C2RA

Our portfolio of animal core facilities

November 2019

Institut Pasteur

DTPS

Center for animal resources and research

Institut Pasteur / Technology and scientific programs department - 25-28, rue du Docteur Roux - 75724 Paris Cedex 15. **Photo credits**: Institut Pasteur's library / François Gardy. **Design and achievement**: Sponsorship and communication direction / Image Service / Jean-François Charles.

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At Institut Pasteur, we have always combined cellular and animal models as we believe it allows reaching a precise understanding of diseases and developing relevant preventive and therapeutic strategies, to the benefit of human health. We care about laboratory animals and are committed to reduce their usage through the implementation of alternative experimental models.

Christophe Joubert,

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

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INTRODUCTION

A favorable environment for animal research

Providing Institut Pasteur research teams with a favorable and enabling technological environment to advance their discoveries is a priority of the strategic plan of the institute.

Support in animal research and animal models at the highest level of technology is provided through the center for animal resources and research (C2RA) and allows animal experimentation to be performed in the best ethical and regulatory conditions.

To support research in a cost-effective manner and achieve higher usage and impact of cutting-edge equipment requiring high-level expertise for its operation, a set of strategic technological resources are gathered within the center for technological resources and research (C2RT). Detailed information of center for technological resources and research (C2RT) is available in a companion brochure.

Mission of the Center of Animal Resources and Research

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

C2AT aims at:

- Providing researchers with state-of-the-art equipment, services and technical expertise to enable 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

Organized in three core facilities covering a large range of technological areas, C2RA is a key component of Institut Pasteur's research ecosystem, by providing researchers with state-of-the-art equipment, services and technical expertise to enable success of their projects:

- Center for Production and Infection of Anopheles (CEPIA)
- Central Animal Facility (AC)
- Mouse Genetics Engineering Center (CIGM)

A development of core facilities in close interaction with Institut Pasteur research Departments and teams

The core facilities of the C2RA work in close connection with the scientific departments at several levels. This ensures that their activities, developments and strategy are aligned with the needs of Institut Pasteur research community:

- organizational level: CEPIA and CIGM are affiliated to the department of technology and scientific programs (DTPS) and to a scientific department. AC is affiliated to DTPS.
- 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 to define a strategic vision in terms of developments, acquisition of large equipment, recruitment of personnel and the associated funding strategies.

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.*

Head of Core Facility: Patricia Baldacci

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.

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.

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.

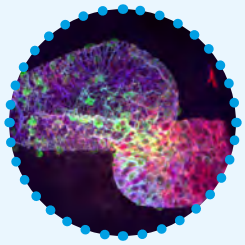
You will be asked to provide additional information concerning risk prevention, animal experimentation etc.


SINGLE USE ONLY

Central Animal Facility (CAF)

Providing access to a wide range of animal models and experimental settings in accordance with the 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 produced data using animal models critically depends on the physical and microbiological environment provided to the animals. Animal research requires that all personnel be adequately trained and projects be authorized.



Head of Core Facility: Christophe Joubert

Contact

Mail (general): animalerie@pasteur.fr
Mail (administrative issues): sec-anim@pasteur.fr
Mail (animal welfare issues): sbea@pasteur.fr
Website: http://webcampus.pasteur.fr/jcms/c_87140/fr/accueil-animalerie

Mission

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

What we do

The different CAF teams are in charge of every aspect of animal use in research.
We continuously ensure animal care and welfare in different animal facilities of Institut Pasteur Campus.
We are in charge of the husbandry of different animal species: mice, rats, hamsters, guinea-pigs, gerbils, rabbits and quails. We also ensure a daily observation in accordance with the regulation.
Our animal facilities include a wide range of environment and confinement: germ-free, specific and opportunistic pathogen free, specific pathogen-free, confined (BSL3) rodents infected with various pathogens (bacteria, virus, fungi).

We provide the breeding and production of mouse strains carrying various types of genetic modifications in accordance with the needs of researchers. We also provide the breeding and production of germ-free and gnotobiotic mice.
We offer access to different experimental spaces and setups (surgery, behaviour setup, in-vivo imaging lab in BSL3 – managed by UTechS PBI).
We organise regulatory trainings, continuous training, experimental techniques teaching (we have a dedicated teaching space).
We offer a wide range of services including strain importation, quarantine and rederivation, strain cryopreservation, technical assistance (gnotobiology, neurosciences, BSL3 experiments…).
We provide veterinary advice and care and we assure periodic health monitoring of the different colonies. We provide access to veterinary drugs.
We provide animal welfare advice prior to the project evaluation by the Institut Pasteur ethic committee.
We are in contact with official authorities for project authorisations and for veterinary inspections.
We realise preliminary risk (biological, chemical) assessment of project prior to the submission to Service de Prévention des Risques.

