

GUIDELINES

lInstitut Pasteur continuously invests to provide its research teams with access to a state-of-the-art environment through core facilities, Technology and Service Units (UTechS), biological and animal resources located on its campus.

These resources are coordinated by the Technology Department (DT) through four Centers:

- The Center for Technological Resources and Research (C2RT)
- The Center for Animal Resources and Research (C2RA)
- The Biological Resource Centre (CRBIP)
- The Informatic Resources and Research (C2RI)

Through their expertise, services and shared equipment, the core facilities and resources of these four centers support research teams in the technological and animal research components of their projects from grant writing to project implementation and publication.

The entities of the four centers of the DT, as shared resources, aim to support all the research teams of the campus. They are also open to external users from national and international research organizations or private institutions.

The guidelines outlined in this document aim to facilitate interactions between the users and the core facilities and resources of these four centers teams throughout the life of a project. In addition, they are also intended to allow as many people as possible to access these resources. The guidelines were established in 2019 by the technology and scientific programs department (DTPS) in collaboration with all the Scientific Departments and were validated by the scientific direction committee (CODIS).

They apply to any type of project involving a user and a C2RT/C2RA/CRBIP/C2RI team (including training, assisted sessions, routine or non-routine service, scientific collaboration, etc.).

This document presents an updated version of these best practice guidelines. To ensure continuous improvement, they may evolve over time.

	Key practices applicable to both users and C2RT/C2RA/CRBIP/C2RI teams	Key practices specific to users / research teams	Key practices specific to C2RT/C2RA/CRBIP/C2RI teams
Upstream of a project between a user and a C2RT/C2RA/CRBIP/C2RI team	<p>Discuss about the user's request as early as possible after its filing in order to identify the technological challenges and qualify the feasibility of the project.</p> <p>Discuss the constraints faced by the user and by the C2RT/C2RA/CRBIP/C2RI team as soon as possible.</p>	<p>Specify the key elements of the request, the expected results and how the request fits into the research project.</p>	<p>Acknowledge receipt of the user's request. Recall the principle of equal access to C2RT/C2RA/CRBIP/C2RI core facilities. Present the core facility's operation modalities and the criteria used for prioritizing / selecting projects.</p> <p>Indicate what level of involvement of the user will be necessary for the successful implementation / completion of the project.</p> <p>Provide the user/PI with an estimate of the cost of the project and of the expected timeframe, including approximate time periods between the main steps of the process.</p>
Definition & planning	<p>Frame the project while remaining flexible. Define the key elements (for example project objectives, project steps and associated milestones, the nature of the work to be done (routine or non-routine), the distribution of roles and responsibilities, the necessary resources, the associated deadlines and fees).</p> <p>Define in particular how each project participant shall be involved (both on the side of the requesting laboratory and the platform).</p> <p>Indicate the risks/ uncertainties related to the project and how they would be handled.</p> <p>Establish a «roadmap» of the project together with the associated cost estimate (when applicable) and send it to the PI for validation.</p>	<p>Define the contact people for the project implementation (scientific and administrative).</p> <p>Ensure that all the people who will be directly involved take part in the definition and planning phase of the project.</p>	<p>Define the contact people for the scientific and administrative components of the project especially if the project goes beyond the routine activities of the core facility.</p> <p>If, from the Core Facility's viewpoint, the project goes beyond routine activities and requires significant intellectual involvement, inform the user and his/her PI/group leader from the beginning. Define, in agreement with the PI, the expectations regarding authorship (see appendix below).</p>

