Erasmus+

Institut Pasteur, 2026-2027

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INSTITUT Pasteur

Education

DEPARTMENT

Projects 2026-2027

Erasmus+

Institut Pasteur, 2026-2027

RESEARCH CENTER

Legal name: **Institut Pasteur**
Address: **25-28 rue du Dr. Roux, 75724 Cedex 15, PARIS**
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Brief description of your Institution

The Institut Pasteur is a private non-profit foundation that contributes to the prevention and treatment of diseases through research, education, and public health activities. Its campus in Paris hosts more than 3000 individuals, 153 research units, organized in 13 departments.
Research: priority is given to fight infectious diseases, as well as to study the impact of climate change on health, the origin of pathologies (cancer, genetic, neurodegenerative, and allergic diseases) and to explore health and diseases at extremities of life (Pasteur 2030 Strategic Plan).
Education: every year 600 young scientists from all over the world follow high-level courses in various fields related to research in microbiology, immunology, cellular biology, epidemiology, genetics, and disease control. Over 850 trainees from 77 different countries come to perfect their skills or conduct their Master or Doctoral trainings in the Institute's laboratories.

Description of the work program(s)

See projects on following pages

N° of placements available for work programs:

The laboratories at the Institut Pasteur have proposed 34 projects for Erasmus internships. Students may also contact other laboratories at Pasteur to apply for an internship, even if the laboratories have not presented a project (https://research.pasteur.fr/en/team-heads).

FACILITIES

- **Accommodation**: a limited number of rooms for rent are reserved for Pasteur at the student residence "Cité Universitaire".
- **Canteen**: partially subsidized canteen is available on the Pasteur Campus.
- **Reimbursement of the public transportation pass (monthly/yearly):** the Institut Pasteur reimburses your Navigo pass at 75%.
- **Additional salary:** additional salary of approximately 650 euros/month (for internships longer than 60 days) is paid by the host lab (4.50 euros/hour, 7 hours/day).

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Institut Pasteur, 2026-2027

Title of the work program 1

Functional characterization of novel genes involved in bacterial outer membrane biogenesis

Description of the work program

The bacterial cell envelope is primarily divided into two architectures: **monoderm (Gram-positive)** and **diderm (Gram-negative).** Both types of envelopes possess an inner membrane and a peptidoglycan layer, but only diderm bacteria have an outer membrane (OM). To synthesize and transport the various components of the OM, diderm bacteria rely on numerous complex systems. Most of these systems have been studied in the model bacterium *Escherichia coli*.

To broaden our understanding of the mechanisms involved in OM biogenesis in bacteria, our laboratory has developed a new experimental model, the diderm Firmicute *Veillonella parvula*, a main member of the human microbiome. Interestingly, in *V. parvula* most of the genes involved in OM biogenesis are clustered within a single genetic locus. This gene cluster notably encodes three copies of **Skp**, a periplasmic chaperone involved in the transport and assembly of OM proteins. In the model bacterium *E. coli*, this function is carried out by several proteins, including SurA, Skp, and DegP, with SurA being considered the primary pathway. In this context, the precise role of Skp remains only partially understood. In contrast, *V. parvula* lacks an identifiable SurA homolog and appears to rely exclusively on its multiple copies of Skp to perform this function. This unusual organization suggests that Skp plays a particularly important role in OM biogenesis in this bacterium and offers a unique opportunity to investigate its function in greater detail.

The internship project will consist in generating deletions of the different **skp** gene copies present in *V. parvula* and characterizing the resulting mutants. For this, the student will employ different approaches involving molecular biology (cassette construction), microbiology (growth curves, spot assays), and microscopy (OM alterations). In parallel, the student will investigate a second gene of unknown but essential function located within the OM biogenesis gene cluster. To do so, they will implement a novel approach based on the CRISPR/Cas9 system, recently developed in the laboratory. This strategy aims to enrich a population of *V. parvula* carrying a genetic background in which the gene is no longer essential. The resulting mutants are therefore expected to harbor compensatory mutations that bypass the essentiality of the target gene. The student will perform several rounds of CRISPR-based selection by transforming *V. parvula* with plasmids carrying different guide RNAs and antibiotic resistance markers, thereby maintaining continuous selective pressure against **the target gene**. Finally, the student will isolate the resulting mutants and identify the compensatory mutations selected during the experiment, providing valuable insights into the function of **this gene** and its potential involvement in OM biogenesis.

Tutor/supervisor

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Institut Pasteur, 2026-2027

Lab webpage	https://research.pasteur.fr/fr/team/evolutionary-biology-of-the-microbial-cell/
Profile on ORCID (if applicable):	

I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

Beaud Benyahia B, Taib N, Beloin C, Gribaldo S. Terrabacteria: redefining bacterial envelope diversity, biogenesis and evolution. Nat Rev Microbiol. 2025 Jan;23(1):41-56. doi: 10.1038/s41579-024-01088-0. Epub 2024 Aug 28. PMID: 39198708.

Megrian D, Taib N, Witwinowski J, Beloin C, Gribaldo S. One or two membranes? Diderm Firmicutes challenge the Gram-positive/Gram-negative divide. Mol Microbiol. 2020 Mar;113(3):659-671. doi: 10.1111/mmi.14469. PMID: 31975449.

Grasekamp KP, Beaud Benyahia B, Taib N, Audrain B, Bardiaux B, Rossez Y, Izadi-Pruneyre N, Lejeune M, Trivelli X, Chouit Z, Guerardel Y, Ghigo JM, Gribaldo S, Beloin C. The Mla system of diderm Firmicute Veillonella parvula reveals an ancestral transenvelope bridge for phospholipid trafficking. Nat Commun. 2023 Nov 23;14(1):7642. doi: 10.1038/s41467-023-43411-y. PMID: 37993432; PMCID: PMC10665443.

Scientific or technical background required for work program

General Microbiology

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Institut Pasteur, 2026-2027

Title of the work program 2

Host–Pathogen Interactions during tuberculosis

Description of the work program

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), is one of the deadliest diseases caused by a single infectious agent, alongside COVID-19. According to the latest WHO report, an estimated 10 million people developed TB, and the disease claimed 1.3 million lives in 2024. Despite considerable efforts, TB remains a major global public health challenge. There is still no highly effective vaccine against pulmonary TB in adults, and multidrug-resistant (MDR) strains of Mtb continue to emerge. Combating TB therefore requires new strategies and a better understanding of host–pathogen interactions.

In our laboratory, we are developing several research projects aimed at:

- Identifying new molecules that enhance the antimicrobial or bactericidal functions of innate immune cells and/or improve the efficacy of anti-tuberculosis drugs.
- Understanding and evaluating the long-term consequences of TB on the body, including the brain.

Depending on the duration of the internship, candidates will work on one of these projects. They will use a combination of cell biology, microbiology, and immunology techniques. In particular, they will learn how to isolate human blood cells, differentiate them into macrophages (the primary cellular targets of Mtb), and infect them with fluorescent Mtb strains or attenuated mycobacteria. Host–pathogen interactions will then be investigated using advanced imaging approaches. Some projects will also involve the use of a murine model of TB. Additional techniques routinely used in the laboratory include transcriptomics, advanced microscopy, and flow cytometry.

Tutor/supervisor

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Profile on ORCID (if applicable):	

☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

1. Sayes, F. et al. Improved immune responses and tuberculosis protection by aerosol vaccination with recombinant BCG expressing ESX-1 from *Mycobacterium marinum*. PLoS Pathog. 2026 Feb 23;22(2):e1013992.
2. Maure, A. et al. A host-directed oxadiazole compound potentiates antituberculosis treatment via zinc poisoning in human macrophages and in a mouse model of infection. PLoS Biol. Apr 29;22(4):e3002259 (2024).
3. Giraud-Gatineau, A. et al. The antibiotic bedaquiline activates host macrophage innate immune resistance to bacterial infection. eLife 9, doi:10.7554/eLife.55692 (2020).

4. Bottai, D. et al. TbD1 deletion as a driver of the evolutionary success of modern epidemic *Mycobacterium tuberculosis* lineages. Nat Commun 11, 684, doi:10.1038/s41467-020-14508-5 (2020).
5. Coya, J. M. et al. Tri-mannose grafting of chitosan nanocarriers remodels the macrophage response to bacterial infection. J Nanobiotechnology 17, 15, doi:10.1186/s12951-018-0439-x (2019).

Scientific or technical background required for work program

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- Strong motivation, scientific curiosity and interest in microbiology, immunology or neurosciences
- Good verbal and written English communication skills are expected
- Research experience in cell culture and/or animal manipulation is regarded very favorably

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Institut Pasteur, 2026-2027

Title of the work program 3

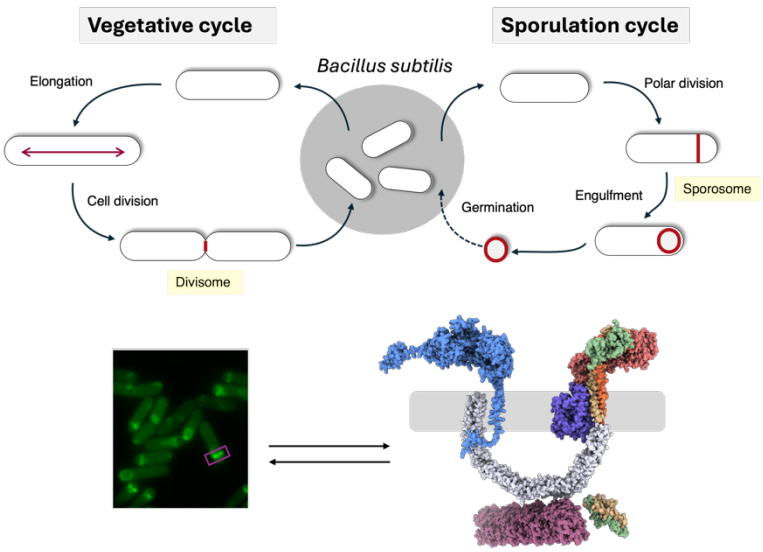
Genetic and structural characterisation of the sporosome in *Bacillus subtilis*.

Description of the work program

Bacteria deploy an arsenal of molecular strategies to survive unfavourable conditions such as nutrient starvation, oxidative stress and exposure to toxic molecules. One of the most extreme of these survival strategies is **sporulation**, in which the cell follows a genetically programmed differentiation pathway that produces a dormant spore able to withstand extreme conditions such as desiccation, UV radiation or even antibiotic exposure for hundreds of years. Understanding the molecular principles behind this process is the central question of the project.

Sporulation is widespread among members of the Firmicutes, a group that includes i**mportant human pathogens** such as *Bacillus anthracis* and *Clostridioides difficile*. When nutrients are available, bacterial cells divide by binary fission (the vegetative cycle), a highly coordinated process in which the cell divides at midcell to produce two identical daughter cells. Cell division is carried out by a macromolecular complex known as **the divisome**, which spans the cytoplasm, membrane and cell wall to drive constriction. Remarkably, the same machinery also carries out the first steps of sporulation, dividing the cell close to one pole when conditions become unfavourable; in this context, it is referred to as the **polar divisome**. Although the core machinery that constricts the cell is shared between the vegetative and sporulation cycles, key differences exist, which is why we have renamed the polar divisome **the sporosome**. The sporosome is a specialised divisome that forms two unequally sized compartments, each following a different genetic fate. The main goal of the project is to understand the differences in assembly, structure and regulation between the divisome and the sporosome.

To answer these questions, the lab uses an integrative approach that combines *in vitro* biochemical characterisation and structure determination by crystallography and cryo-electron microscopy with *in vivo* cell imaging and genetic engineering. The project will use ***Bacillus subtilis* as a model organism,** for which we have an extensive genetic toolkit, including CRISPR/Cas9, and engineered strains for native protein purification.



The discoveries made in this project will not only advance our understanding of the fundamental process of cell differentiation in bacteria but will also likely identify new **potential drug targets,** specifically targeting sporulating cells, with a direct impact on biomedical research.

Figure 1. Overview of the project. **(top)** Cell cycle of *B. subtilis* **(bottom)** Simplified view of the methodological approach

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Tutor/supervisor

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☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

1. Sogues A, Martinez M, Gaday Q, et al. Essential dynamic interdependence of FtsZ and SepF for Z-ring and septum formation in Corynebacterium glutamicum. Nat Commun. 2020;11(1):1641. Published 2020 Apr 2. doi:10.1038/s41467-020-15490-8
2. Sleutel M, Sogues A, Remaut H. Auto-crosslinking sporesilk fibers promote endospore and Cry toxin clustering. Nat Commun. 2026;17(1):3809. Published 2026 Mar 11. doi:10.1038/s41467-026-70495-z
3. Martinez M, Petit J, Leyva A, et al. Eukaryotic-like gephyrin and cognate membrane receptor coordinate corynebacterial cell division and polar elongation. Nat Microbiol. 2023;8(10):1896-1910. doi:10.1038/s41564-023-01473-0
4. Carloni G, Gaday Q, Megrian D, et al. Mechanistic insights into SteAB regulation of cell wall hydrolase RipA in Mycobacterium tuberculosis. mBio. 2026;17(3):e0370025. doi:10.1128/mbio.03700-25

Scientific or technical background required for work program

We are looking for a **curious and motivated student** with an interest in microbiology and/or structural biology. The candidate should have a theoretical background in either molecular biology, biochemistry or microbiology. Previous laboratory experience would be beneficial, but is not required. This project offers an excellent opportunity to acquire a broad range of molecular, genetic and structural techniques while contributing to answering fundamental questions with real biomedical implications.

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Title of the work program 4

Role of substrate rigidity and mechanotransduction in cancer cell plasticity

Description of the work program

Glioblastoma (GBM) is a primary brain tumor and a paradigmatic poor-prognosis cancer, in which cellular plasticity drive diffuse invasion, adaptive resistance to radio-chemotherapy, and near-inevitable relapse. Microenvironmental cues, including hypoxia, perivascular niches, immune and glial cells, and the extracellular matrix (ECM) are key instructors of GBM identity, proliferation, migration, and survival. Because glial cells are exquisitely mechanosensitive, substrate rigidity can reprogram cytoskeletal architecture and mechanics, thereby influencing adhesion, migration, invasion, and proliferation. Thereby, the ECM stiffness influences GBM phenotypes like durotaxis and proliferation. The brain's mechanical landscape changes markedly with aging and disease. Tissue characterization indicates global softening and regional stiffening during aging and neurodegenerative diseases, driven by gliosis, extracellular matrix (ECM) remodeling, and increased crosslinking. GBMs further disrupts this milieu: tumor borders often stiffened via extracellular matrix deposition and remodelling. However, the full extent and the consequence of local tissue stiffness and GBM progression remain unclear.
We propose that ECM rigidity drives GBM plasticity and therapy resistance via mechanotransduction. Understanding how GBM cells interpret and respond to rigidity is critical for explaining why GBM is highly invasive in the soft brain and for identifying mechanobiology-informed therapeutic strategies. We hypothesize substrate rigidity rewires cytoskeletal composition and organization in GBM cells, creating distinct mechano-phenotypes that govern adhesion dynamics, motility programs, and cell proliferation and survival control. We predict GBM displays broadened stiffness tolerance and enhanced mechanoadaptation compared to normal astrocytes, mediated by specific cytoskeletal and mechanotransduction nodes.

The objectives of the project will be:
1- Quantify how substrate rigidity alters GBM cell functional behaviors (adhesion, migration/invasion, proliferation) and resistance to treatment (irradiation and temozolomide treatment). Patient-derived glioblastoma cells will be used in 2D and 3D hydrogels with tunable rigidities (0.5 kPa (healthy brain) to 10 kPa (tumor core/fibrotic areas)).

2- Identify major mechanotransduction pathways involved in rigidity-dependent GBM cell behavior by targeting mechanosensitive cytoskeletal regulators and pathways (e.g., Western Blot/qPCR of YAP/TAZ, Rho/ROCK, FAK) using genetic or pharmacologic tools. The expression of major mechanosensitive markers will be correlated with patient survival data (using public databases like TCGA) or immunohistochemistry on human tissue sections.

3- This approach will be coupled with transcriptomic/proteomic profiling to map rigidity-dependent networks for potential future PhD project.
These tools and methods are all commonly used in the lab.

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Institut Pasteur, 2026-2027

Tutor/supervisor

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☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

- van Bodegraven E.J., Infante E., Peglion F., Pereira D., Kesenci Y., Roca V., Perfettini I., Terriac E., Geay J., Soto L., Sluijs J., Rietveld R., Seetharaman E., Boëda B., Olivo-Marin J.C., Asnacios A., Boquet-Pujadas A., Manneville J.B., Etienne-Manneville S. *Cytoplasmic intermediate filaments promote glioblastoma cell invasion by controlling nuclear deformations and mechanosensitive expression of MMP14.* **Cell Rep.** 2025 Nov 14;44(11):116553. doi: 10.1016/j.celrep.2025.116553. PMID: 41241939

Preprints:

- Infante Elvira, Terriac Emmanuel, Gelin Matthieu, Siegfried Hugo, Pereira David, Roca Vanessa, Varet Hugo, Khalilian Sara, Rietveld Reinier, Asnacios Atef, van Bodegraven Emma J, Etienne-Manneville Sandrine. *Intratumoral Heterogeneity of Vimentin Modulates Nuclear Mechanotransduction, DNA Damage Response and Cancer Cell Survival. BioRXiv* 2025. https://doi.org/10.1101/2025.06.27.661506 (in press in EMBO Rep)

- Clara Gomez-Cruz, Matthieu Gelin, Lucas Pradeau-Phelut, Arrate Munoz-Barrutia, Sandrine Etienne-Manneville, Daniel Garcia-Gonzalez. *Transient cytoskeletal anisotropy encodes short-term mechanical memory. BioRXiv* 2026. https://www.biorxiv.org/cgi/content/short/2026.03.09.710573v1 (in press in Adv Mat.)

Scientific or technical background required for work program

This project offers an exceptional opportunity for biology students to specialize in the emerging field of cancer mechanobiology within the vibrant scientific hub of central Paris. Candidates should possess a solid foundation in cell and molecular biology, with practical experience in mammalian cell culture and standard molecular techniques (e.g., fluorescence microscopy, protein analysis). Beyond technical skills, we seek curious minds eager to explore how physical forces govern biological behavior. You will join a diverse, international team and benefit from mentorship in cutting-edge biophysical methods. This Erasmus placement is designed to strengthen your profile for future PhD programs, providing both

advanced scientific training and a unique international experience in one of the world's most dynamic cities.