Our expertise includes

- Laboratory animal science
- Laboratory animal veterinary science
- Animal welfare and animal ethics
- Biosafety and risk assessment

Some examples of success stories

- Identification of new loci involved in the host susceptibility to *Salmonella typhimurium* in collaborative cross mice. Zhang J *et al*. *BMC Genomics*, 2018. **19**, 303. https://doi.org/10.1186/s12864-018-4667-0
- A human immune system mouse model with robust lymph node development. Li Y *et al*. *Nat Methods*. 2018, **15**, 623-630. doi: 10.1038/s41592-018-0071-6. Epub 2018 Jul 31.
- Colorectal cancer specific conditions promote *Streptococcus gallolyticus* gut colonization. Aymeric L*et al*.. *Proc Natl Acad Sci U S A*. 2018 Jan 9;**115**, E283-E291.

How to work with us/how to apply for support

Forms for work application and support are available on CAF websites: http://webcampus.pasteur.fr/jcms/c_87140/fr/accueil-animalerie

Access to FAQ: http://webcampus.pasteur.fr/jcms/c_87298/fr/faq.

Certifications and Networks

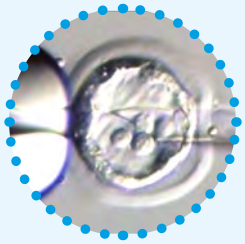
Animal facilities authorisations:

http://webcampus.pasteur.fr/jcms/c_481366/fr/agrement-des-animaleries-18-aout-2014.

Center for Murine Genetics Engineering (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 nuclease systems.

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

- 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)
- Meioc KO ice 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, PHEnotying, DIstribution and Archiving of model organiscms) network since 2016.

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

ANNEXES

GUIDELINES

Relationships between users and C2RT/C2RA core facilities members & Acknowledgement of contributions from C2RT/C2RA core facilities members

Institut Pasteur continuously invests to provide its research teams with access to a state-of-the-art environment through core facilities and technology and service units (UTechS) located on its campus.

These resources are coordinated by the technology and scientific programs department (DTPS) through two centers: the technological resources and research center (C2RT) and the animal resources and research center (C2RA).

Through their expertise, services and shared equipment, the C2RT/C2RA core facilities support research teams in the technological and animal research components of their projects from grant writing to project implementation and publication.

The entities of C2RT and C2RA, 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 C2RT/C2RA teams all along the life of a project. In addition, they are also intended to allow as many people as possible to access these resources. The guidelines have been established by the technology and scientific programs department (DTPS) in collaboration with all the Scientific Departments and have been validated by the scientific direction committee (CODIS).

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

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

	Key practices applicable to both users and C2RT/C2RA teams	Key practices specific to users / research teams	Key practices specific to C2RT/C2RA teams
Upstream of a project between a user and a C2RT/C2RA team	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**. Discuss the constraints faced by the user and by the C2RT/C2RA team as soon as possible.	Specify the **key elements** of the request, the **expected results** and how the request fits into the research project.	Acknowledge receipt of the user's request. Recall the principle of **equal access** to C2RT/C2RA core facilities. Present the core facility's operation modalities and the **criteria used for prioritizing /selecting projects**. Indicate what level of involvement of the user will be necessary for the successful implementation / completion of the project. 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.
Definition & planning	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**). Define in particular how each project participant shall be involved (both on the side of the requesting laboratory and the platform). Indicate the **risks/ uncertainties** related to the project and how they would be handled. Establish a **«roadmap»** of the project together with the associated cost estimate (when applicable) and send it to the **PI for validation**.	Define the **contact people** for the project implementation (scientific and administrative). Ensure that all the people who will be directly involved take part in the **definition and planning phase** of the project.	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. 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).

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

Appendix

Acknowledgement of the contributions of C2RT / C2RA 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 equipement have been used. If the project goes beyond the routine activities of the core facility and requires significant intellectual 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 or C2RA): « we thank (names of people involved) of (official name of the core facility or UTechS) of C2RT / C2RA for ..... » or, by default, «we thank the staff of (official name of the core facility y or UTechS) of C2RT / C2RA for ..... »

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

research.pasteur.fr/center/C2RT

research.pasteur.fr/center/C2RA

Format for co-authorship: Name of the co-author, Name the entity (official name of the core facility or UTechS), center of affiliation (C2RT or C2RA), Institut Pasteur, Paris (75015) 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 and scientific programs. As a last resort the case shall be addressed to the ethics committee of Institut Pasteur.

Affiliation of C2RA Core Facilities to Scientific Departments

Core Facilities	Heads	Departements
Central Animal Facility	Christophe Joubert	
Center for Production and Infection of Anopheles	Patricia Baldacci	Parasites and insect vectors
Center for Murine and Genetics Engineering	Francina Langa Vives	Developmental and stem cell biology

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