	Key practices applicable to both users and C2RT/C2RA/CRBIP/C2RI teams	Key practices specific to users / research teams	Key practices specific to C2RT/C2RA/CRBIP/C2RI teams
Execution and follow-up	<p>Interact periodically throughout the project, and monitor achievements and difficulties encountered if any.</p> <p>Inform each other as soon as possible of any change that may affect the project.</p>	<p>Alert the Core Facility team as early as possible if any change occurs in the project expectations. Jointly define the changes to be made. If these changes are important, it may be better to close the project and define a new one.</p>	<p>Alert the user and research team leader/PI as early as possible if any difficulty occurs in the implementation of the project.</p> <p>Discuss with the user and with his/her group leader or PI to define the actions to be taken to overcome the encountered difficulties.</p> <p>Alert the user and his/her PI if the intellectual contribution of the core is greater than originally planned. If appropriate, close the project and define a new one.</p>
Closing of the project and beyond	<p>In case the project needs to be overhauled, close it and file a new application.</p> <p>Hold a final meeting to review the results. Invite if needed the PI/group leader to participate in this meeting.</p> <p>To ensure continuous improvement, share the encountered difficulties, the adequacy of the solutions provided during the project, the possible improvements.</p>	<p>Provide feedback on the exploitation of the results obtained and their integration into the overall project framework.</p> <p>Acknowledge the contribution of the Core Facility team. When appropriate invite them to contribute to the drafting of the publication (see appendix below).</p> <p>Proceed to the payment of the related invoices.</p>	<p>Hand over the deliverables that were agreed on and, if necessary, the associated raw data.</p> <p>When appropriate, assist the user in the drafting of the publication(s) associated with the project (see appendix).</p>

Appendix

Acknowledgement of the contributions of DT core facility members in manuscripts and grants

Acknowledgment of the contributions of core facility staff in publications and grants (application and reports) is regarded as a key indicator of the impact of their activities. It is also an element that is taken into account by funders when evaluating funding applications filed by core facilities, as well as by evaluation bodies when rating core facility staff and deciding on their career progression.

Guideline 1

Acknowledge the contribution of a core facility in publications and grants (both application and reports) every time its services and/or equipment have been used. If the project goes beyond the routine activities of the core facility and requires significant involvement, the PI or the head of the research group involved and the head of the core facility jointly agree on the most appropriate way to acknowledge the contribution of the core staff (acknowledgment or invitation to be a co-author).

Guideline 2

Format of acknowledgement in a publication: name whenever possible the person (s) who contributed or by default the core facility as a whole, and indicate the official name of the entity along with its center of attachment (C2RT, C2RA, C2RI or CRBIP): « we thank (names of people involved) of (official name of the core facility or UTechS) of C2RT, C2RA, C2RI or CRBIP for » or, by default, «we thank the staff of (official name of the core facility y or UTechS) of C2RT, C2RA, C2RI or CRBIP for »

The official names of the entities of C2RT, C2RA, C2RI and CRBIP are available at:

research.pasteur.fr/center/C2RT
research.pasteur.fr/center/C2RA
research.pasteur.fr/center/C2RI
research.pasteur.fr/center/CRBIP

Format for co-authorship:

Name of the co-author, Institut Pasteur, Université de Paris, C2RT, C2RA, C2RI or CRBIP, F-75015 Paris, France.

Guideline 3

A core facility staff member may refuse to be a co-author of a publication. In this case, the core facility will be mentioned in the acknowledgments (see guideline 2).

Guideline 4

Disagreements over the type of recognition shall first be handled by the head of the core facility/UtechS and the PI, who will make their best efforts to find an agreement meeting their respective expectations as well as those of their collaborators.

If a mutually agreeable solution cannot be found, the PI or the head of the core facility /UtechS shall refer the matter to the vice president for technology. As a last resort the case shall be addressed to the ethics committee of Institut Pasteur.