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Institut Pasteur, 2026-2027

Title of the work program 5

Unlocking Functional Origins of Muscle Resilience in Muscular Dystrophies

Description of the work program

Not all muscles in the body are equivalent. Extraocular muscles (EOMs), which control eye movement, are distinct from all other muscles due to their unique resistance to neuromuscular diseases and their remarkable evolutionary conservation across vertebrates. The coexistence of both vulnerable and resilient muscles within the same organism provides compelling in vivo evidence that sustained regenerative capacity is possible, even in severe conditions such as Duchenne muscular dystrophy. However, the mechanisms underlying EOM resilience remain largely unknown, making EOMs a powerful model for uncovering muscle-specific protective processes.

This project aims to address the following key questions : Why are EOM myofibers more robust ? What mechanisms drive EOM regeneration ? Can we harness EOM myofiber properties to strengthen vulnerable limb and trunk muscles ?

Our single-nucleus multiomics data have revealed that spared muscles are built upon unique gene regulatory networks triggering distinctive contractile programs compared to other cranial and limb muscles. Preliminary analysis already identified a transcription factor that when mutated induces dystrophic features in EOMs. In this project, we aim to implement functional analysis of these regulators in the dystrophic context in vivo and determine determine whether enforcing these programs in limb muscles is sufficient to mitigate dystrophic pathology.

Tutor/supervisor

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Lab webpage	https://research.pasteur.fr/en/team/stem-cells-and-development/
Profile on ORCID (if applicable):	0000-0003-3244-3378

☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

1. Impaired stem cell migration and divisions in Duchenne muscular dystrophy revealed by live imaging. Sarde L, Letort G, Varet H, Laville V, Fernandes J, Tajbakhsh S, Evano B. Nat Commun. 2026 Jan 28;17(1):1769. doi: 10.1038/s41467-026-68474-5.

2. Co-option of neck muscles supported the vertebrate water-to-land transition. Heude E, Dutel H, Sanchez-Garrido F, Prummel KD, Lalonde R, Lam F, Mosimann C, Herrel A, Tajbakhsh S. Nat Commun. 2024 Dec 4;15(1):10564. doi: 10.1038/s41467-024-54724-x.

3. Extraocular muscle stem cells exhibit distinct cellular properties associated with non-muscle molecular signatures. Girolamo DD, Benavente-Diaz M, Murolo M, Grimaldi A, Lopes PT, Evano B, Kuriki M, Gioftsidi S, Laville V, Tinevez JY, Letort G, Mella S, Tajbakhsh S*, Comai G*. Development. 2024 Feb 15;151(4):dev202144. doi: 10.1242/dev.202144. Epub 2024 Feb 21.

4. Interplay between Pitx2 and Pax7 temporally governs specification of extraocular muscle stem cells. Kuriki M, Korb A, Comai G*, Tajbakhsh S*. PLoS Genet. 2024 Jun 14;20(6):e1010935. doi: 10.1371/journal.pgen.1010935.
5 . Local retinoic acid signaling directs emergence of the extraocular muscle functional unit. Comai GE, Tesařová M, Dupé V, Rhinn M, Vallecillo-García P, da Silva F, Feret B, Exelby K, Dollé P, Carlsson L, Pryce B, Spitz F, Stricker S, Zikmund T, Kaiser J, Briscoe J, Schedl A, Ghyselinck NB, Schweitzer R, Tajbakhsh S. PLoS Biol. 2020 Nov 17;18(11):e3000902. doi: 10.1371/journal.pbio.3000902.

6. B. Evano, D. Gill, I. Hernando-Herraez, G. Comai, T. M. Stubbs, P.-H. Commere, W. Reik, S. Tajbakhsh, Transcriptome and epigenome diversity and plasticity of muscle stem cells following transplantation. Plos Genet 16, e1009022 (2020).

7. Reciprocal signalling by Notch-Collagen V-CALCR retains muscle stem cells in their niche. Baghdadi MB, Castel D, Machado L, Fukada SI, Birk DE, Relaix F, Tajbakhsh S, Mourikis P. Nature. 2018 May;557(7707):714-718. doi: 10.1038/s41586-018-0144-9. Epub 2018 May 23.

Scientific or technical background required for work program

We are looking for highly motivated and creative « Medicine-Sciences » students. This internship is particularly suited for medical students with an interest in Neuromuscular disorders, Ophthalmology and vision sciences.
The student will become familiar with a number of techniques routinely used in the lab including: mouse handling, histology, AAV-mediated gene expression, confocal microscopy and image processing. Prior expertise in mouse genetics, image analysis and coding would be highly appreciated. The candidate should feel comfortable working in English, be able to critically discuss experimental results and be updated on the related literature. Students will be fully integrated in the scientific life of the lab and department (seminars, lab retreat, training).
The internship should last between 6-12 months.

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Title of the work program 6

Mapping the evolutionary and molecular basis of skeletal muscle diversity

Description of the work program

Among head muscles, extraocular muscles (EOMs) are by far the most specialized muscles of the vertebrate body enabling a whole range of precise motor actions essential for our visual experience. EOMs differ markedly from limb muscles in terms of embryological origin, regenerative capacity and disease susceptibility in neuromuscular disorders, yet remain remarkably conserved in structure from lamprey to human. While trunk, limb and most cranial muscles derive from well-defined mesodermal territories, the implication of the tissues arising at gastrulation in the origin of EOMs is still debated.
This project aims to uncover how the distinctive molecular identity of EOMs is established during early development and determine whether the molecular and structural features defining EOM identity are conserved across vertebrate evolution. The project builds on previous work from our group on EOM development and muscle stem cell properties, as well as on unpublished multiomic data revealing atypical myonuclear signatures in EOM progenitors and myofibres.
We will construct a 4D spatiotemporal map of EOM emergence from early embryogenesis onward in the mouse. Whole-mount immunostaining + 3D confocal imaging and single molecule in situ hybridization will characterize progenitor distribution in lineage-traced embryos. Newly identified EOM markers will be examined in other jawed vertebrates (including cartilaginous fish) to assess conservation of EOM specification and myofibre regulatory programs.

Tutor/supervisor

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Lab webpage	https://research.pasteur.fr/en/team/stem-cells-and-development/
Profile on ORCID (if applicable):	0000-0003-3244-3378

☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

1. Interplay between Pitx2 and Pax7 temporally governs specification of extraocular muscle stem cells. M. Kuriki, A. Korb, G. Comai, S. Tajbakhsh, PLOS Genet. 20, e1010935 (2024).

2. Identification of bipotent progenitors that give rise to myogenic and connective tissues in mouse. A. Grimaldi, G. Comai, S. Mella, S. Tajbakhsh. Elife 11, e70235 (2022).

2. Co-option of neck muscles supported the vertebrate water-to-land transition. Heude E, Dutel H, Sanchez-Garrido F, Prummel KD, Lalonde R, Lam F, Mosimann C, Herrel A, Tajbakhsh S. Nat Commun. 2024 Dec 4;15(1):10564. doi: 10.1038/s41467-024-54724-x.

3. Extraocular muscle stem cells exhibit distinct cellular properties associated with non-muscle molecular signatures. Girolamo DD, Benavente-Diaz M, Murolo M, Grimaldi A, Lopes PT, Evano B, Kuriki M, Gioftsidi S, Laville V, Tinevez JY, Letort G, Mella S, Tajbakhsh S*, Comai G*. Development. 2024 Feb 15;151(4):dev202144. doi: 10.1242/dev.202144. Epub 2024 Feb 21.

4. Local retinoic acid signaling directs emergence of the extraocular muscle functional unit. Comai GE, Tesařová M, Dupé V, Rhinn M, Vallecillo-García P, da Silva F, Feret B, Exelby K, Dollé P, Carlsson L, Pryce B, Spitz F, Stricker S, Zikmund T, Kaiser J, Briscoe J, Schedl A, Ghyselinck NB, Schweitzer R, Tajbakhsh S. PLoS Biol. 2020 Nov 17;18(11):e3000902. doi: 10.1371/journal.pbio.3000902.

6. Transcriptome and epigenome diversity and plasticity of muscle stem cells following transplantation. B. Evano, D. Gill, I. Hernando-Herraez, G. Comai, T. M. Stubbs, P.-H. Commere, W. Reik, S. Tajbakhsh, Plos Genet 16, e1009022 (2020).

Scientific or technical background required for work program

The student will become familiar with a number of techniques routinely used in the lab including: mouse handling, histology, single molecule FISH, confocal microscopy and image processing. Prior expertise in mouse genetics, image analysis and coding would be highly appreciated.
The candidate should feel comfortable working in English, be able to critically discuss experimental results and be updated on the related literature. Students will be fully integrated in the scientific life of the lab and department (seminars, lab retreat, training).
The internship should last between 6-12 months.

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Institut Pasteur, 2026-2027

Title of the work program 7

Feature engineering for malaria genomic epidemiology

Description of the work program

This 6-month plus work program, ideally starting January 2027, is part of a French National Research Agency (ANR) funded project, UniGEM (Unified inference for Genomic Epidemiology of Malaria). Using simulation-based inference with deep-learning, UniGEM aims to build a neural network to estimate epidemiological parameters of *P. falciparum*, the deadliest malaria parasite species (read [1] to learn more about the ideas behind UniGEM).

Within UniGEM, this work program aims to engineer the features input into the neural network and to compute their values using real malaria parasite data. These values will be used in a subsequent phase of the UniGEM project (beyond the scope of the Erasmus + work program) to assess the realism of simulated data, and to estimate epidemiological parameters globally.

P. falciparum data are sourced from MalariaGEN, a network of data contributors coordinated by a team of sequencing experts at the Liverpool School of Tropical Medicine; see www.malariagen.net. The newest and largest *P. falciparum* data release, Pf8, includes whole-genome sequence (WGS) data for over 33,000 samples collected from 122 admin-level-one locations in 34 countries across South America, Africa, Asia, and Oceania between 1966 and 2022 [2]. Ninety-nine studies contributed samples to Pf8. Most sampled from malaria-positive patients in clinical field studies. The WGS data were generated centrally at the Wellcome Sanger Institute and are thus highly standardised; 24,409 analysis-ready samples passed central quality control. Among these, data on 1,544,381 biallelic single nucleotide polymorphisms in coding regions have been used to partition samples into 10 populations worldwide, and to estimate FWS (a per-sample intra-infection inbreeding coefficient) [2].

Internship work programme: The internship will start with training, before Pf8 data are partitioned and summarised. The intern will be encouraged to package their workflow into a reproducible and modular pipeline. These steps are described in more detail below.

Training: The internship will start with MalariaGEN online training, and training through tutorials provided by PGEforge, a community-driven platform designed to simplify Plasmodium genomic data analysis; see https://mrc-ide.github.io/PGEforge/.

Data partitioning: The analysis-ready samples will be extracted and partitioned into subsets by country and, if necessary, by genetic populations within countries, i.e., on a more granular level than that reported in [2], likely using principal coordinate analysis.

Summarise P. falciparum populations in a vectorised format, where each statistic is a candidate
node in layer zero of a neural network: For all subsets with more than 20 samples a suite of summary statistics will be generated. Statistics will include summaries of distributions over multiplicities of infection (i.e., numbers of genetically distinct groups of parasites per infection), inbreeding coefficients, allele frequencies, linkage disequilibrium, pairwise relatedness, identity-by-descent segment lengths, etc. Some statistics will be generated using software designed specifically to analyse malaria parasite genetic data; see [3].

Engineering: The intern will be encouraged to package their workflow into a well-documented, modular, and parallelisable pipeline that can be used to efficiently generate vectors of per-population statistics given any set of samples. This pipeline will be used in a subsequent phase of the UniGEM

project (beyond the scope of the internship) to generate summary statistics for synthetic datasets used to train, develop and test the neural network.

Location: This internship is supervised by Aimee Taylor, chargée de recherche, Infectious Disease Epidemiology and Analytics (IDEA) Unit, Department of Global Health, Institut Pasteur, Paris. Michael White directs IDEA. It is a highly international and multidisciplinary unit, with expertise in mathematical
modelling and machine learning, wet-lab expertise in multiplex serological and genetic assays, expertise in diagnostic development and production, and expertise coordinating field studies and clinical trials. Major projects the intern will learn about through group meetings include PvSTATEM, a large cluster-randomised clinical trial with collaborators in Ethiopia and Madagascar, and ULTIMASero, a large cohort study with collaborators in Senegal, Cameroon, and Madagascar.

What the intern will gain: experience working with the largest open dataset of genome variation in any non-human eukaryotic species, conducting a broad range of population genetic analyses, engineering deep-learning inputs, pipeline engineering, and an enhanced open-science profile.

Publication prospects: The intern will be invited to co-author all publications of UniGEM activities that make use of the internship's results. Depending on the internship's progress, there is also potential for a software note describing the pipeline and its application to Pf8.

PhD prospect: This internship could potentially progress into a PhD funded through PRAIRIE (Paris Artificial Intelligence Research Institute). As such, candidates interested in PhD studies at the artificial intelligence / epidemiology interface are encouraged to apply.

Recommended reading:
[1] F. Camponovo et al., "Measurably recombining malaria parasites," Trends Parasitol., vol. 39, no. 1, Jan. 2023.
[2] Malaria Genomic Epidemiology Network (MalariaGEN) et al., "Pf8: an open dataset of Plasmodium falciparum genome variation in 33,325 worldwide samples," Wellcome Open Res., vol. 10, June 2025.
[3] A. R. Taylor et al., "Review of MrsFreqPhase methods: methods designed to estimate statistically malaria parasite multiplicity of infection, relatedness, frequency and phase," Malar. J., vol. 23, no. 1, Oct. 2024.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

F. Camponovo et al., “Measurably recombining malaria parasites,” Trends Parasitol., vol. 39, no. 1, Jan. 2023.

A. R. Taylor et al., “Review of MrsFreqPhase methods: methods designed to estimate statistically malaria parasite multiplicity of infection, relatedness, frequency and phase,” Malar. J., vol. 23, no. 1, Oct. 2024.

Scientific or technical background required for work program

- Strong programming skills (R or Python or other)
- Familiarity with Git / GitHub for version control
- English proficiency (B2 level or higher)
- Experience handling large genomic datasets is desirable
- Basic understanding of population genetics is desirable

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Institut Pasteur, 2026-2027

Title of the work program 8

Applied Epidemiology and Outbreak Preparedness Research – Outbreak Investigation Task Force (OITF), Institut Pasteur

Description of the work program

The Emerging Diseases Epidemiology Unit at Institut Pasteur (Paris) focuses on the study of emerging pathogens. The unit has been involved in the investigation of numerous recent epidemics, including SARS, H1N1 influenza, MERS, Zika, Ebola, pneumonic plague, COVID-19 and mpox. It is headed by Prof. Arnaud Fontanet, who also directs the Pasteur Pandemic Preparedness Initiative (P3I), which coordinates the Institute's pandemic preparedness and response activities.

Within this unit, the Outbreak Investigation Task Force (OITF) develops and supports applied epidemiological research during and between epidemics, aiming to rapidly generate evidence for public health decision-making while building methods, tools and capacities to strengthen preparedness for, and investigation of, future epidemics. The OITF is a multidisciplinary rapid-response team bringing together experts in early outbreak research, field epidemiology, anthropology, diagnostics, genomic surveillance and mathematical modelling.

We are looking for a mid-experienced scientific or medical PhD with a background and genuine interest in global health and infectious diseases to join the OITF for a period of 6 months to 1 year. The successful candidate will work primarily on one of the projects below, selected at the start of the placement according to the state of ongoing activities, operational needs, and the candidate's own interests and availability, with the possibility to contribute on a more occasional basis to other epidemic preparedness or response activities.

Project 1 – Epidemiological research during an outbreak (TAMBUA-BDBV project): Participation in a sero-epidemiological study conducted following the ongoing outbreak of Bundibugyo ebolavirus disease in the Democratic Republic of the Congo. This study aims to better document past or unrecognised infections, community and occupational exposures, and the characteristics of healthcare workers – in collaboration with the INRB, IRD and ITM. Depending on timing, tasks may include finalising study tools and the analysis plan, data preparation and quality control, descriptive and analytical work, epidemiological interpretation, feedback to partners, and contribution to a scientific report and/or article.

Project 2 – Sentinel Sero-surveillance in a climate and health context in Madagascar: Contribution to the development, implementation, or analysis of serological data for multiple pathogens coming from sentinel surveillance sites in Madagascar – in collaboration with the Institute Pasteur of Madagascar. The project aims to reinforce existing systems and build local capacity, providing climate and health indicators to inform public health decision-making and protect vulnerable populations.

Project 3 – Epidemic preparedness and simulation exercise (SimEx): Contribution to the preparation, delivery and evaluation of a global pandemic simulation exercise organised with the Pasteur Network in Brazil in March 2027. Activities may include reviewing existing exercises, building the scenario and facilitating the exercise on site. The candidate may also contribute to the after-action review and recommendations to strengthen preparedness and response capacities across the Pasteur Network.

Project 4 – EPOPT: protocols for early outbreak investigation: Contribution to the Early Phase Outbreak Protocol Templates (EPOPT) project, developed by the OITF with Institut Pasteur de Bangui and other Pasteur Network partners. This project aims to build a library of standardised, modular and rapidly adaptable epidemiological protocols for the early phases of an outbreak. Following a launch workshop planned for October 2026, tasks may include reviewing and mapping existing protocols, identifying gaps and adaptation needs, drafting and harmonising generic protocols, CRFs, core

variables and analysis plans, considering options for expedited ethical review and rapid implementation, and preparing the piloting of certain tools during a future outbreak.

By the end of the placement, the candidate will have strengthened their ability to translate a real-world outbreak challenge into a rigorous, operational public health question. Skills developed may include: structured literature review; study design and implementation in an outbreak context; development of protocols, analysis plans and data-collection tools; ethical, regulatory, logistical and operational considerations specific to research conducted during a health emergency; data management, cleaning and quality control; descriptive and, depending on the project, multivariate or infectious-disease-specific statistical analysis; interpreting results in their epidemiological and operational context; the principles of epidemiological surveillance and field epidemiology; the architecture of global health governance; multidisciplinary and international teamwork; and communicating results through presentations, public health notes, reports or scientific articles.

The candidate will be part of the OITF team, supervised primarily by Michael Casera (OITF Coordinator) and Natalie Fischer (Deputy Coordinator), with regular supervision meetings to define priorities, track progress on the main project, and support methodological and analytical choices. Depending on the project selected, co-supervision may also be provided by a researcher, biostatistician, anthropologist, biologist or other expert from Institut Pasteur or the Pasteur Network. The candidate will also be welcome to take part in the scientific meetings of the Emerging Diseases Epidemiology Unit, relevant OITF and P3I activities, and seminars, conferences and courses organised by Institut Pasteur and its partners.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

Geoffroy A, Jeang D, Baidjoe A et al. Research priorities for characterising Bundibugyo virus. The Lancet, 2026; 408211

Jeang D, Randrianasolo L et al. Integrated Sentinel Serosurveillance in Madagascar: A Model for Routine Multi-Pathogen Monitoring. Journal of Global Health, 2026 – in review.

Villa J et al. Field investigation suggests an earlier, wider Bundibugyo virus disease epidemic in Mongbwalu, Democratic Republic of the Congo. The Lancet, 2026 – submitted.

Harimanana AN, N'Takpé JB et al. Preliminary findings from a prospective household mpox transmission study in Antananarivo, Madagascar, 2026. State-of-the-Art Mpox Symposium, Kampala, Uganda, 2026 – abstract for oral presentation.

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Institut Pasteur, 2026-2027

Scientific or technical background required for work program

A completed or ongoing PhD (or equivalent, e.g. MD-PhD) in epidemiology, public health, infectious disease research or a related field, with demonstrated interest in global health and outbreak response. Prior exposure to field epidemiology, outbreak investigation, or infectious disease surveillance is an asset. Solid grounding in epidemiological methods and biostatistics, with practical experience using a statistical software environment (e.g. R) for data management and analysis is an asset. Ability to work independently as well as within a multidisciplinary, international team, including under the time constraints typical of an outbreak response. Strong scientific writing skills and fluency in English; working knowledge of French is an advantage given the Institute's environment. Availability for a placement of 6 months to 1 year, with some flexibility on start date.

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Institut Pasteur, 2026-2027

Title of the work program 9

Using AI to explore antibiotic resistance in the human gut microbiota

Description of the work program

Goal: The goal of this project is to use machine-learning and artificial-intelligence methods to identify antibiotic-resistance proteins in the human intestinal microbiota.
The proposed work will continue research undertaken within the NASPEC project whose broader goal includes developing new antibiotics that target pathogens and protect commensal bacteria. Previous work in the host laboratory used protein language models, sequence motifs and structure-based methods (AlphaFold) to identify potential β-lactamases in genomic and metagenomic data. Collaborators in NASPEC have experimentally characterised a number of candidate proteins that can serve to evaluate and improve the existing predictions.
The student will use Python and existing analysis pipelines to evaluate and improve methods based on protein language models. The student will have the opportunity to write their own code, test new models and compare their predictions with conventional sequence-based approaches. The resulting methods will be applied to human gut metagenomic data to explore the diversity and distribution of potential antibiotic-resistance proteins and to identify candidates for further experimental study.
At the end of the internship, the student will have gained experience in Python programming, machine learning, protein-sequence analysis and metagenomics. Previous experience with AI or protein language models is not required, as training in these methods will form part of the project. Potential students may also have a strong computer science background, in which case they will be given the opportunity to learn more about antibiotics and human microbiota biology in the course of the project.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

1. Baud, A. & Kennedy, S. P. Targeted Metagenomic Databases Provide Improved Analysis of Microbiota Samples. Microorganisms 12, 135 (2024).

2. Ruppé, E. et al. Prediction of the intestinal resistome by a three-dimensional structure-based method. Nature Microbiology 4, 112–123 (2019).

3. Volant, S. et al. SHAMAN: a user-friendly website for metataxonomic analysis from raw reads to statistical analysis. BMC Bioinformatics 21, 345 (2020).

Scientific or technical background required for work program

- Previous programming experience in Python
- Some familiarity with Git
- Interest in machine learning, bioinformatics, microbiology or metagenomics
- Motivation and willingness to learn new computational methods
- Rigorous organisation and record keeping
- Good written and oral communication skills
- Ability to work independently and collaboratively
- English or French language skills

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Institut Pasteur, 2026-2027

Title of the work program 10

Impact of repeated acoustic trauma on presbycusis

Description of the work program

Institut presentation

The Hearing Institute (Institut de l'Audition, IdA, Paris 12eme) is a new center for basic and translational neuroscience research in the field of hearing, which opened in 2020 at the initiative of the Fondation Pour l'Audition and the Institut Pasteur. The overarching goal of the Institute is to elucidate the principles underpinning the workings of the auditory system, auditory perception and cognition from the molecular to the cognitive level. Optical techniques are key for this endeavor.

Scientific Context

Age-related hearing loss (presbycusis) progressively impairs auditory function in approximately one-third of individuals over 65. A central feature of this pathology is damage to cochlear hair cells. Epidemiological studies indicate that environmental factors—particularly repeated exposure to loud noise—contribute to its variability and severity, although the underlying mechanisms remain poorly understood. Emerging evidence suggests that temporary threshold shifts (TTS) caused by acoustic overexposure (e.g., concerts, machinery) disrupt tip links—nanoscale protein complexes (CDH23/PCDH15) essential for sound transduction. While this disruption is reversible, we hypothesize that repeated TTS episodes may compromise tip link integrity and ultimately accelerate presbycusis. This project seeks to elucidate how recurrent acoustic trauma affects tip link structure and regeneration.

Internship Objectives

The student will characterize the structural and functional consequences of acoustic trauma on hair cell tip links in mouse models. Key aims include:

1. Quantifying tip link breakage after single/repeated TTS using super-resolution microscopy.
2. Correlating ultrastructural damage with functional hearing thresholds.

Methodology

The internship integrates three experimental phases:

- **Acoustic Trauma Induction:** The student will expose mice to calibrated noise (8–16 kHz, 95 dB SPL, 2 hours) to induce TTS. Auditory Brainstem Responses (ABRs) and otoacoustic emissions will monitor pre/post-trauma hearing thresholds.

- **Cochlear Dissection & Immunolabeling:** The student will carry out dissection of cochlea and immunostaining of CDH23, PCDH15, and actin. She/he will then visualize the sample under confocal or STED microscope.
- **Structural-Functional Correlation:** Using confocal/STED imaging, the student will quantify tip link integrity via CDH23/PCDH15 colocalization. Time-series sampling (1h–48h post-trauma) will track regeneration dynamics. Data will be cross-referenced with ABR thresholds to establish mechanistic links between tip link disruption and hearing loss.

Training and Skills Development

The student will gain rare expertise in auditory neuroscience techniques: murine auditory phenotyping, cochlear dissection, microscopy (confocal/STED), and quantitative image analysis. They will participate in interdisciplinary team meetings, contributing to experimental design and data interpretation.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

1. Gagliardini M.*, Mechaussier S.*, Campos Pina C.*, …., Gourevitch B.*, Paul Avan A.*, Michalski N.*, "Deciphering Auditory Hyperexcitability in Otogl Mutant Mice Unravels an Auditory Neuropathy Mechanism", Advanced Science, **12**(19), 2410776, 2025.
2. Gourévitch, B., Edeline, J.-M., Occelli, F. & Eggermont, J. J. Is the din really harmless? Long-term effects of non-traumatic noise on the adult auditory system. *Nat. Rev. Neurosci.* **15**, 483–491 (2014).
3. Brunstein, M. & Oheim, M. Dependence of descriptors of co-localization on microscope spatiotemporal resolution and the choice of regions of interest: Brunstein and Oheim. *Microsc. Res. Tech.* **80**, 220–230 (2017).
4. Wagner, E. L. & Shin, J.-B. Mechanisms of Hair Cell Damage and Repair. *Trends in Neurosciences* **42**, 414–424 (2019).

Scientific or technical background required for work program

We seek a master's student in neuroscience, cell biology, or biomedical engineering with a strong academic record. Prior experience in histology or microscopy is advantageous but not essential. The ideal candidate should be meticulous, with problem-solving aptitude and enthusiasm for translational sensory research.

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Institut Pasteur, 2026-2027

Title of the work program 11

Mechanisms of the influence of intestinal dysbiosis induced by a Western diet on the brain response to nicotine in mice

Description of the work program

Tobacco smoking is responsible for more than seven million deaths each year. While major genetic advances have improved our understanding of vulnerability to nicotine addiction, the contribution of environmental factors remains insufficiently explored. Among these factors, the gut microbiota has emerged as a central component of the gut–brain axis, a bidirectional communication system increasingly implicated in various neuropsychiatric disorders. However, its role in the neural mechanisms underlying reward and addiction remains to be elucidated.

The rewarding effects of drugs initially rely on activation of the mesolimbic system, composed of dopaminergic neurons projecting from the ventral tegmental area (VTA) to the nucleus accumbens (NAc). Our team was the first to demonstrate that gut microbiota depletion potentiates nicotine-induced activation of the VTA and alters its motivational properties in mice. In addition, preliminary data suggest that a Western diet, rich in fat and sugar and low in fiber, may also modify the sensitivity of the mesolimbic system to nicotine, in association with profound alterations of the gut microbiota, notably including short-chain fatty acid (SCFA)-producing bacteria.

SCFAs, the main metabolites derived from dietary fiber fermentation, are key mediators of gut–brain communication. They regulate gut hormone secretion, can cross the blood–brain barrier, and act as epigenetic regulators through inhibition of histone deacetylases. They also contribute to immune homeostasis by limiting inflammation. Recent findings from our laboratory indicate that modulation of SCFA levels may influence VTA activation under dysbiotic conditions, suggesting their involvement in regulating the brain's response to nicotine.

Among the mechanisms considered, modulation of gut hormones appears central. Preliminary observations suggest that a Western diet may alter the balance of circulating forms of ghrelin. Ghrelin, an orexigenic hormone, activates its receptor GHS-R1A, which is expressed in several reward-related regions including the VTA and NAc, and stimulates dopamine release. In contrast, other hormones regulated by SCFAs (GLP-1, leptin, insulin, PYY) exert anorexigenic effects and tend to reduce reward sensitivity. Disruption of this hormonal balance could therefore contribute to the heightened nicotine sensitivity observed under dysbiotic conditions.

The aim of this project is to better establish the link between SCFAs, gut hormonal signaling, and the brain response to nicotine under Western diet–induced dysbiosis, by assessing multiple levels in mouse models: neuronal activation, neurotransmission, and nicotine-related motivational behaviors..

This project builds on the laboratory's previous work and hopes to move closer to a translational perspective aimed at better understanding how environmental factors such as diet and the microbiota contribute to individual vulnerability to nicotine addiction.

Bibliography:

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Ikemoto S, Bonci A. Neurocircuitry of drug reward. Neuropharmacology. 2014;76:329 341. doi: 10.1016/j.neuropharm.2013.04.031.

Lakosa A, Rahimian A, Tomasi F, Marti F, Reynolds LM, Tochon L, David V, Danckaert A, Canonne C, Tahraoui S, de Chaumont F, Forget B, Maskos U, Besson M. Impact of the gut microbiome on nicotine's motivational effects and glial cells in the ventral tegmental area in male mice. Neuropsychopharmacology. 2023;48(6):963 974. doi:10.1038/s41386 023 01563 x.

Angoa Pérez M, Kuhn DM. Evidence for modulation of substance use disorders by the gut microbiome: hidden in plain sight. Pharmacol Rev. 2021;73(3):571 596. DOI: 10.1124/pharmrev.120.000144

García Cabrerizo R, Carbia C, O'Riordan KJ, Schellekens H, Cryan JF. Microbiota gut brain axis as a regulator of reward processes. J Neurochem. 2021;157(6):1495 1524. doi:10.1111/jnc.15284.

Jerlhag E, Engel JA. Ghrelin receptor antagonism attenuates nicotine induced locomotor stimulation, accumbal dopamine release and conditioned place preference in mice. Drug Alcohol Depend. 2011;117(1):126 131. doi: 10.1016/j.drugalcdep.2011.01.010.

Meckel KR, Kiraly DD. A potential role for the gut microbiome in substance use disorders. Psychopharmacology (Berl). 2019;236(5):1513 1530. doi:10.1007/s00213 019 05232 0.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

de Chaumont F*, Icick R*, Gorwood P, Granon S, Forget B, Bouarab C, Mattioni J, Bourgeron T, Maskos U, Ramoz N, Besson M$. The influence of CHRNA5 and D398N missense variation on social and emotional behaviors in rodents and humans. Trans Psychiatry. 2025;15(1):507. PMID: 41309559.

Lakosa A*, Rahimian A*, Tomasi F*, Marti F, Reynolds LM, Tochon L, David V, Danckaert A, Canonne C, Tahraoui S, de Chaumont F, Forget B, Maskos U, Besson M. Impact of the gut microbiome on nicotine's motivational effects and glial cells in the ventral tegmental area in male mice. Neuropsychopharmacology. 2023;48(6):963-974. PMID: 36932179.

Forget B, Icick R, Robert J, Correia C, Prevost MS, Gielen M, Corringer PJ, Bellivier F, Vorspan F, Besson M*, Maskos U*. Alterations in nicotinic receptor alpha5 subunit gene differentially impact early and later stages of cocaine addiction: a translational study in transgenic rats and patients. Prog Neurobiol. 2021;197:101898. PMID: 32841724.

Scientific or technical background required for work program

The candidate should have a strong background in neuroscience and, preferably, a good knowledge of neuropsychiatric disorders and their neurobiological correlates, particularly the circuits and mechanisms involved in addiction. Knowledge of immunology would be an important asset. Ideally, the candidate will have previous training in rodent handling, behavioral testing, and brain tissue preparation and analysis (e.g., dissection, sectioning, immunohistochemical labeling, etc.).

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Institut Pasteur, 2026-2027

Title of the work program 12

Exploring the diverse ways of coronavirus cell entry through a structural approach

Description of the work program

Coronaviruses are considered to be one of the biggest threats for zoonotic transmission to humans, following the recent COVID-19 pandemic. Other than SARS-CoV-2, the causative agent of COVID-19, more coronaviruses have recently spilled over from animals to humans including SARS-CoV, responsible for the SARS epidemic in 2002-2003, and MERS-CoV, responsible for the MERS outbreak in 2012-2013 and multiple transmissions from camels to humans thereafter.
These viruses are able to enter their hosts' cells and subsequently cause disease through interaction between the Spike glycoprotein on the virion and one or more receptor proteins on the host cell. The ability to use a host's cellular receptor, however, largely differs between coronaviruses. This is primarily determined by the sequence and structure of the Spike's receptor binding domain, controlling the host tropism of each coronavirus.
In this project, the student will use an array of AI-based protein structure prediction methods to generate 3D models of Spike receptor binding domains across all known coronaviruses. The student will then use comparative approaches to explore differences and similarities between the mechanisms that coronaviruses use to enter their hosts on the structural level.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

Lytras S, Ghafari M, and Grove J (2026) Studying the Deep Evolution of Viruses in the Era of Artificial Intelligence Structure Prediction. ***Annual Review of Virology***, 13. doi: 10.1146/annurev-virology-100424-122154

Tolentino JE, …, **Lytras S,** Sato K (2025) Structural and phenotypic plasticity of the RBD loop2 region is a key determinant for HKU5r-CoVs' emergence in mink. ***BioRxiv*** – *preprint.* doi: 10.1101/2025.10.22.684003

Mifsud JCO, **Lytras S**, *et al.* (2024) Mapping glycoprotein structure reveals defining events in the evolution of the Flaviviridae. ***Nature***, 633(8030):695-703. doi: 10.1038/s41586-024-07899-8

Scientific or technical background required for work program

Interest in structural virology and applications of AI structure predictions to virus proteins. Prior experience with phylogenetic and/or structure prediction methods is recommended.

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Institut Pasteur, 2026-2027

Title of the work program 13

Application of deep mutational scanning to emerging RNA viruses

Description of the work program

Viruses emerging and re-emerging into the human population generally exhibit genotypic changes which result in phenotypes previously unobserved or different to previously circulating strains. Such mutations are often relevant to public health responses and in some cases, result in immune escape e.g. neutralizing polyclonal sera or monoclonal antibodies or reduction in the efficacy of treatments, among other effects.

Systematic experimental evolutionary approaches such as deep mutational scanning (DMS) can be utilized to investigate the impact of single amino acid mutations, insertions and deletions from a known viral background. DMS generates a catalogue of per-residue functional scores that can then be used to rapidly map the consequences of amino-acid mutations observed in nature without the immediate necessity for laboratory characterization, potentiating public health responses. DMS has been extensively applied to SARS-CoV-2 during the COVID-19 pandemic and has allowed characterization of variants of interest or concern.

The general objective of this project is to contribute to the development and optimization of deep mutational scanning-based assays for the definition of evolutionary space around existing genotypes from RNA viruses of public health importance.

This project is laboratory based and thus will develop the student's general molecular biology skills i.e. cloning, PCR, cell culture, NGS library preparation, pseudovirus production. The laboratory additionally has the capacity for dry-lab based skills that the student would be able to participate in if it matches their interests.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

- Taieb F, Baidaliuk A, Durand A, Prot M, Jidar K, Hochedez P, Consigny PH, Itani O, Simon-Loriere E. Phylogenetic analysis of chikungunya virus in travellers returning from La Reunion Island. J Travel Med. 2025 Aug 1:taaf079. doi: 10.1093/jtm/taaf079. PMID: 40748267.

- Ou TP, Guillebaud J, Baidaliuk A, Tum S, Chheang D, Delaune D, Prot M, Bruder E, Machado RRG, Pum L, Hul V, Hoem T, Ly S, Auerswald H, Arnaud F, Sato K, Smith GJ, Dussart P, Karlsson EA, Chevalier V, Cappelle J, Duong V, Simon-Loriere E. Characterization and evolutionary history of novel SARS-CoV-2-related viruses in bats from Cambodia. Nat Commun. 2026 Jul 23;17(1):9002. doi: 10.1038/s41467-026-75954-1. PMID: 42642437; PMCID: PMC13507159.
- Planas D, Staropoli I, Michel V, Lemoine F, Donati F, Prot M, Porrot F, Guivel-Benhassine F, Jeyarajah B, Brisebarre A, Dehan O, Avon L, Bolland WH, Hubert M, Buchrieser J, Vanhoucke T, Rosenbaum P, Veyer D, Péré H, Lina B, Trouillet-Assant S, Hocqueloux L, Prazuck T, Simon-Loriere E, Schwartz O. Distinct evolution of SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 lineages combining increased fitness and antibody evasion. Nat Commun. 2024 Mar 13;15(1):2254. doi: 10.1038/s41467-024-46490-7. PMID: 38480689
- Gámbaro F, Pérez AB, Prot M, Agüera E, Baidaliuk A, Sánchez-Seco MP, Martínez-Martínez L, Vázquez A, Fernandez-Garcia MD, Simon-Loriere E. Untargeted metagenomic sequencing identifies Toscana virus in patients with idiopathic meningitis, southern Spain, 2015 to 2019. Euro Surveill. 2023 Nov;28(45):2200913. doi: 10.2807/1560-7917.ES.2023.28.45.2200913. PMID: 37943504.