Affiliations of C2RT UTechS/CFs to Scientific Departments

Technological domain	Core Facilities	Heads	Departements
Omics, Proteomics and Single Cell	Biomics	Marc Monot	Genomes and Genetics
	Mass Spectrometry for Biology UTechS	Julia Chamot-Rooke Mariette Matondo	Structural Biology and Chemistry
	Metabolomics	Sandrine Aros	Microbiology
	Cytometry and Biomarkers UTechS	Milena Hasan Sophie Novault	Immunology
Multiscale imaging	Photonic Bio-Imaging	Spencer Shorte Nathalie Aulner	Cell Biology and Infection
	Ultrastructural Bio-Imaging UTechS	Adeline Mallet	Cell Biology and Infection
	Nano-Imaging	Matthijn Vos	Structural Biology and Chemistry
	Hearing Institute Bioimaging Core facility	Maia Brunstein	Hearing Institute
Nanobody discovery, Protein production, Molecular Biophysics and Structural Biology	Production and Purification of Recombinant Proteins	Stéphane Pêtres	Structural Biology and Chemistry
	Antibody Engineering	Pierre Lafaye	Structural Biology and Chemistry
	Molecular Biophysics	Patrick England	Structural Biology and Chemistry
	Crystallography	Ahmed Haouz	Structural Biology and Chemistry
	Biological NMR	Iñaki Guijarro	Structural Biology and Chemistry
Screening, Microfluidics and organ on chips	Chemogenomic and Biological screening	Fabrice Agou	Structural Biology and Chemistry
	Biomaterials and Microfluidics	Samy Gobaa	Developmental and stem cell biology
	Diagnostic Test Innovation & Development	Thierry Rose	Global Health

Affiliations of C2RA Core Facilities to Scientific Departments

Core Facilities	Heads	Departements
Central Animal Facility (CAF)	Jean Jaubert	—
CAF / Animal Welfare Body and Regulatory Monitoring	Myriam Mattei	—
CAF / Washing-areas - Maintenance - Logistics	François Rimlinger	—
CAF / Center François Jacob facility and related activities, Embryology	Franck Bourgade	—
CAF / Centre for Gnotobiology, Technical Assistance	Marion Bérard	—
CAF / A3, Metchnikoff, Monod/Fernbach facilities and related activities	Laëtitia Breton	—
Center for Production and Infection of Anopheles	Sabine Thiberge	Parasites and insect vectors
Mouse Genetics Engineering Center - CIGM	Francina Langa Vives	Developmental and stem cell biology
Hearing Institute Animal and Phenotyping Core Facility	Marta Lindner	Hearing Institute
The Histopathology Platform	David Hardy	—
Human Disease Models platform	Mathilde Dusséaux	—