Scientific or technical background required for work program

Skills listed below are advantageous but not a pre-requisite of the program:

- General molecular biology techniques
  - Cloning
  - PCR
  - Nucleic acid extraction
  - Gel electrophoresis

- Cell culture and aseptic technique

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Institut Pasteur, 2026-2027

Title of the work program 14

Visualizing Homologous Recombination one molecule at a time: A structural and functional study of RadA2 Recombinases

Description of the work program

Since the discovery of the DNA double helix, decades of intensive research have revealed how cellular and viral systems have evolved highly complex molecular machines to copy and maintain their genomes. Homologous recombination (HR) is an evolutionarily conserved DNA repair pathway, which restores genome integrity by using an intact homologous sequence to repair damaged DNA. HR depends on recombinases, which assemble nucleoprotein filaments capable of catalysing strand exchange. Recently, we reported cryo-EM structures of RadA, capturing the presynaptic (ssDNA), synaptic (D-loop) and postsynaptic (dsDNA) states of HR in archaea. A comprehensive phylogenetic analysis of archaeal and eukaryotic recombinases, including newly sampled Asgard archaeal and viral sequences, identified a divergent, likely virus-derived RadA2 clade of recombinases. Structural differences between RadA and RadA2 are predicted to affect key motifs, with implications for filament stability and recombination fidelity. Indeed, RadA2 proteins share certain important features with the eukaryotic recombinases in the ATP- and DNA-binding motifs, including substitutions in the Walker A motif, the A-cap, and the L2 loop, not present in the canonical RadA. It is tempting to speculate that the relaxed fidelity exploited by viral RadA2 for generating genomic diversity and mosaicism has been harnessed by archaeal cells and by the emerging eukaryotes.

The objective of this project is to characterize representative members of the RadA2 recombinase family using an integrative biology approach. By combining structural, biochemical, biophysical, and single-molecule methods, we aim to elucidate how sequence divergence within RadA2 translates into functional differences in filament assembly, stability, and recombination activity. Particular emphasis will be placed on identifying the molecular determinants underlying the potentially relaxed fidelity of RadA2 and their evolutionary relationship to eukaryotic recombinases. A synergistic combination of cryo-EM and single-molecule techniques has the potential to provide real-time visualization of homologous recombination intermediates, both under standard biochemical conditions and in the presence of DNA substrates or structures that challenge recombinase filament assembly and strand exchange.

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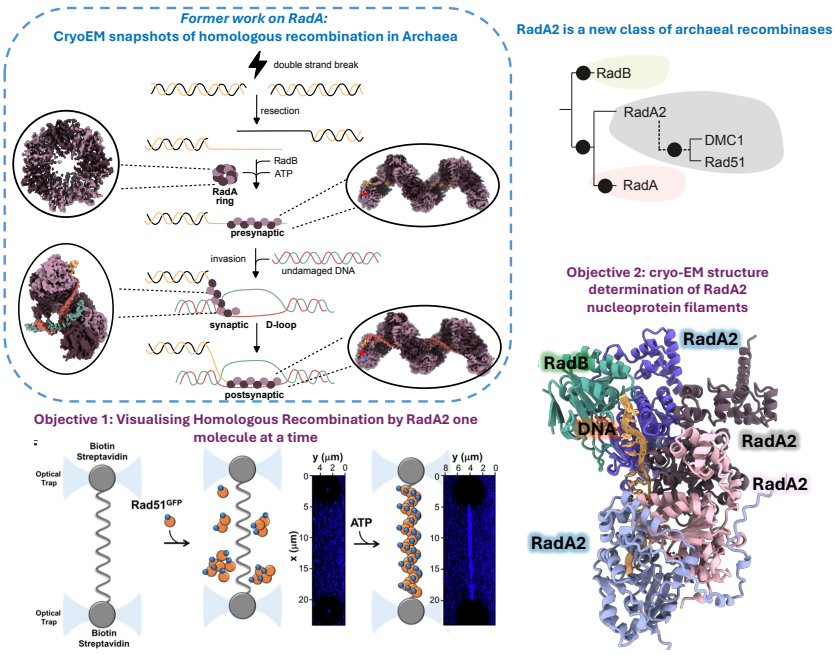
Institut Pasteur, 2026-2027



Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

- Imbert et al. Structural and functional analyses of archaeal recombinases clarify the evolution of homologous recombination in eukaryotes. Under review in Nature Communications.

- Betancurt-Anzola et al. The A, B, C, D's of replicative DNA polymerase fidelity: utilizing high-throughput single-molecule sequencing to understand the molecular basis for DNA polymerase accuracy. Nucleic Acids Res. 2025 53(21):gkaf1143 DOI: https://doi.org/10.1093/nar/gkaf1143

- Markel Martínez-Carranza et al. Communication between DNA polymerases and Replication Protein A within the archaeal replisome. Nature Communications 2024 15, 10926. DOI: https://doi.org/10.1038/s41467-024-55365-w

- Betancurt-Anzola et al. Molecular basis for proofreading by the unique exonuclease domain of Family-D DNA polymerases. Nature Communications 2023 Dec 14;14(1):8306. DOI: https://doi.org/10.1038/s41467-023-44125-x

- Madru et al. DNA-binding mechanism and evolution of replication protein A. Nature Communications. 2023 14(1):2326. DOI: https://doi.org/10.1038/s41467-023-38048-w

Scientific or technical background required for work program

We are seeking for a highly motivated candidate that is able to work effectively within a team. The candidates should have a solid background in molecular biology, protein biochemistry, or biophysics. An interest in innovative technologies and cutting-edge methodological approaches is essential, along with curiosity and enthusiasm for interdisciplinary research.

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Institut Pasteur, 2026-2027

Title of the work program 15

Application of a Lymphoid Organ-on-chip to the evaluation of candidate antiviral vaccines

Description of the work program

Predicting the immunogenicity of candidate vaccines in humans remains a challenge. To address this issue, we have developed a lymphoid organ-on-chip (LO chip) model based on a microfluidic chip seeded with human peripheral blood mononuclear cells (PBMC) at high density within a 3D matrix. Perfusion of the SARS-CoV-2 Spike mimicked a vaccine boost, by inducing a massive amplification of memory B cells and Spike-specific antibody secretion. (R. Jeger-Madiot et al., J Exp Med 2024).

The student will aim at comparing the immune responses induced in the LO chip by candidate antiviral vaccines based on different platforms, including classic mRNA-liponanoparticles (LNPs), self-amplifying mRNA LNPs, and mRNA-LNPs encoding self-assembling virus-like particles. The kinetics of antigen expression, the innate responses induced in antigen presenting cells, and the differentiation of specific B and T cells will be evaluated by spectral flow cytometry, while CD4+ T cell / B cell interactions will be probed by confocal microscopy. This project should help develop a human-relevant 3D model for evaluating a broad variety of vaccination and immunotherapeutic strategies.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

- Jeger-Madiot R*, Planas D, Staropoli I, ..., Gobaa S, and Chakrabarti LA*. (2024) Modeling memory B cell responses in a Lymphoid Organ-Chip to evaluate mRNA vaccine boosting. **Journal of Experimental Medicine** 221(10):e20240289.

- Claireaux M., Robinot R., ..., Lambotte O., and Chakrabarti L.A.* (2022) Low CCR5 expression protects HIV-specific CD4+ T cells of elite controllers from viral entry. **Nature Communications** 13:521

Scientific or technical background required for work program

Students are expected to have a formation in Immunology.

Students should be familiar with procedures to perform cell culture under sterile conditions. An expertise with primary human T cell culture and/ or spectral flow cytometry would be an asset.

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Institut Pasteur, 2026-2027

Title of the work program 16

Study of the impact of bacteria and fungi on the invasive process of *Entamoeba histolytica* using human colon-on-chip model

Description of the work program

Entamoeba histolytica is a protozoan parasite that colonizes the human colon. It is estimated that around 60 % of the population in developing countries might be harboring *Entamoeba* in an asymptomatic manner, and only ~20% of the cases develop intestinal amoebiasis which is characterized by colonic mucosa invasion and destruction. The stimuli triggering the parasite to switch from commensal to virulent state are unknown. In asymptomatic infection, *E. histolytica* interacts with the microbiome and feeds on bacterial microbiota. Our hypothesis is that the outcome of amoebiasis could be influenced by the composition of the gut microbiome.

The student will address her/his project following two axes:

1- The study of the direct impact of chosen fungi or bacteria on *E. histolytica* virulence: she/he will identify and quantify virulence factors of *E. histolytica* in their presence.
2. The study of the invasive process of *E. histolytica* in the presence of bacteria or fungi: she/he will use: human colon-on-chip model which reproduces the tree-dimensional colonic architecture and can be mechanically stretch to mimic peristalsis; Real time and fixed samples imaging, spinning disk confocal microscope, and image quantification plugins; The infection dynamics (under stretch and not) will be quantified by different measures over the time such as bacterial colonization area, amoeba displacement and tissue connectivity.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

1. M. Manich, P. Bochet, A. Boquet-Pujadas, T. Rose, G. Laenen, N. Guillén, JC.Olivo-Marin and E. Labruyère. Fibronectin induces a transition from amoeboid to a fan morphology and modifies migration in *Entamoeba histolytica*. PLoS Pathog. 2024. DOI: 10.1371/journal.ppat.1012392.
2. Boquet-Pujadas A, Feaugas T, Petracchini A, Grassart A, Mary H, Manich M, Gobaa S, Olivo-Marin JC, Sauvonnet N, Labruyère E. 4D live imaging and computational modeling of a functional gut-on-a-chip evaluate how peristalsis facilitates enteric pathogen invasion. **Science Advences**. **2022**. PMID: 36269830

Scientific or technical background required for work program

Cell biology, Microbiology, laboratory experiment

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Institut Pasteur, 2026-2027

Title of the work program 17

How systemic disease imposes a distinct quiescent state on tissue-resident stem cells

Description of the work program

Background. Adult stem cells reside in a reversible quiescent (G0) state that is actively maintained and that preserves their capacity to respond to injury. Our laboratory has identified a distinct quiescent state, which we term G_{Path}, induced in skeletal muscle stem cells (MuSCs), mesenchymal progenitors (Fibro-Adipogenic Progenitors, FAPs) and neural stem cells by pathologies arising at a distance from those tissues. The two systemic diseases we are studying are the respiratory influenza virus infection, and a non-metastatic subcutaneous tumour model of cancer cachexia in mice. G_{Path} is paradoxical. Cells downregulate multiple canonical regulators of quiescence, any one of which would normally be expected to promote quiescence exit, yet they do not enter the cell cycle during homeostasis. Instead they are smaller, metabolically depressed (reduced mitochondrial mass and membrane potential, lower oxygen consumption and ATP production), show broad downregulation of extracellular matrix programmes together with an immune-associated signature, and display altered chromatin accessibility. In MuSCs, timed EdU incorporation, Cyclin D1 and Ki67 kinetics, phospho-Rb accumulation and live imaging place the dominant delay before S-phase entry. Functionally, muscle regeneration after injury is delayed and qualitatively impaired. Circulating cytokines including TNFα reproduce part of the phenotype; providing soluble activin receptor type IIB (sActRIIb-Fc) rescues it partially.

Several questions remain open: **is G_{Path} reversible once the primary pathology resolves; which signalling nodes enforce the delay in proliferative commitment; and how much of the state is imposed directly by circulating factors?**

As part of this project, trainee will work with a senior researcher to establish a recovery time course in influenza-infected mice, analysing MuSCs and FAPs at the peak of pathology and at successive recovery time points after viral clearance. Readouts: cell number and size by flow cytometry, mitochondrial mass and membrane potential, a quiescence gene panel by qRT-PCR, and proliferative competence by EdU incorporation. Downstread signaling will be examined in the influenza model and phospho-SMAD2/3 in both models. The trainee will isolate MuSCs from pathological and control mice, plate them under growth-permissive conditions with or without pharmacological inhibitions and quantify Cyclin D1, Ki67, EdU positivity at defined intervals after plating, complemented by time-lapse videomicroscopy of time-to-first-division. The trainee will also use our existing transcriptomic and chromatin-accessibility datasets to define core gene sets promoting stem cell deregulation, and will use it to score the experimental conditions generated during the placement. No prior programming experience is required; guided introduction to R is provided.

Tutor/supervisor

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☑ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

1. Gayraud-Morel B., Di Girolamo D., et al., Tajbakhsh S. Systemic pathologies induce a distinct quiescent state in tissue-resident stem cells. *Cell Stem Cell, in revision*.

2. Di Girolamo D., et al., Tajbakhsh S. Extraocular muscle stem cells exhibit distinct cellular properties associated with non-muscle molecular signatures. *Development* 151, dev202144 (2024). doi:10.1242/dev.202144
3. Di Girolamo D., Tajbakhsh S. Pathological features of tissues and cell populations during cancer cachexia. *Cell Regeneration* 11, 15 (2022). doi:10.1186/s13619-022-00108-9
4. Evano B., Tajbakhsh S. Skeletal muscle stem cells in comfort and stress. *npj Regenerative Medicine* 3, 24 (2018). doi:10.1038/s41536-018-0062-3
5. Latil M., et al., Tajbakhsh S. Skeletal muscle stem cells adopt a dormant cell state post mortem and retain regenerative capacity. *Nature Communications* 3, 903 (2012). doi:10.1038/ncomms1890
6. Rocheteau P., Gayraud-Morel B., Siegl-Cachedenier I., Blasco M.A., Tajbakhsh S. A subpopulation of adult skeletal muscle stem cells retains all template DNA strands after cell division. *Cell* 148, 112–125 (2012). PMID: 22265406

Scientific or technical background required for work program

Training in cell biology, developmental biology, physiology, immunology or a related biomedical discipline. Prior hands-on experience with mammalian cell culture, immunostaining and light microscopy is expected; experience with flow cytometry, mouse experimentation or molecular biology (qRT-PCR, western blot) is an advantage. Candidates must highly motivated and willing to invest, work with laboratory mice. We look for rigour, autonomy in record-keeping, and a genuine interest in stem cell biology and tissue regeneration. Basic statistics is expected; familiarity with Fiji/ImageJ and any experience with R is welcome. Working language is English.

Techniques acquired. Mouse disease models, in vivo experimentation under approved ethics protocols; tissue dissection, enzymatic digestion; FACS isolation; primary cell culture at physiological oxygen; EdU proliferation assays; immunofluorescence and confocal microscopy; time-lapse videomicroscopy; flow-cytometry-based metabolic assays and qRT-PCR and western blotting; cryosectioning, histology; quantitative image analysis; statistics and data presentation (Prism, R).

Environment and expected outcome. The Stem Cells & Development Unit comprises around fifteen people (senior scientists, postdocs, PhD students, engineers) and works in English. The trainee will have day-to-day supervision from a senior scientist in the unit, direct access to Institut Pasteur core facilities (cytometry, imaging, animal facility, bioinformatics), and will present at weekly lab meetings and journal clubs.

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Institut Pasteur, 2026-2027

Title of the work program 18

Mechanisms of SARS-CoV-2 infection and neurodegeneration

Description of the work program

SARS-CoV-2, the virus responsible for COVID-19, has mainly been associated with respiratory disease, but increasing evidence indicates that infection can also affect the central nervous system and lead to neurological and cognitive alterations. The molecular mechanisms underlying these effects and their possible contribution to neurodegenerative processes remain poorly understood. Alzheimer's disease (AD) and Parkinson's disease (PD) are characterized by the accumulation of pathological proteins, including amyloid-β and hyperphosphorylated tau in AD, and α-synuclein in PD. Although the mechanisms responsible for the aggregation and spreading of these proteins have been extensively investigated, the possible role of viral infections and inflammation in modulating these processes remains an important open question.

Recent evidence suggests that SARS-CoV-2 infection may induce neuroinflammation, cellular stress, mitochondrial dysfunction and alterations in protein homeostasis, potentially affecting the aggregation and spreading of pathological proteins. Here, using *confocal microscopy* and *in situ cryo-electron microscopy approaches*, we will investigate the cellular and structural mechanisms linking SARS-CoV-2 infection to neurodegeneration. In particular, we will study how SARS-CoV-2 interacts with neuronal and glial cells, how infection affects tau and α-synuclein homeostasis, and whether viral-induced cellular alterations promote protein aggregation and spreading. The combination of confocal microscopy and cryo-EM will allow us to investigate the localization and ultrastructural organization of viral and pathological proteins, providing new insights into the molecular mechanisms connecting SARS-CoV-2 infection with neurodegenerative processes.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

Sartori-Rupp, A*. Cordero-Cervantes, D*. Pepe, A.* et al. Nat Commun 10, 342. 2019

Dilsizoglu Senol, A. Pepe A. et al. Sci Rep 9, 5741. 2019.

Grudina C et al., Neurobiol Dis 2019

Chastagner, et al. EMBO Molecular Medicine 12, e12025, 2020

Cordero, Zurzolo. EMBO J 40, e105789, 2021
Pepe, A. et al. Science Advances 8, eabo0171.2022
Chakraborty R et al., Cell Death Dis. 2023

Scientific or technical background required for work program

We are looking for a highly motivated candidate who has already demonstrated an excellent ability to carry out experiments during previous placements. A background in cell biology is required, as well as a good level of written and spoken English. Skills in cell culture, microscopy and/or image analysis and cryo-EM data analysis are welcome.

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Institut Pasteur, 2026-2027

Title of the work program 19

Deciphering Actin Filament Polarity in Tunneling Nanotubes by Cryo-Electron Tomography and AI-Based Image Analysis

Description of the work program

This project aims to elucidate the molecular organization and polarity of actin filaments within tunneling nanotubes (TNTs), specialized cellular structures involved in intercellular communication and the transfer of cellular components. We have established a novel end-to-end computational pipeline combining cryo-electron tomography (cryo-ET), molecular template matching, and AI-driven image segmentation to visualize and trace actin filaments within TNTs at near-molecular resolution.
By systematically optimizing tomographic reconstruction and developing deep learning–based analysis tools, we identified an optimal strategy for reliable actin filament detection and established a scalable workflow for 3D filament segmentation and polarity assignment. Preliminary analyses suggest that individual TNTs may display a defined and homogeneous actin polarity, providing new insights into the mechanisms governing TNT formation, stability, and intracellular transport.
The student will be involved in the 3D segmentation and analysis of actin filaments, using the established computational workflow, and will contribute to subtomogram averaging of individual actin filaments to determine their molecular orientation and polarity. This interdisciplinary project will provide the student with hands-on training in cryo-ET image analysis, computational structural biology, and AI-based image processing, while contributing to the mechanistic understanding of TNT-mediated intracellular transport.

Tutor/supervisor

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☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

Sartori-Rupp, A*. Cordero-Cervantes, D*. Pepe, A.* et al. Nat Commun 10, 342. 2019

Dilsizoglu Senol, A. Pepe A. et al. Sci Rep 9, 5741. 2019.

Grudina C et al., Neurobiol Dis 2019

Chastagner, et al. EMBO Molecular Medicine 12, e12025, 2020

Cordero, Zurzolo. EMBO J 40, e105789, 2021

Pepe, A. et al. Science Advances 8, eabo0171.2022

Chakraborty R et al., Cell Death Dis. 2023

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Institut Pasteur, 2026-2027

Scientific or technical background required for work program

We are looking for a highly motivated candidate with a strong interest in computational image analysis and structural biology. Familiarity with Linux/Unix and command-line tools is required, as well as a basic knowledge of cryo-EM/cryo-ET. Experience with cryo-EM image analysis software and basic 3D image processing and segmentation skills are welcome. Knowledge of Python would be an advantage, as well as an interest in AI-based image analysis and structural biology.

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Institut Pasteur, 2026-2027

Title of the work program 20

Microbiota and sex dependent programming of T cell immunity

Description of the work program

Sex differences are a fundamental feature of our immune responses, but the mechanisms through which they are established and maintained are still incompletely understood and generally understudied. Puberty is a major physiological transition for the immune system, and the gut microbiota is an important regulator of T-cell activation and differentiation. However, **how hormonal and microbial signals interact to shape sex-specific T-cell immunity** is still largely unknown.

Our project investigates this question using **mouse models**. We have identified a marked sex bias in liver T-cell immunity that appears after puberty and is strongly influenced by microbial signals. This system provides an opportunity to **investigate how sex hormones, developmental timing and the environment interact to shape sex-biased T-cell states**.

The Erasmus student will contribute to this ongoing work by characterising the emergence of sex-biased T-cell phenotypes and their relationship with the gut microbiota. Depending on the duration and progress of the project, the work will include **spectral flow-cytometric analyses** of immune cells, in vivo T cell transfers, confocal imaging, faecal sampling for **microbiota profiling**, controlled microbiota-transfer experiments, **meta-genomics** and **single cell RNA sequencing**. The student will receive training in mouse immunology, flow cytometry, experimental design, data analysis and scientific communication. This internship will be embedded in a project funded by the Branco Weiss Fellowship Society in Science and will be supervised on a day-to-day basis by Dr Valentina Venzin.

Tutor/supervisor

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☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

- Chi L, … , Belkaid Y. Sexual dimorphism in skin immunity is mediated by an androgen-ILC2-dendritic cell axis. 2024. *Science*. 384(6692).
- Belkaid Y, Harrison OJ. Homeostatic Immunity and the Microbiota. Immunity. 2017 Apr 18;46(4):562-576.
- Naik, S., Bouladoux, N., … Belkaid, Y. (2012). Compartmentalized control of skin immunity by resident commensals. *Science*, *337*(6098), 1115–1119.
- Venzin, V., … Iannacone, M. (2025). $CD4^+$ T cells license Kupffer cells to reverse $CD8^+$ T cell dysfunction induced by hepatocellular priming. *Nature immunology*, *26*(8), 1352–1366.

Scientific or technical background required for work program

Applicants should have completed at least three years of undergraduate study in biology, immunology, microbiology or a related field. Interest in host-microbiota interactions and T-cell immunobiology and a good command of English are required. Prior laboratory experience (mouse handling/immunology) is desirable but not essential; training in mouse work and flow cytometry will be provided.

Erasmus+

Institut Pasteur, 2026-2027

Title of the work program 21

Investigating flagellar structures in trypanosomes

Description of the work program

Cilia and **flagella** are sophisticated organelles made of 9 doublet microtubules and composed of up to 1,000 proteins. They perform multiple functions in motility, sensing or morphogenesis. Despite their conservation in most eukaryotes, they display amazing variations between species or between cell types of the same organism, with addition of sometimes large components, contributing to flagellum motility or other functions.

One such example is the paraflagellar rod (PFR) of protists of the Excavate group, a large lattice-like structure attached to some microtubule doublets. This is composed of at least 150 proteins whose organisation and function remains to establish. The student will use several electron and light microscopy approaches including **expansion microscopy** to reveal and explore the organisation of these proteins in the parasite *Trypanosoma brucei*. Functional impact of the morphological differences will be evaluated with a combination of fluorescent protein tagging to monitor **protein trafficking** and **Crispr-Cas9** approaches.

Environment: the host lab has exhaustive expertise in molecular and cellular biology, as well as in imaging at multiple level (live imaging, expansion microscopy, super-resolution, scanning and transmission electron microscopy) and has access to high-end facilities of the Institut Pasteur. It has trained numerous students over the years coming from more than 15 countries and 5 continents.

Lab website: https://research.pasteur.fr/en/team/trypanosome-cell-biology/
Social networks: https://bsky.app/profile/bastinlab.bsky.social
https://www.linkedin.com/in/philippe-bastin-157b893b2/

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

1. **Bertiaux, E.**, **Mallet, A., Fort, C.**, Blisnick, T., Bonnefoy, S., Jung, J., Lemos, M., Marco, S., Vaughan, S., Trepout, S., Tinevez, J.Y., and Bastin, P. (2018). Bidirectional intraflagellar transport is restricted to two sets of microtubule doublets in the trypanosome flagellum. **J Cell Biol** *217*, 4284-4297. Top 5% Altmetrics.

2. **Bertiaux, E**., Morga, B., Blisnick, T., Rotureau, B., and Bastin, P. (2018). A Grow-and-Lock Model for the Control of Flagellum Length in Trypanosomes. **Curr Biol** *28*, 3802-3814 e3803.
3. **Mallet, A.**, and Bastin, P. (2022). Restriction of intraflagellar transport to some microtubule doublets: An opportunity for cilia diversification? **Bioessays** *44*, e2200031. Front cover.
4. Bonnefoy, S., Alves, A.A., Bertiaux, E., and Bastin, P. (2024). LRRC56 is an IFT cargo required for assembly of the distal dynein docking complex in Trypanosoma brucei. **Mol Biol Cell** *35*, ar106.
5. **Abbuhl, D**., Pruzincova, M., Stepanek, L., Bouscasse, E., Azevedo, R., Matondo, M., Varga, V., Bonnefoy, S., and Bastin, P. (2025). A novel approach to tagging tubulin reveals MT assembly dynamics of the axoneme in Trypanosoma brucei. **J Cell Sci** 138(20):jcs264145.
6. Alves, A.A., Jung, J., Moneron, G., Vaucelle, H., **Fort, C., Buisson, J**., Schietroma, C., and Bastin, P. (2025). Intraflagellar Transport Selectivity Occurs with the Proximal Portion of the Trypanosome Flagellum. **J Cell Biol** 224(10):e202501088.
7. **Hecquet, A**., Bonnefoy, S., Bastin, P. (2026) The trypanosome flagellum as model for parasitology, cell biology and ciliopathies. **Semin Cell Dev Biol**.184:103689.

Names of current or former PhD students in bold

Scientific or technical background required for work program

Cellular and molecular biology, microscopy

Erasmus+

Institut Pasteur, 2026-2027

Title of the work program 22

Knowledge Management System for cross-disciplinary research on human behavior

Description of the work program

Understanding human behavior requires integrating evidence produced across a wide range of methods and disciplines –from genetics, neurophysiology, and evolutionary biology to anthropology, psychology, philosophy, and cognitive sciences. Yet behavioral sciences currently face a major digital bottleneck: datasets, theoretical models, and research findings are increasingly digital, but they remain hard to connect because they use different vocabularies, formats, and standards of evidence. The goal of this project is to contribute to the development of a Knowledge Management System (KMS) that can host heterogeneous research data on human behavior, using eating behavior as a case study. The system will structure information together with its conceptual relationships, provenance, dependency rules, hypotheses, and uncertainty metrics, so that evidence from different fields can be queried and reasoned across. The work will involve regular exchanges with an interdisciplinary network of more than a dozen scholars across various domains.

The intern will work closely with the Dr. Aschard and the interdisciplinary network to support the design, prototyping, and documentation of the KMS. The internship offers a unique opportunity to participate at the ground level of an ambitious interdisciplinary project at the intersection of knowledge engineering, behavioral science, and philosophy of science.

The internship will be adapted to the intern's profile: candidates with a stronger technical background can focus more on system design and prototyping; candidates with a stronger behavioral-science background can focus more on ontology, conceptual mapping, and network coordination.

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Selected publications or patents of the Research Group offering the work program

- **The influence of environment on bacterial co-abundance in the gut microbiomes of healthy human individuals**. Boetto C, et al. Commun Biol. 2025. PMID:41198867
- **Polygenic risk score prediction accuracy convergence.** Henches L, et al. HGG Adv. 2025. PMID:40375557
- **Multitrait Analysis to Decipher the Intertwined Genetic Architecture of Neuroanatomical Phenotypes and Psychiatric Disorders.** Auvergne A, et al. Biol Psychiatry Cogn Neurosci Neuroimaging. 2025 PMID:39260564
- **Identifying chronic obstructive pulmonary disease subtypes using multi-trait genetics**. Ziyatdinov A, et al. EBioMedicine. 2025. PMID:40010152
- **An approach to identify gene-environment interactions and reveal new biological insight in complex traits.** Zhu X, et al. Nat Commun. 2024. PMID:38649715

Scientific or technical background required for work program

The candidate should have a strong background in computer science and/or behavioral sciences. Good analytical and conceptual skills, and excellent communication abilities are required.

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Institut Pasteur, 2026-2027

Title of the work program 23

Can tissue-resident macrophages remember early life?
Exploring long-term programming after prenatal immune activation.

Description of the work program

Tissue-resident macrophages are specialized immune cells that populate organs early during development and subsequently acquire functions adapted to their local environment. Unlike many circulating immune cells, several populations of tissue-resident macrophages originate from embryonic progenitors and can persist throughout life through local self-renewal. This unique developmental history raises an interesting question: **can an inflammatory event, occurring during embryonic life, leave a lasting imprint on macrophages that remains detectable in adulthood?**
We investigate this question using a mouse model of maternal immune activation. Pregnant mice are exposed at embryonic day 9.5 (E9.5) to the viral mimic Poly(I:C), inducing a transient inflammatory response during a critical period of embryonic immune development. Our current results indicate that this prenatal perturbation modifies inflammatory responses in adult offspring. However, whether these alterations are intrinsically maintained within tissue-resident macrophages or depend on their adult tissue environment remains unknown.

The goal of this internship will be to determine whether adult tissue-resident macrophages retain a memory of prenatal immune exposure when removed from their tissue environment and studied ex vivo. The student will:

1. Establish and optimize the isolation and ex vivo culture of Kupffer cells, the resident macrophages of the liver, assessing cell yield, viability and preservation of their identity.
2. Characterize their response to LPS over time by combining RT-qPCR and intracellular flow cytometry to measure inflammatory gene expression and cytokine production.
3. Compare Kupffer cells from control and prenatally Poly(I:C)-exposed offspring, including male and female animals, to identify sex-dependent alterations in their inflammatory response.
4. Extend the approach to alveolar macrophages, a tissue-resident macrophage population particularly suitable for ex vivo culture, to determine whether developmental programming is shared across macrophage populations or is tissue-specific.

The project will provide hands-on training in primary macrophage isolation and culture, ex vivo stimulation, flow cytometry, intracellular cytokine staining, RT-qPCR and quantitative data analysis.

Tutor/supervisor

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Institut Pasteur, 2026-2027

Selected publications or patents of the Research Group offering the work program

Lazarov T, Loyher PL, Yang H, Choo ZN, Deng Z, Nowotschin S, Kuo YY, Zhou T, Alberdi-Gonzalez A, Stumm R, Mass E, **Gomez Perdiguero E**, Hadjantonakis AK and Geissmann F. *Characterization of the mammalian prodefinitive angio-hematopoeitic lineage.* **(2025) Science Immunology** Nov7;10(113):eadt6616. doi: 10.1126/sciimmunol.adt6616.

Monticelli S, Sommer A, AlHajj Hassan Z, Garcia Rodriguez C, Adé K, Cattenoz P, Delaporte C, **Gomez Perdiguero E**[*] and Giangrande A[*]. *Early-wave macrophages: novel string-puller of late hematopoiesis*. **(2024) Developmental Cell** May 20;59(10):1284-1301.e8. doi: 10.1016/j.devcel.2024.03.013.. *These authors contributed equally. **Corresponding author.**

Weinberger T, Messerer D, Joppich M, Fischer M, Garcia C, Kumaraswami K, Wimmler V, Ablinger S, Räuber S, Fang J, Liu L, Han W Liu, Winterhalter J, Lichti J, Tomas L, Esfandyari D, Percin G, Martin Salamanca S, Hidalgo A, Waskow C, Engelhardt S, Todica A, Zimmer R, Pridans C, **Gomez Perdiguero E** and Schulz C. *Resident and recruited macrophages differentially contribute to cardiac healing after myocardial ischemia*. **(2024) eLife**. doi: 10.7554/eLife.89377.1.

Freyer L, Lallemand Y, Dardenne P, Sommer A, Biton A and **Gomez Perdiguero E**. *Erythro-Myeloid Progenitor Origin of Hofbauer cells in the Early Mouse Placenta***. (2022) Development** 149:200104. doi: 10.1242/dev.200104. **Corresponding author.**

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Soares-da-Silva F, Freyer L, Elsaid R, Burlen-Defranoux O, Iturri L, Sismeiro O, Pinto-do-Ó P, **Gomez Perdiguero E** and Cumano A. *Yolk sac, but not hematopoietic stem cell-derived progenitors, sustain erythropoiesis throughout murine embryonic life*. **(2020) Journal of Exp Med** 18 (4): e20201729 doi: 10.1084/jem.20201729.

Gomez Perdiguero E*, Klapproth K*, Schulz C, Busch K, Crozet L, Trouillet C, Geissmann F[•] and Rodewald HR[•]. *Tissue-resident macrophages originate from yolk-sac-derived erythro-myeloid progenitors*. (**2015) Nature** 518(7540):547-51. *,[•] These authors contributed equally.

Scientific or technical background required for work program

Candidates should be currently enrolled in a program in Immunology, Molecular Biology, Biomedical Sciences, Biotechnology, or a related field. Previous laboratory experience is expected, while experience in flow cytometry, primary cell culture, RT-qPCR or mouse experimentation would be advantageous but is not mandatory. Candidates should have a strong interest in immunology and macrophage biology, be motivated to engage in experimental optimization and troubleshooting, and be comfortable working both independently and collaboratively. Good proficiency in English is required.

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Institut Pasteur, 2026-2027

Title of the work program 24

Generation of isogenic CHRFAM7A knockout hiPSC lines to investigate human-specific regulation of α7 nicotinic signalling

Description of the work program

The α7 nicotinic acetylcholine receptor, encoded by *CHRNA7* at chromosome 15q13.3, is a highly Ca^{2+}-permeable ligand-gated ion channel expressed in neural progenitors and developing cortical neurons, including inhibitory interneurons. In addition to its established functions in cholinergic neurotransmission, cognition and synaptic plasticity, α7-nAChR signalling may contribute to early developmental processes such as progenitor proliferation, neuronal differentiation, migration, neurite development and activity-dependent maturation. Alterations affecting the dosage or function of *CHRNA7* have been associated with neurodevelopmental and neuropsychiatric conditions, including epilepsy and schizophrenia, as well as with neuronal vulnerability in Alzheimer's disease. In humans, α7-nAChR biology is further regulated by *CHRFAM7A*, a human-lineage-specific chimeric gene containing a partial duplication of *CHRNA7*. Its product, dupα7, can associate with α7 subunits and influence receptor assembly, intracellular trafficking and membrane availability. Experimental studies indicate that *CHRFAM7A* expression can attenuate α7-dependent calcium responses, including in human iPSC-derived neurons. Since *CHRFAM7A* is absent from conventional rodent genomes, human iPSC models are essential for investigating its endogenous functions. The *CHRFAM7A* locus presents substantial interindividual variability in copy number, genomic configuration and allelic composition. Of particular interest, the Δ2bp variant in exon 6 introduces a frameshift and a premature stop codon, but its consequences for dupα7 expression and function in human neural cells remain incompletely understood.

The objective of this Erasmus project is to generate an isogenic allelic series of *CHRFAM7A*-edited hiPSC lines in two parental backgrounds, each carrying two genomic copies of *CHRFAM7A*: one two-copy line without the Δ2bp variant and one two-copy line carrying the Δ2bp variant. In each background, the project will aim to isolate both monoallelic knockout clones, in which one *CHRFAM7A* copy remains intact (*CHRFAM7A*+/−), and, whenever technically achievable, complete biallelic knockout clones in which both copies are disrupted (*CHRFAM7A*−/−). This allelic series will make it possible to compare parental *CHRFAM7A*+/+ cells with *CHRFAM7A*+/− and *CHRFAM7A*−/− clones within the same genetic background. The design will therefore assess not only the consequences of complete *CHRFAM7A* loss but also potential gene-dosage effects. This is particularly relevant because the proportion of dupα7 relative to α7 may influence receptor assembly, trafficking and functional availability. The two parental backgrounds will additionally determine whether the effects of reducing or eliminating *CHRFAM7A* are reproducible or modified by the Δ2bp-associated allelic context. In the Δ2bp-positive line, baseline characterization will establish whether the variant is present in one or both *CHRFAM7A* copies. The parental hiPSC lines will be edited by nucleofection of CRISPR/Cas9 ribonucleoprotein complexes designed to disrupt *CHRFAM7A* while preserving the highly homologous *CHRNA7* locus. Nucleofected cells will be enriched by fluorescence-activated cell sorting and deposited as single cells for monoclonal expansion. Recovered colonies will undergo an initial molecular screening to identify edited clones and determine whether one or both *CHRFAM7A* copies have been disrupted. Candidate *CHRFAM7A*+/− and *CHRFAM7A*−/− clones will then be validated using locus-specific PCR and Sanger sequencing. Positive clones will be progressively expanded and cryopreserved. A second independent screening after expansion and banking will confirm the stability of the genotype, the number of intact *CHRFAM7A* copies and the preservation of the *CHRNA7* locus. Final clones will also be assessed for hiPSC morphology, pluripotency, absence of mycoplasma and genomic

integrity. The expected outcome is an isogenic panel comprising parental *CHRFAM7A*+/+ cells, validated *CHRFAM7A*+/− clones and, where technically possible, *CHRFAM7A*−/− clones in both the Δ2bp-negative and Δ2bp-positive backgrounds. Whenever possible, at least two independently derived clones of each relevant genotype will be retained to reduce the influence of clone-specific effects. The final resource will include cryopreserved stocks, a complete clone genealogy and a traceable molecular-validation dossier.