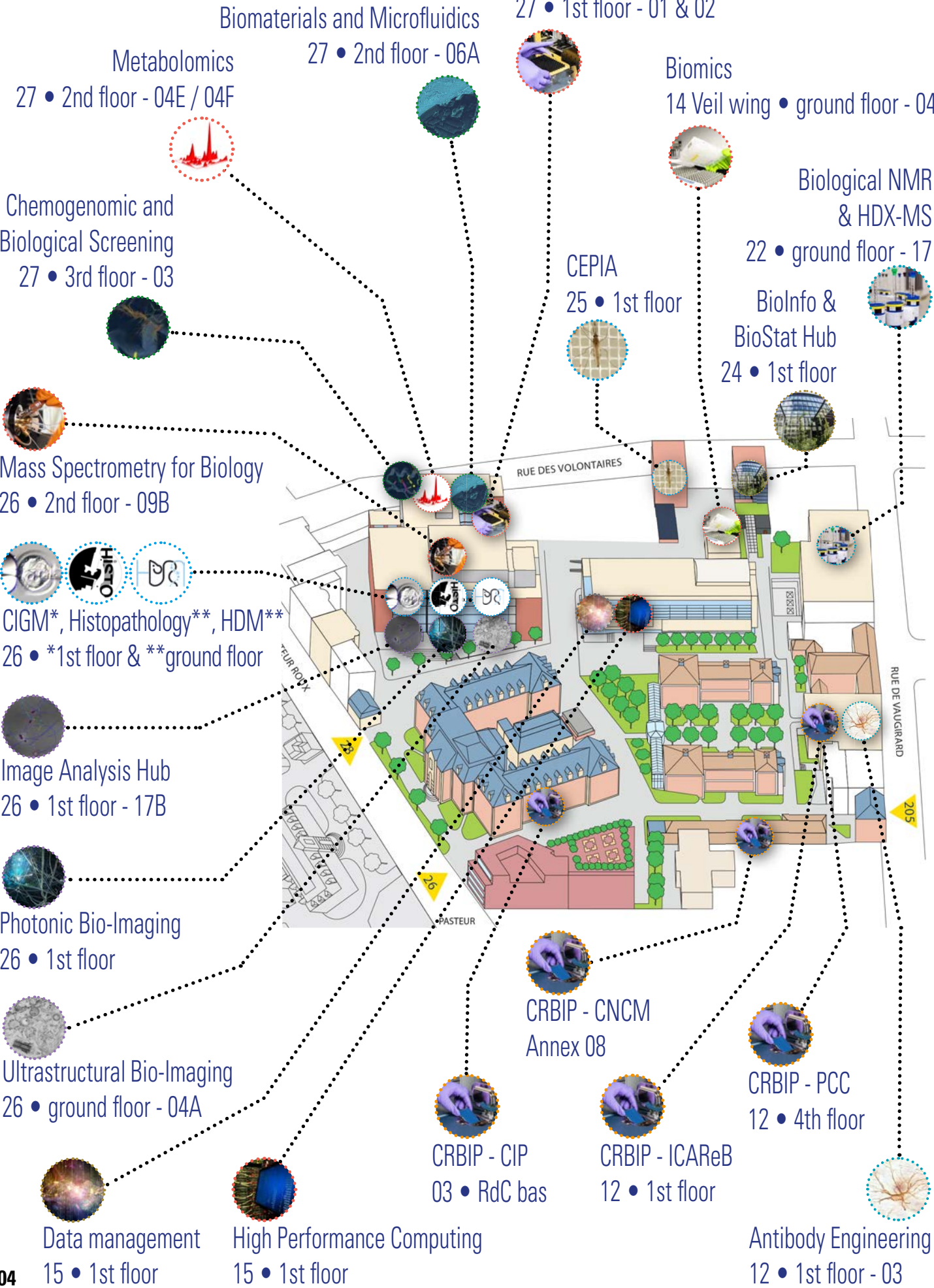
Affiliations of C2RI Core Facilities to Scientific Departments

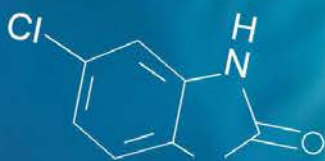
Core Facilities	Heads	Departements
Image Analysis Hub (IAH)	Jean-Yves Tinevez	Developmental and stem cell biology
High Performance Computing CF (HPC)	Yousef Ghorbal	—
Data Management CF (DMcf)	Anne-Caroline Delétoile	—
Bioinformatics and Biostatistics Hub	Marie-Agnès Dilies Hervé Ménager	Computational biology
Hearing Institute Data Acquisition and Neural Signal Processing Facility	Clara Dussaux	Hearing Institute

Affiliations of CRBIP Core Facilities to Scientific Departments

	Core Facilities	Heads	Departements
Biological Resource Center of Institut Pasteur (CRBIP)	CIP	Dominique Clermont	Microbiology
	CNCM	Raquel Hurtado Ortiz	Microbiology
	ICAReB	Emmanuel Roux	—
	PCC	Muriel Gugger	• Microbiology • Structural bBiology and chemistry

Location of UTechS/CFs





TO FIND OUT MORE ABOUT

The Center for Technological Resources and Research (C2RT)

- research.pasteur.fr/center/C2RT
- c2rt@pasteur.fr

The Center for Animal Resources and Research (C2RA)

- research.pasteur.fr/center/C2RA
- c2ra@pasteur.fr

The Center for Informatics Resources and Research (C2RI)

- research.pasteur.fr/center/C2RI
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