Future biological applications: The generated isogenic lines will provide a causal human model for investigating whether *CHRFAM7A* acts only as a regulator of mature α7-nAChRs or also influences earlier developmental programmes. Following the resource-generation stage, parental and knockout hiPSCs will be differentiated into ventral forebrain progenitors and cortical interneurons. These models will support the analysis of neural progenitor specification, proliferation and differentiation, followed by interneuron migration, neurite development and acquisition of mature cellular identities. At the receptor level, future experiments will examine α7-nAChR intracellular trafficking, surface availability and pharmacologically evoked Ca^{2+} responses. At later stages, the consequences of *CHRFAM7A* loss may be evaluated at the level of neuronal maturation and network activity. The isogenic panels will also be used to investigate whether *CHRFAM7A* modifies interneuron vulnerability under Alzheimer-related conditions. Controlled exposure to amyloid-β or oxidative stress will allow assessment of calcium dysregulation, receptor redistribution, stress responses and neuronal survival. In longer-term studies, selected cells may be evaluated following xenotransplantation to study their maturation, migration and integration into functional brain circuits.

Additional work package (contingent on CRISPR pipeline feasibility): modelling BMI1 loss in sporadic Alzheimer's disease. BMI1 is a core component of the Polycomb Repressive Complex 1 that maintains heterochromatin integrity and neuronal genomic stability; its expression is selectively silenced in the brains and iPSC-derived neurons of patients with sporadic, late-onset Alzheimer's disease, and its experimental loss is sufficient to trigger genomic instability and neurodegeneration-like phenotypes in human neurons. If the student demonstrates good command of the CRISPR/Cas9 ribonucleoprotein nucleofection, FACS-based clonal isolation and PCR/Sanger-based molecular validation pipeline described above for *CHRFAM7A*, the same strategy will be extended, as a second, optional work package, to generate CRISPR/Cas9-mediated knockout of *BMI1*. Using nucleofection of CRISPR/Cas9 ribonucleoprotein complexes, FACS-based single-cell sorting and monoclonal expansion, and locus-specific PCR/Sanger sequencing validation, the student will aim to isolate and validate heterozygous *BMI1*+/− hiPSC clones and complete *BMI1*−/− clones, alongside isogenic parental controls. These clones will then be differentiated into mature neurons to extract and quantify AD-relevant phenotypes, including axonal and dendritic alterations, amyloid-β and tau dysregulation, thereby extending the isogenic hiPSC toolbox developed in this project to a second, mechanistically distinct model of sporadic Alzheimer's disease.

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Institut Pasteur, 2026-2027

☒ I authorise the IP Erasmus+ team to publish the project proposal on the pasteur.fr website

Selected publications or patents of the Research Group offering the work program

- Görgülü I, Jagannath V, Pons S, et al. The human-specific nicotinic receptor subunit *CHRFAM7A* reduces α7 receptor function in human induced pluripotent stem cell-derived and transgenic mouse neurons. *European Journal of Neuroscience*. 2024;60:4893-4906. doi:10.1111/ejn.16474.
- Llach Pou M, Thiberge C, Pons S, Maskos U, Cloëz-Tayarani I. *CHRFAM7A* overexpression in human iPSC-derived interneurons dysregulates α7-nAChR surface expression and alters response to oligomeric β-amyloid peptide. *bioRxiv*. 2024. doi:10.1101/2024.06.04.597325. Preprint, not peer reviewed.
- Llach Pou M, Thiberge C, Van der Zwan M, et al. Developmental changes of human neural progenitor cells grafted into the ventricular system and prefrontal cortex of mouse brain in utero. *Cells*. 2023;12:1067. doi:10.3390/cells12071067.
- D'Alessio R, Koukouli F, Blanchard S, et al. Long-term development of human iPSC-derived pyramidal neurons quantified after transplantation into the neonatal mouse cortex. *Developmental Biology*. 2020;461:86-95. doi:10.1016/j.ydbio.2020.01.009.
- Deflorio C, Blanchard S, Carisì MC, Bohl D, Maskos U. Human polymorphisms in nicotinic receptors: a functional analysis in iPS-derived dopaminergic neurons. *FASEB Journal*. 2017;31:828-839. doi:10.1096/fj.201600932R.
- Koukouli F, Rooy M, Tziotis D, et al. Nicotine reverses hypofrontality in animal models of addiction and schizophrenia. *Nature Medicine*. 2017;23:347-354. doi:10.1038/nm.4274.

Scientific or technical background required for work program

Required profile

• Advanced Bachelor's or Master's-level training in molecular and cellular biology, neuroscience, stem-cell biology, genetics, biotechnology or a related discipline.

• Demonstrated hands-on experience with sterile mammalian cell culture, including aseptic handling, passaging, cell counting and freezing or thawing. Experience working carefully and consistently with sensitive cell cultures is essential.

• Strong organizational skills and attention to experimental traceability, including accurate sample identification, maintenance of laboratory records and reliable execution of repetitive experimental tasks.

• Patience, precision and the ability to work according to established biosafety procedures and standard operating procedures.

• Ability to read scientific literature and communicate results in English within an international research environment.

• Motivation to learn genome-editing, clonal-isolation and molecular-validation approaches. Previous experience with these techniques is not required, as appropriate training will be provided during the placement.

Preferred but not required

• Previous experience with human pluripotent stem cells, including assessment of colony morphology, routine maintenance or pluripotency quality control.

• Familiarity with DNA extraction, PCR, agarose-gel electrophoresis, primer design or basic sequence interpretation.

• Exposure to CRISPR/Cas9 genome editing, ribonucleoprotein delivery, flow cytometry, single-cell sorting, monoclonal expansion, Sanger sequencing or amplicon-sequencing analysis.

• Basic experience with data analysis using GraphPad Prism, R or Python.

Experience with CRISPR/Cas9, clonal isolation or sequencing will be considered an advantage but is not a prerequisite. The essential technical requirement is previous practical experience in mammalian cell culture.

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Institut Pasteur, 2026-2027

Title of the work program 25

Imaging Shigella infection responses and bacterial spread in epithelia using novel microfluidic chip device and label-free imaging technologies

Description of the work program

Project summary

The intestinal epithelium forms a dynamic barrier that maintains tissue homeostasis and responds rapidly to microbial infection. At the cell level, the initially infected enterocytes communicate with uninfected neighbouring cells and coordinate local responses, but the temporal relationship between bacterial and immune signalling spread, cell morphology, organelle remodelling (like mitochondria, nucleus, lipid droplets), and cell fate remains poorly understood. This project will use Targeted Infection Chips that have been recently developed by the host team (TIC; see Fig.1), a microfluidic device that allows single-cell infection and high-resolution microscopy, together with NanoLive (https://www.nanolive.com) holotomographic imaging technique or an complementary label-free approach called **quantitative phase imaging (QPI; Phasics;** https://www.phasics.com/en/applications/quantitative-phase-imaging/**)** to study *Shigella flexneri* infection in epithelial cells at single-cell resolution. This represents a unique opportunity to combine our unique organ-on-a-chip methodologies with advanced imaging techniques to understand dynamic cellular processes in responses to infection spread within the intestinal epithelium.

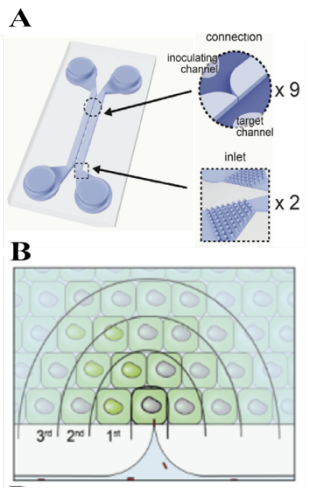

Figure 1: Design of the Targeted Infection Chip (TIC).

Background and rationale

The intestinal epithelium is not only a physical barrier but also a coordinated communication system (Odenwald & Turner, 2017). Infected epithelial cells activate signalling pathways and transmit inflammatory or stress-related signals to neighbouring cells. These cell-cell signalling events influence epithelial morphology, barrier function, antimicrobial responses, metabolism, and cell survival. During infection with the major enteroinvasive bacterial pathogen *Shigella*, the balance between bacterial dissemination and host signalling is particularly important because bacterial spread can generate localised infection foci and amplify tissue damage (Perdomo *et al*, 1994). To study these processes, the hosting laboratory has developed a novel microfluidics device - the Targeted Infection Chip (TIC). The TIC enables controlled infection of selected epithelial cells. Unlike conventional infection assays, TIC-based experiments can distinguish primary responses in infected cells from secondary responses in neighbouring cells. The integration of TIC with high-resolution imaging has been established to measure a variety of cell signalling, like inflammatory responses, however these methods require immunofluorescent labelling of cellular components and is not adaptable with patient derived tissue samples, where fluorescent labelling options are limited. Consequently, label-free imaging represents a cutting-edge approach to dynamically monitor living cells without the need for fluorescent labels or fixation. Applying these technologies to patient-derived tissue models offers a unique opportunity to capture cellular responses in a more physiologically relevant context while preserving tissue viability.

The aim of this project is to establish and compare two label-free imaging approaches and their compatibility with the TIC, for monitoring epithelial responses to bacterial infection and inflammatory stimuli. The first approach will combine **NanoLive holotomographic imaging with fluorescence imaging using a p65-GFP reporter cell line**, while the second will use **QPI (Phasics)** as an alternative label-free approach. The project will determine which imaging system, or combination of systems, is most suitable for long-term, non-invasive monitoring of epithelial cell responses at single-cell resolution (Aim1). Further, targeted infection on TIC will be performed using *Shigella flexneri* as a model infectious organism, to study cellular responses to infection and cell-cell signalling (Aim2). This provides a unique opportunity to advance the TIC's potential for future studies on more physiologically relevant tissues, while retaining epithelial heterogeneity and barrier properties.

Aim 1: Establish and compare label-free imaging approaches for TIC-based epithelial models

The first aim will establish a reproducible TIC workflow for epithelial cell culture and evaluate two label-free imaging technologies for monitoring epithelial responses to infection and inflammatory stimuli. Two complementary imaging approaches will then be established and evaluated on the TIC. The first will use the **NanoLive holotomographic microscope (that detects intracellular bacteria and within their different cellular environments)**, enabling label-free three-dimensional imaging of living cells together with fluorescence imaging of the **p65-GFP reporter cell line the host lab already has established. This combination will allow to monitor dynamic changes in cellular morphology and intracellular organisation while simultaneously measuring activation of the NF-κB inflammatory pathway, induced by pharmacological stimulation directly on the chip (e.g., TNF-α treatment). The second approach will** use **quantitative phase imaging (QPI; Phasics)** as an alternative label-free technology. QPI will be evaluated for its ability to image epithelial cells within the TIC and to quantify changes in cell morphology, cell mass/density, cell-cell interactions, and cellular integrity during infection or inflammatory stimulation. The two label-free approaches will be compared in the TIC model. **NanolLive** offers 3D information on cell morphology and quantification of intracellular structures juxtaposed to the invading bacteria, and it can be combined with p65-GFP fluorescence but may be more sensitive to the optical properties of the TIC itself, based on the fabrication material (PDMS). **Phasics QPI** offers a complementary, label-free approach and is compatible with any kind of fluorescent microscope and does not require additional work on our TIC design. However, its ability to resolve intracellular structures and work alongside fluorescence will need to be evaluated.

An image-analysis pipeline will be developed to segment and track individual epithelial cells over time. For the NanoLive/p65-GFP approach, these phenotypic parameters can be detected by using the company based AI-tool and will be correlated with p65-GFP dynamics. Equivalent quantitative features will be extracted from QPI.

The outcome of this aim will be a validated TIC-based imaging workflow and a direct comparison of NanoLive holotomography combined with fluorescence and Phasics quantitative phase imaging. This comparison will identify the most suitable label-free imaging technology, or combination of technologies, for longitudinal single-cell monitoring of epithelial responses to bacterial infection and inflammatory stimuli in TICs, a ground work for Aim2 and future studies on patient-derived tissue models.

Aim 2: Infect the TIC with *Shigella* and quantify bacterial spreading, mitochondrial and lipid droplet reprogramming in infected and neighbouring cells

Following evaluation of the two label-free imaging approaches, the most suitable workflow will be used to investigate the cellular response to *Shigella* infection. We will determine how *Shigella* spreads through the epithelium and whether infection induces mitochondrial fragmentation and lipid droplet changes in infected and neighbouring epithelial cells. The student will perform targeted infection of the TIC with *Shigella*. Wild-type *S. flexneri* and an *icsA*-mutant, which cannot spread from cell-to-cell, will be used to infect selected epithelial cells while the surrounding monolayer remains intact for continuous observation. Here, changes in bacterial spread dependent signalling can be observed.

Bacterial spreading: Label-free imaging will allow to track bacterial spread over time and identify three cell populations: directly infected cells, subsequently infected neighbours (for wild-type), and uninfected bystander cells. The extent and kinetics of bacterial dissemination across the epithelial monolayer will be quantified and linked to changes in host organelles at the single-cell level (see next paragraphs). The *icsA*-mutant will provide a complementary condition in which cells are exposed to infection without cell-to-cell bacterial spread.

Mitochondrial reprogramming: Changes in mitochondrial morphology will be quantified over time, using NanoLive's AI-powered Smart Mitochondrial AssayLIVE or comparable Fiji macros (in case of QPI usage), mitochondrial network continuity, size, elongation, distribution, and fragmentation will be measured, building on previous work linking *Shigella* infection to mitochondrial fragmentation and cell death (Sirianni *et al*, 2016; Lobato-Márquez *et al*, 2023; Brokatzky *et al*, 2024).

Lipid droplet reprogramming: The project builds on recent findings that *S. flexneri* actively remodels host lipids, depleting the cellular lipid pool and driving the formation of large lipid bodies (Ascari *et al*, 2023). Using NanoLive's AI-powered Smart Lipid Droplet AssayLIVE or comparable Fiji macros (in case of QPI usage), we will quantify lipid droplet number, size, dry mass, area, and spatial distribution in infected and neighbouring cells (Pérez-Montero *et al*, 2023).

Spatial propagation of the response: For both mitochondrial and lipid droplet responses, the key question is whether changes are restricted to infected cells or also arise in bystander cells before bacteria arrive, which would indicate a communication-driven response. Already-developed image analysis pipelines, in collaboration with Julie Mabon of Jean-Christophe Olivo-Marin's Lab (Institut Pasteur), will be integrated to map bacterial infection, host organelle responses, and spatial neighbourhoods.

The project will provide a dynamic, single-cell view of how *Shigella* spreads through the epithelium, reshapes host organelles, and potentially triggers responses in uninfected neighbouring cells ahead of bacterial arrival.

Significance

This project will establish a TIC-based, non-invasive imaging workflow to study *Shigella* infection and epithelial cell-cell communication at single-cell resolution. By combining fluorescence-based inflammatory readouts with label-free imaging, the project will link bacterial dissemination with the timing and spatial propagation of epithelial responses, including changes in cell morphology, mitochondrial fragmentation and lipid droplet dynamics.

Label-free imaging is particularly valuable because it enables living cells to be monitored continuously without the need for fluorescent labelling, fixation or repeated staining. This provides a unique comprehensive view of cellular dynamics over time whilst minimising manipulation of the system. It also creates an opportunity to detect early cellular responses that may be missed by endpoint or fluorescence-only approaches, and it works with non-labelled pathogens. Importantly, this approach could be particularly valuable for future studies using patient-derived tissues, where fluorescent labelling can be more challenging and may be limited by tissue complexity and accessibility. Establishing label-free imaging within the host lab's TIC will therefore provide an innovative approach for studying infection and inflammation in increasingly complex and physiologically relevant tissue models, with high spatial and temporal resolution.

The project will determine whether cellular responses are restricted to directly infected cells or are transmitted to neighbouring cells before bacterial entry, an important and longstanding question in infection biology for which technological approaches to monitor these early events in living tissues remain limited.

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Institut Pasteur, 2026-2027

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Institut Pasteur, 2026-2027

Selected publications or patents of the Research Group offering the work program

1. Lippmann J, Gwinner F, Rey C, Tamir U, Law HK, Schwikowski B, Enninga J, Bacterial Internalization, Localization, and Effectors Shape the Epithelial Immune Response during Shigella flexneri Infection, Infect. Immun. 2015 Sep;83(9):3624-37.
2. Mellouk N., et al. (2024). Post-translational targeting of Rab35 by the effector IcsB of Shigella determines intracellular bacterial niche formation. Cell Reports, 43(4).
1. Valenzuela-Valderas KN, Farrashzadeh E, Chang YY, Shi Y, Raudonis R, Leung BM, Rohde JR, Enninga J, Cheng Z, RACK1 promotes Shigella flexneri actin-mediated invasion, motility, and cell-to-cell spreading., iScience 2023 Nov; 26(11): 108216.
2. Walocha, R., et al. (2024). Organoids and organ-on-chip technology for investigating host-microorganism interactions. Microbes and Infection, 26(7).
3. Brokatzky, D., et al. (2024). Septins promote macrophage pyroptosis by regulating gasdermin D cleavage and ninjurin-1-mediated plasma membrane rupture. Cell Chemical Biology, 31(8), 1518-1528.e6.

Scientific or technical background required for work program

The successful implementation of this project requires a student with a solid understanding in epithelial cell biology, and host-pathogen interactions, complemented by practical skills in mammalian cell culture, bacterial infection models, and image analysis. Also, knowledge in advanced imaging is a plus. The fellow is expected to have:

- **Advanced knowledge of cell and molecular biology**, including epithelial barrier function, cell-cell junctions, organelle dynamics (mitochondria, nucleus).
- **Experience with host-pathogen systems**, preferably with intracellular bacterial pathogens (e.g. *Shigella*, *Salmonella*).
- **Hands-on expertise in mammalian cell culture** under sterile conditions, and designing time-lapse imaging experiments.
- **Practical skills in microbiology and infection assays**, such as bacterial culture, and safe handling of BSL-2 organisms.
- Basic statistical analysis and visualization of time-series and spatial data is advantageous.

Additional background in **microfluidics, organ-on-chip technologies, or organoid culture** is highly desirable but not mandatory, as specific training on the Targeted Infection Chip (TIC) and Nanolive holotomographic imaging will be provided during the fellowship. Willingness to learn new imaging modalities, adopt computational workflows, and work at the interface of infection biology and quantitative cell biology is essential. The lab environment is highly supportive and the language spoken is English.

Erasmus+

Institut Pasteur, 2026-2027

Title of the work program 26

BMI1 loss of function and axonal degeneration in late onset sporadic Alzheimer: an integrated in vitro and in vivo computational approach

Description of the work program

Late onset sporadic Alzheimer's disease (AD), the most common form of AD, is characterized by progressive neurodegenerative dysfunction driven primarily by the accumulation of ß amyloid plaques (plaques Aß), leading to cognitive decline. While advanced age and APOE4 predisposition remain the strongest risk factor, the molecular pathways contributing to it remain completely elusive. BMI1 gene, a member of the polycomb repressive complex 1 (PRC1), plays a role in chromatine compaction, maintenance of genomic stability, neuronal homeostasis and cellular senescence. Recent work has identified a selective alteration of BMI1 expression in sporadic AD brains suggesting that its dysfunction contributes to neuronal vulnerability to Aß toxicity (Flamier et al., 2018). Beyond amyloid and tau pathology, synaptic (dendrite spine loss) and axonal integrity are among the earliest structural consequence of neurodegeneration and correlate closely with cognitive impairment in AD patients. However, the specific consequences of BMI1 loss on axonal cytoskeletal architecture such as axonal breakage, swelling, and caliber changes of neurite diameter, remain uncharacterized and quantitatively unexplored.
This project aims to characterize and quantify BMI1 deficiency induced axonal alteration by developing a reproducible and automated Python based image analysis pipeline for the quantitative assessment of axonal degeneration in BMI1 deficient neurons in vitro and in vivo.

Methodology
The in vitro arm have already been carried out, with deactivation of BMI1 using shRNA targeting the sequence of BMI1, or using a scramble sequence (control), in human iPSC-derived mature neurons. These neurons were immunostained for axonal cytoskeletal markers (tubulin) and imaged by confocal microscopy providing the raw imaging data for this project. Preliminary observations show axonal breaking points, swellings, and reduced neurite diameter. The first part of the project will focus on the analysis, detection and quantification of axonal fragmentation (breaks), swellings and neurite diameter in vitro at different timepoint of cell maturation (DIV7, DIV14, DIV30).

To quantify axonal breakage objectively, a Python based image analysis pipeline has been developed that: (1) segments axons via intensity-based tubular-structure (vesselness) filtering and thresholding, (2) reduces the binary mask to a skeleton, (3) computes fragmentation metrics such as fragment rate, mean fragment continuity, endpoint density, gap-bridge rate, (4) explicitly detects individual break-pairs allowing visual and statistical validation of the phenotype across conditions. This pipeline will be refined, validated across additional conditions and timepoints, and extended to quantify axonal swelling (local diameter along the skeleton). To assess and quantify dendritic loss and synaptic structure alteration, neurons were immunostained with a dendrite marker (MAP2) combined with a spine-specific marker PSD-95 (postsynaptic sites) and synaptophysin (presynaptic terminals). Using python and pretrained deep learning models, the detection of PSD-95 and synaptophysin puncta and quantification of their density per unit and spatial apposition will be performed to compare the conditions.

Further, this pipeline could serve to detect early axonal alteration in BMI1 deficient iPSCs-derived neurons xenografted into the prefrontal cortex (PFC) of immunodeficient NOD-SCID mice. In vivo models involving the transplantation of human neurons into mouse brains are powerful approaches to analyze human-relevant cellular and particularly the molecular mechanisms that occur in the early

stages of AD(1–3). The analysis of early alterations will be performed at different timepoints after transplantation (2 weeks and 1 month post-transplantation).
The aim will be to assess whether axonal breakage and swelling phenotypes observed in vitro are reproduced and evolve within a physiological brain environment. Confocal images of grafted axons (identified by human specific nuclear marker STEM101 and hNCAM) are provided to this project for analysis. Python pipeline workflow will be adapted to the complexity of brain tissue and validated against appropriate biological controls.

Overall, the project will establish a quantitative and reproductible pipeline to measure neuronal and axonal degeneration. The work will combine computational image processing, Python programming that provide a bioinformatics oriented approach for the characterization of BMI1-associated neuronal pathology.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

1. Vitrac A, Pons S, Balkota M, Lemière N, Raïs C, Bourgeois JP, et al. A chimeric mouse model to study human iPSC-derived neurons: the case of a truncating SHANK3 mutation. Sci Rep. 7 août 2020;10(1):13315. doi:10.1038/s41598-020-70056-4 PubMed PMID: 32769989; PubMed Central PMCID: PMC7414912.
2. Llach Pou M, Thiberge C, Van der Zwan M, Devi Govindan A, Pons S, Maskos U, et al. Developmental Changes of Human Neural Progenitor Cells Grafted into the Ventricular System and Prefrontal Cortex of Mouse Brain in Utero. Cells. 31 mars 2023;12(7):1067. doi:10.3390/cells12071067 PubMed PMID: 37048140; PubMed Central PMCID: PMC10093207.
3. Thiberge C, Pou ML, Vitrac A, Maskos U, Cloëz-Tayarani I. Humanized Chimeric Mouse Models to Study Human Neural Development and Pathogenesis of Brain Diseases. In: Martin S, Laumonnier F, éditeurs. Translational Research Methods in Neurodevelopmental Disorders [Internet]. New York, NY: Springer US; 2022 [cité 29 janv 2026]. p. 135-58. Disponible sur: https://doi.org/10.1007/978-1-0716-2569-9_8 doi:10.1007/978-1-0716-2569-9_8

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Institut Pasteur, 2026-2027

Scientific or technical background required for work program

The project is primarily computational, in vitro and in vivo works (iPSC differentiation, BMI1 silencing, immunostaining, xenografting) has been carried out. The core project of this Erasmus work programme will focus on the design, validation, and application of the image analysis and statistical pipeline.

Essential skills :

- Python programming for scientific computing and image analysis
- Image processing and analysis: filtering, thresholding, morphological operations, skeletonization; handling of multi-dimensional microscopy formats (.czi) and z-stack data
- Image segmentation techniques, thresholding, connected component labeling
- Statistics related to quantification, data visualization
  Deep learning inference with pretrained models (PyTorch) and ability to adapt or fine-tune a pretrained model on new data

Additional skills :

- Biological understanding : general neuron morphology (axons, dendrites, cytoskeleton) and cell biology
- Familiarity with the biological concepts of amyloid-β pathology, neuronal differentiation, axonal integrity and neurodegeneration will facilitate interpretation of the imaging data
- Experience with confocal microscopy, immunofluorescence images and quantitative image analysis would be advantageous

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Institut Pasteur, 2026-2027

Title of the work program 27

Mosquito-microbiota dynamics: colonization niches, blood meal effects, and viability.

Description of the work program

Aedes mosquitoes are vectors for several **arthropod borne viruses** (arboviruses) which represent a significant global burden. As mosquito populations are expanding and acquiring resistance to insecticides, it is crucial to develop new vector control strategies.

Mosquitoes acquire arboviruses when **feeding on infected vertebrates**. After ingestion, blood is stored in the midgut and digested. This period is critical for mosquito infection by the virus: only the viruses that successfully infect **mosquito gut** cells will replicate, disseminate throughout the mosquito body, and infect multiple organs. Once viruses reach the salivary glands and infect the saliva, the mosquito can transmit the virus to naïve vertebrates during subsequent blood meals. Therefore, the mosquito gut represents the first barrier to infections. When viruses reach the mosquito gut, they encounter a microenvironment that can hinder their ability to infect mosquito cells. In particular, the gut hosts a diverse **microbiota**, which proliferates significantly during a blood meal and influences gut homeostasis impacting, in turn, pathogen infection.

The mosquito microbiota has gained interest as a tool to build vector-control measures. However, major gaps persist on our understanding of **mosquito–microbiota interactions**. We do not know whether the microbiota colonization stabilizes in discrete gut niches or reflects continuous acquisition–loss dynamics, and how blood meals remodel this landscape. We do not know whether ingested bacteria are alive in the mosquito gut and metabolically active. To address these questions, the student will work with bacterial strains isolated from field mosquitoes (namely, *Bacillus*, *Cedecea*, *Asaia* and *Pantoea*). The student will transform these strains with plasmid encoding antibiotic resistance and a fluorescent marker (mCherry, eGFP, CFP or YFP). Then, the student will be in charge of investigating the following aspects:

- Assessing bacterial clearance in the mosquito gut. We will re-colonize germ-free (GF) adult mosquitoes for three days with one or multiple bacterial strains by contaminating mosquito sugar with bacterial cultures. A group of mosquitoes will be kept continuously with bacteria (*colonized*), while another group will be transferred daily in new boxes with sterile sugar (*cleared*). In this way, *cleared* mosquitoes will be exposed to decreasing amounts of bacteria and the re-contamination from the food source will be reduced with time. Colony forming units (CFUs) will be assessed daily for five days to confirm the differences in microbiota loads between *colonized* and *cleared* mosquitoes.

- Identifying gut-specific bacterial colonization. *Colonized* and *cleared* mosquitoes will be dissected to isolate their digestive system. Guts will be observed via confocal microscopy, to identify the localization of fluorescent bacteria.

- Analyzing bacterial dynamics post-blood meal. Once the best conditions to obtain *colonized* and *cleared* mosquitoes will be assessed, bacterial counts and tissue localization via confocal microscopy will be assessed at multiple time-points post-blood feeding (6h, 24h, 48h). This will provide insights into how microbiota dynamics shift during blood digestion.

- Assessing bacterial viability in the gut. To confirm the presence of a living microbiota and determine whether some bacteria are lysed in specific gut regions, SYTOX dead cell stain or equivalent will be mixed in the sugar and fed to colonized and cleared mosquitoes exposed to unlabeled bacteria. Guts will be dissected, fixed and observed with a confocal microscope. Fluorescence will indicate bacteria with a damaged membrane (likely dead cells). If *in vivo* staining proves challenging, post-

fixation staining protocols will be implemented. Both sugar-fed and blood-fed mosquitoes will be analyzed at different time-points to compare bacterial viability across feeding conditions.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

Romoli O, Schönbeck JC, Hapfelmeier S, Gendrin M. Production of germ-free mosquitoes via transient colonisation allows stage-specific investigation of host-microbiota interactions. *Nat Commun*. 2021 Feb 11;12(1):942. doi: 10.1038/s41467-021-21195-3. PMID: 33574256; PMCID: PMC7878806.

Romoli O, Henrion-Lacritick A, Blanc H, Frangeul L, Saleh MC. Limitations in harnessing oral RNA interference as an antiviral strategy in *Aedes aegypti*. *iScience*. 2024 Feb 16;27(3):109261. doi: 10.1016/j.isci.2024.109261. PMID: 38433898; PMCID: PMC10907830.

Scientific or technical background required for work program

Ideally the student should have some microbiology background (bacterial culture, working under sterile conditions). Experience with confocal microscopy is appreciated.

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Institut Pasteur, 2026-2027

Title of the work program 28

Metabolism, Degradation, and Inflammation in a Synucleinopathic Neuroimmune Axis

Description of the work program

Parkinson's disease (PD) is a neurodegenerative disease that kills dopaminergic neurons, with α-synuclein (α-syn) aggregates perturbing neuronal degradative pathways and damaging mitochondrial functions, leading to neuroinflammation. Our lab has demonstrated that α-syn and mitochondria can be transferred between microglia and α-syn-burdened neurons via tunneling nanotubes (TNTs) to aid in clearance. CD4+ T cells also play a significant role in the initial inflammatory response to α-syn-laden neurons; however, their functional properties diminish over time in PD patients. Here, we seek to elucidate the effects of α-syn on the neuronal-microglia-CD4+ T cell network, specifically on mitochondrial metabolism, autophagic degradation, and inflammatory responses. We found that α-syn can be internalized in Jurkat (CD4+ T) cells and colocalize with lysosomes. Repeated treatments of α-syn on Jurkat cells drives the cells towards a Th1 and exhaustive phenotype, as has been shown in circulatory CD4+ T cells in PD patients. Repeated treatment also decreased oxygen consumption rate and increased glycolysis in a step-wise manner. When naïve Jurkat cells are tri-cultured with α-syn-treated SH-SY5Y and HMC cells, they preferentially form TNTs with SH-SY5Y cells with some Jurkat/SH-SY5Y connections containing mitochondria, which is lost when HMC3 are absent and suggests an instigating role by HMC3 cells on Jurkat/SH-SY5Y cells. This tri-culture results in a reduction of α-syn within SH-SY5Y cells although HMC and Jurkat mitochondrial membrane potential decrease. Moreover, there is augmented lysosomal activity in SH-SY5Y cells in a tri-culture compared to a bi-culture with HMC or Jurkat cells. These suggest that HMC and Jurkat cells cooperate to increase lysosomal degradation to clear α-syn but undergo negative impact towards mitochondrial health. Furthermore, FACS-sorted Jurkat cells from tri-cultures were cultured once more with new α-syn-treated SH-SY5Y and HMC3 cells, resulting in a more significant decrease in α-syn within SH-SY5Y cells. This indicates that Jurkat cells gain memory of α-syn and can assist neuronal cells in clearing it. Further work will examine how this affects metabolism and inflammation of the cells and continued re-culturing with primed cells to determine whether Jurkat cells each exhaustion in this paradigm. Altogether, we aim to understand how metabolic reprogramming, degradation, and inflammatory cascades are affected by a synucleinopathic environment between neuronal, microglial, and CD4+ T cells.

Tutor/supervisor

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Institut Pasteur, 2026-2027

Selected publications or patents of the Research Group offering the work program

Chakraborty, R., Maya, S., Testa, V. et al. α-Synuclein aggregates induce mitochondrial damage and trigger innate immunity to drive neuron–microglia communication. Nat Commun 17, 6462 (2026). https://doi.org/10.1038/s41467-026-73136-7

Chakraborty R, Nonaka, T, Hasegawa, M, and Zurzolo, C, *Tunnelling nanotubes between neuronal and microglial cells allow bi-directional transfer of alpha-Synuclein and mitochondria.* Cell Death Dis, 2023. **14**(5): p. 329. 10.1038/s41419-023-05835-8. https://www.ncbi.nlm.nih.gov/pubmed/37202391

Dilsizoglu Senol A, Samarani, M, Syan, S, Guardia, CM, Nonaka, T, Liv, N, Latour-Lambert, P, Hasegawa, M, Klumperman, J, Bonifacino, JS, and Zurzolo, C, *alpha-Synuclein fibrils subvert lysosome structure and function for the propagation of protein misfolding between cells through tunneling nanotubes.* PLoS Biol, 2021. **19**(7): p. e3001287. 10.1371/journal.pbio.3001287. https://www.ncbi.nlm.nih.gov/pubmed/34283825

Scientific or technical background required for work program

Proficiency in cell culture work, RNA extraction, RT-qPCR, or confocal imaging.

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Institut Pasteur, 2026-2027

Title of the work program 29

Understanding the mechanism of ATRX/SAD-6 recruitment to chromatin for the initiation of gene silencing

Description of the work program

This project finds itself at the intersection of three basic research questions. The first question concerns the initiation of epigenetic silencing (either transcriptional [heterochromatin-mediated] or post-transcriptional [RNAi-mediated]). The second question focuses on the mechanism of action of the conserved chromatin remodeler ATRX (alpha-thalassemia mental retardation X-linked), which has many functions in eukaryotes, including the de novo initiation of epigenetic silencing. The third question pertains to the nature of the primary signal that triggers silencing of repetitive DNA. Here, we are interested in testing the hypothesis that the signal is produced by homologous dsDNA–dsDNA pairing (of intact identical repeats). We have obtained experimental evidence that these three questions are indeed interconnected.

In the lab, we use the fungus Neurospora crassa as an exceptionally advantageous model organism, and all in vivo work in this project is expected to be done in N. crassa as well. The reasons why N. crassa is the ideal model organism to pursue the above questions are as follows. First, throughout evolution, N. crassa has retained all main epigenetic pathways, including fully functional RNAi, DNA methylation, constitutive (“H3K9me3”), and facultative ("H3K27me3") heterochromatin. Second, all these pathways can be inactivated, individually or altogether, without causing substantial fitness defects in N. crassa in the lab. Thus, we can dissect them without running into side effects that typically complicate their analysis in “higher” eukaryotes. Third, N. crassa has evolved several extremely efficient genome-defense processes that use these pathways to induce de novo silencing. This is a very important point: while key epigenetic effectors have been evolutionarily conserved in N. crassa, they are now being very efficiently used to combat incoming deleterious genetic elements. In other words, while N. crassa appears to share its basic epigenetic toolbox with plants and animals (including humans), it uses it much more efficiently than any other model organism, thus representing a true gift of Nature to Science (https://www.nobelprize.org/uploads/2018/06/brenner-lecture.pdf). Fourth, N. crassa is a haploid microbial eukaryote, with a relatively small genome that is free of naturally occurring repetitive DNA and gene paralogs, thus greatly simplifying its genetic analysis. Fifth, N. crassa represents an established model organism, which is very easy to grow, transform, and manipulate in the lab.

While the exact topic of this Erasmus project is subject to further discussion with a prospective candidate, possible research directions may include the following: (1) characterizing the chromatin state of a model locus undergoing SAD-6-dependent silencing, (2) characterizing additional factors required for SAD-6-dependent silencing, and/or (3) reconstituting the remodeling/silencing cycle in vitro. The project is based on our earlier studies (refs. 1-4), where we showed that the ATRX ortholog SAD-6 can mediate both de novo heterochromatin formation and RNAi initiation at sites of perturbed or otherwise dynamic chromatin in N. crassa. As a result, we proposed a general model in which silencing is induced by the act of remodeling per se (rather than the mere existence of an aberrant chromatin state). Intriguingly, we have now discovered that SAD-6 is also required for a pathway that connects homologous dsDNA–dsDNA pairing to the initiation of constitutive heterochromatin (ref. 1). We have also established a screen to identify additional factors in SAD-6-dependent silencing and found many of them to have direct orthologs in humans. These results place our lab at the leading edge of the field to elucidate the molecular logic of ATRX-family remodelers.

Tutor/supervisor

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Erasmus+

Institut Pasteur, 2026-2027

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Selected publications or patents of the Research Group offering the work program

[Preprints]

[1] Carlier F. et al. 2026. SAD-6/ATRX enables broad genome surveillance and defense in fungi. biorxiv, https://www.biorxiv.org/content/10.64898/2026.08.11.744009v1.

[Research papers]

[2] Carlier F. et al. 2024. Remodeling of perturbed chromatin can initiate de novo transcriptional and post-transcriptional silencing. PNAS 121: e2402944121. doi: 10.1073/pnas.2402944121.
[3] Rhoades N, Nguyen TS, Witz G, Cecere G, Hammond T, Mazur AK, Gladyshev E. 2021. Recombination-independent recognition of DNA homology for meiotic silencing in Neurospora crassa. PNAS 118: e2108664118. doi: 10.1073/pnas.2108664118.
[4] Carlier F, Nguyen TS, Mazur AK, Gladyshev E. 2021. Modulation of C-to-T mutation by recombination-independent pairing of closely positioned DNA repeats. Biophys J. 120: 4325-4336. doi: 10.1016/j.bpj.2021.09.014.

[Reviews]

[5] Mazur AK, Gladyshev E. 2023. C-DNA may facilitate homologous DNA pairing. Trends Genet. 39: 575-585. doi: 10.1016/j.tig.2023.01.008.

Scientific or technical background required for work program

The candidate is expected to have a basic understanding of eukaryotic molecular genetics. Prior experience in fungal genetics is a plus, but is not required.

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Institut Pasteur, 2026-2027

Title of the work program 30

A bacterial genetics approach to study interactions between virulence factors in *Pseudomonas aeruginosa*

Description of the work program

Bacterial pathogens employ various mechanisms to deliver virulence factors to the eukaryotic host cells they are infecting. The type III secretion system (T3SS) is a needle-like apparatus produced by certain bacteria, which allows the injection of effectors/virulence factors into the host cell. We are interested in the role of T3SS injected effectors/virulence factors in the pathogenesis of *Pseudomonas aeruginosa*, a pathogen that plays a major role in infections of patients suffering from cystic fibrosis.

One of these effectors, ExoY has the ability to generate different cNMPs (cGMP, cAMP, cUMP and cCMP in this order of preference *in vitro*). The nucleotidyl cyclase activity (NC) of ExoY is activated only inside host cells, but not inside bacteria, a mechanism necessary to protect bacteria from unphysiological levels of cNMPs. We identified several proteins interacting with ExoY. We would now like to understand the role of the interaction between ExoY and these proteins. For this purpose, precise mutants need to be created on the bacterial chromosome using a two-step allelic exchange method. The mutant phenotype of validated mutants will be studied by evaluating the effects on secretion of ExoY and/or other T3SS injected effectors.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

1. Deruelle V, Dupuis G, Raoux-Barbot D, Lim E, Ponce-Lopez R, Teixeira Nunes M, Ladant D, Renault L, **Mechold U.** (2025) Interplay between T3SS effectors, ExoY activation, and cGMP signaling in Pseudomonas aeruginosa infection. *Nat Commun* 2025;**17**(1):69.

2. Belyy, A., Raoux-Barbot, D., Saveanu, C., Namane, A., Ogryzko, V., Worpenberg, L., David, V., Henriot, V., Fellous, S., Merrifield, C., Assayag, E., Ladant, D., Renault, L., and **Mechold, U.** (2016) Actin activates Pseudomonas aeruginosa ExoY nucleotidyl cyclase toxin and ExoY-like effector domains from MARTX toxins. *Nat Commun* **7**, 13582

3. Belyy, A., Mechold, U., Renault, L., and Ladant, D. (2018) ExoY, an actin-activated nucleotidyl cyclase toxin from P. aeruginosa: A minireview. *Toxicon* **149**, 65-71

4. Belyy, A., Santecchia, I., Renault, L., Bourigault, B., Ladant, D., and **Mechold, U.** (2018) The extreme C terminus of the Pseudomonas aeruginosa effector ExoY is crucial for binding to its eukaryotic activator, F-actin. *J. Biol. Chem.* **293**, 19785-19796

5. Raoux-Barbot, D., Belyy, A., Worpenberg, L., Montluc, S., Deville, C., Henriot, V., Velours, C., Ladant, D., Renault, L., and **Mechold, U.** (2018) Differential regulation of actin-activated nucleotidyl cyclase virulence factors by filamentous and globular actin. *PLoS One* **13**, e0206133

6. Silistre, H., Raoux-Barbot, D., Mancinelli, F., Sangouard, F., Dupin, A., Belyy, A., Deruelle, V., Renault, L., Ladant, D., Touqui, L., and **Mechold, U.** (2021) Prevalence of ExoY Activity in Pseudomonas aeruginosa Reference Panel Strains and Impact on Cytotoxicity in Epithelial Cells. *Front Microbiol* **12**, 666097

Scientific or technical background required for work program

The successful candidate should have good English language skills, a solid knowledge in molecular biology, or biochemistry or genetics, should be rigorous and organized and eager to learn new methods.

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Institut Pasteur, 2026-2027

Title of the work program 31

Predicting Optimal Protein Solubility Conditions via Artificial Intelligence

Description of the work program

Protein solubility is a critical bottleneck in academic research and in the development of biologics. It depends on the delicate balance between protein-protein interactions (driving precipitation) and protein-solvent interactions (driving dissolution). Several physicochemical parameters stringly influence this behavior:

- **Folding State:** Native proteins usually bury their hydrophobic core. Denaturation or unfolding exposes these regions, triggering a sharp drop in solubility and rapid aggregation.
- **pH & Charge:** Away from their isoelectric point (pI), proteins carry a net positive or negative charge, causing mutual repulsion and increasing solubility.
- **Ionic Strength:** Buffer conditions play a dual role: at low salt concentrations, ions stabilize the protein in water (**salting-in**), whereas at higher concentrations, ions sequester water molecules, forcing proteins to precipitate (**salting-out**).
- **Other experimental parameters**, such as protein concentration, viscosity and temperature, also significantly affect protein behavior.

Since 2014, the quality control service of the molecular biophysics facility at Institut Pasteur has analyzed over **3,000 recombinant protein samples** using biophysical techniques like Dynamic Light Scattering (**DLS**) and Differential Scanning Fluorimetry (**DSF**). While nearly 1,000 samples were initially insoluble, we successfully optimized solubilization conditions for the vast majority of them (95%, see Berrow et al). This long-term activity has generated a **unique dataset** containing not only protein quality measurements, but also a historical record of **successful and unsuccessful conditions to improve protein solubility and stability**. This large dataset offers a unique opportunity to launch a machine learning process.

We are seeking a motivated student to exploit this database for the development of an ambitious AI-driven study to predict optimal solubility conditions for unknown proteins. Rather than simply predicting whether a protein is likely to be soluble, the project will investigate whether information derived from its primary amino-acid sequence and its AlphaFold model, combined with previous optimization experiments, can be used to **select the best conditions that will improve its solubility and stability**.

The internship will be structured into three main phases:

1. **Database Architecture:** centralize, structure, and clean our 10-year historical dataset by linking each protein to its primary sequence, physicochemical info, formulation conditions and downstream applications.
2. **Predictive modelling:** lay the groundwork for a predictive pipeline capable of forecasting the best solubilization strategies for any new, unknown target protein. The model could therefore address a practical question frequently encountered in biochemistry:
   "Which buffer conditions should we test first to maximize chances for my protein of interest to be well soluble and stable?"
3. **Validation.** New *in vitro* results could then be integrated into the model to iteratively improve its recommendations.

Finally, the student will benefit from the multidisciplinary environment of the Institut Pasteur, and will collaborate with **Dr. Olivier Sperandio, expert in data science and machine learning.**

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

Raynal Bertrand; Lenormand Pascal; Baron Bruno; Hoos Sylviane; England Patrick; Quality assessment and optimization of purified protein samples: why and how? Microbial cell factories 13 1 180 2014

Raynal Bertrand; Brûlé Sébastien; Uebel Stephan; Knauer Stefan H; Assessing and improving protein sample quality Protein-ligand interactions: methods and applications 3-46 2021

Caillet-Saguy Célia; **Brûlé Sébastien**; Wolff Nicolas; **Raynal Bertrand**; PDZ Sample Quality Assessment by Biochemical and Biophysical Characterizations PDZ Mediated Interactions: methods and protocols 89-124 2021

Madru Clément; Dizkirici Tekpinar Ayten; Rosario Sandrine; Czernecki Dariusz; **Brûlé Sébastien**; Sauguet Ludovic; Delarue Marc; Fast and efficient purification of SARS-CoV-2 RNA dependent RNA polymerase complex expressed in Escherichia coli PLOS ONE 16 4 e0250610 2021

Berrow Nick; De Marco Ario; Lebendiker Mario; Garcia-Alai Maria; Knauer Stefan H; Lopez-Mendez Blanca; Matagne André; Parret Annabel; Remans Kim; Uebel Stephan; **Bertrand Raynal**; Quality control of purified proteins to improve data quality and reproducibility: results from a large-scale survey European Biophysics Journal50 3 453-460 2021

De Marco Ario; Berrow Nick; Lebendiker Mario; Garcia-Alai Maria; Knauer Stefan H; Lopez-Mendez Blanca; Matagne André; Parret Annabel; Remans Kim; Uebel Stephan; **Bertrand Raynal**; Quality control of protein reagents for the improvement of research data reproducibility Nature communications 12 1 2795 2021

Burastero Osvaldo; Draper-Barr George; **Raynal Bertrand; Chevreuil Maelenn; England Patrick;** Garcia Alai Maria; Raynals an online tool for the analysis of dynamic light scattering Biological Crystallography79 8 673-683 2023

Bourmancé Lucas; Marie Arul; Puppo Rémy; **Brûlé Sébastien**; Schaeffer Philippe; Toupet Maud; Nitsche Ruben; Elsaesser Andreas; Kish Adrienne; The salty tango of brine composition and UV photochemistry effects on Halobacterium salinarum cell envelope biosignature preservation Communications Biology 8 1 602 2025

Scientific or technical background required for work program

Protein Biochemistry, Protein structure, Bioinformatic tools for visualization and analysis, AI tools such as AlphaFold.

Erasmus+

Institut Pasteur, 2026-2027

Title of the work program 32

CyberStable: Cybergenetic solutions to enforce genetic stability in synthetic biology applications

Description of the work program

Keywords: Synthetic biology, molecular biology, bioengineering, lab automation, protein secretion, yeast

Context

Synthetic biology enables the reprogramming of living systems to perform novel functions. However, this reprogramming imposes a burden on host cells, which must divert finite resources toward executing synthetic tasks. This burden creates selective pressure favouring loss-of-function variants that escape synthetic demands, ultimately leading to population takeover by non-producing cells and bioprocess failure. Despite its critical importance, the relationship between bioproduction burden, cellular stress, and long-term genetic stability of engineered circuits remains poorly characterized.

The CyberStable project addresses this gap through two complementary aims. First, it seeks to quantitatively understand the relationship between transcriptional demand (i.e., induction level), protein production burden, cellular stress responses, and the long-term genetic stability of synthetic circuits. Second, leveraging these insights, it aims to engineer an optogenetic differentiation system comprising a two-population consortium: non-differentiated cells maintain normal growth without expressing the bioproduction machinery and can "differentiate" upon light stimulation into cells that express the bioproduction system while ceasing proliferation.

By decoupling the evolutionarily stable maintenance function (non-differentiated cells) from the burdensome bioproduction task (differentiated cells), this strategy is hypothesized to achieve superior genetic stability compared to conventional single-population approaches.

Internship description

Cecilia Capela, the PhD student leading the CyberStable project, has made significant progress on both aims.

The intern will join her efforts to accelerate and extend this work across the following tasks:

1. **Expanding genetic instability drivers**: the intern will help to identify new candidate proteins that challenge circuit stability; build light-inducible yeast strains expressing those candidates; characterize protein production in batch cultures and continuous bioreactor cultivation.
2. **Building the differentiation system**: the intern will help to develop a growth-arrest module for differentiated cells; integrate it with the protein-production system; characterize the performance and long-term stability of the complete optogenetic differentiation system.

Supervision, location and contact details

The work will be done in the InBio research group. InBio is an interdisciplinary research group, combining wet and dry biology in the same lab. InBio is an Inria – Institut Pasteur joint research group. It is hosted at Institut Pasteur and affiliated to Inria Paris.

The internship will be jointly supervised by Cecilia Capela, Sara Napolitano and Gregory Batt.

Contact: cecilia.capela@pasteur.fr, sara.napolitano@pasteur.fr and gregory.batt@inria.fr

Erasmus+

Institut Pasteur, 2026-2027

Tutor/supervisor

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

[1] Aditya, C., Bertaux, F., Batt, G. *et al.* A light tunable differentiation system for the creation and control of consortia in yeast. *Nat Commun* **12**, 5829 (2021). https://doi.org/10.1038/s41467-021-26129-7

[2] Sosa-Carrillo, S., Galez, H., Napolitano, S. *et al.* Maximizing protein production by keeping cells at optimal secretory stress levels using real-time control approaches. *Nat Commun* **14**, 3028 (2023). https://doi.org/10.1038/s41467-023-38807-9

[3] Bertaux, F., Sosa-Carrillo, S., Gross, V. *et al.* Enhancing bioreactor arrays for automated measurements and reactive control with ReacSight. *Nat Commun* **13**, 3363 (2022). https://doi.org/10.1038/s41467-022-31033-9

[4] Biosensors for optimization of recombinant protein secretion through pooled library screening in bioreactors. Patent Application.

Scientific or technical background required for work program

The candidate should have a strong background in **molecular biology** and **quantitative biology**, or related fields, with a strong interest in quantitative and interdisciplinary approaches to understand biological and cellular processes. We particularly value:

- Solid knowledge of **molecular biology** and experience with standard molecular biology techniques (e.g., Golden Gate Assembly, bacteria transformation, PCR, yeast transformation).
- An interest in **quantitative biology**, including the analysis and interpretation of experimental data.
- Basic knowledge of calculus and differential equations (engineering background is a strong plus).
- Basic Python programming skills, particularly for data analysis and modelling.
- A good level of English, both written and spoken, as the team is highly international.
- A willingness to work in an interdisciplinary and collaborative team, bringing together experimental biology, quantitative biology, and computational approaches.
- Curiosity, autonomy, and enthusiasm for learning and working across different disciplines.

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Institut Pasteur, 2026-2027

Title of the work program 33

Functional study of cellular factors and organelles rewired by hepaciviruses upon hepatocyte infection

Description of the work program

Chronic hepatitis C is a human liver disease resulting in metabolic disorders, such as steatosis, an abnormal lipid accumulation in hepatocytes. Lipid droplets, which are key subcellular organelles involved in the storage of neutral lipids, as well as cellular lipoproteins are essential for hepatitis C virus (HCV) morphogenesis. Mechanistic aspects of the rewiring of host hepatocyte organelles, factors and pathways by HCV, as well as their pathological consequences are not fully understood. Based on affinity purification and mass spectrometry identification of the interactomic network of a key HCV nonstructural protein, we now focus on selected hepatic factors linked to the biogenesis or function of lipid droplets and peroxisomes. The Erasmus+ intern will contribute to functional studies of the role of these factors in the hepacivirus life cycle and the impact of such protein/protein interactions on hepatocyte pathway deregulations. This project relies on the use of infection cell culture systems for both HCV and a rat hepacivirus (RHV) surrogate model; it involves molecular biology techniques and advanced imaging approaches.

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

- Paul *et al.* Unscrambling HCV-induced rewiring of host cell factors and organelles involved in lipid metabolism. Presented at the HCV-Flavi 2026 International Symposium, Copenhagen, Sept. 2026
- Yoo *et al.* Characterization of liver metabolism dysregulation in Sprague Dawley rats chronically infected with Norway rat hepacivirus RHV-rn1. Presented at the HCV-Flavi 2026 International Symposium, Copenhagen, Sept. 2026
- Brunet, Choucha, Gransagne *et al.* A measles-vectored vaccine candidate expressing prefusion-stabilized SARS-CoV-2 spike protein brought to phase I/II clinical trials: candidate selection in a preclinical murine model. *J. Virol.*, 2024, May 14;98(5):e0169323. PMID: 38563763
- Launay *et al.* Safety and immunogenicity of a measles-vectored SARS-CoV-2 vaccine candidate, V591/Tmv-083, in healthy adults: Results of a randomized, placebo-controlled Phase I study. *Ebiomedicine*, 2022, Jan 75:103810. PMID: 35045362
- Escriou *et al.*, Patent: Measles-vectored COVID-19 immunogenic compositions and vaccines. PCT/EP2021/053540 filed on February 12, 2021.
- Boukadida *et al.* NS2 proteases from hepatitis C virus and related hepaciviruses share composite active sites and previously unrecognized intrinsic proteolytic activities. *PloS Pathog., 2018,* 14(2):E1006863. PMID: 29415072
- Aicher *et al.* Differential regulation of the Wnt/ß-catenin pathway by hepatitis C virus recombinants expressing core from various genotypes. *Sci. Rep., 2018,* Jul 25;8(1):11185. PMID: 30046100

Scientific or technical background required for work program

Hands-on experience with molecular biology techniques, cell culture and/or fluorescent microscopy would be an asset.

Erasmus+

Institut Pasteur, 2026-2027

Title of the work program 34

Developing a novel measles-based vaccine platform, resistant to measles preimmunity and amenable to intranasal delivery.

Description of the work program

The large global burden of viral infections and especially the COVID-19 pandemic shows the need for new approaches in vaccine development. Plug-and-play vaccine platform technology that would enable fast development of a vaccine candidate against an emerging pathogen, large-scale immunization of pediatric and adult populations and induction of mucosal responses in the respiratory tract, is a grail.

The measles vector (MV) platform technology derived from the safe and highly efficacious live-attenuated measles virus vaccine has long held promise as a universal vaccine platform. However, our phase I clinical study of the V591 measles-vectored COVID-19 vaccine candidate expressing a prefusion stabilized full-length spike protein, revealed a significant impact of pre-existing anti-measles immunity* on the response to V591, leading to discontinuation of further development (Launay, 2022) and highlighting the caveat of the original MV platform.

The Erasmus+ student will contribute to explore some of the possible modifications to the measles vector to enable it to escape pre-existing immunity and be delivered by the respiratory route.

This work will involve engineering and characterization of new vectors, both *in vitro* and in animal models. It will rely on a diversity of techniques, from molecular and cellular virology to immunology.

* (induced by previous exposure to the pediatric measles vaccine)

Tutor/supervisor

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Selected publications or patents of the Research Group offering the work program

- Ku et al. intranasal vaccination with a lentiviral vector protects against sars-cov-2 in preclinical animal models. *Cell Host & Microbe*, 2021, Feb 10;29(2):236-249.E6.
- Gransagne et al. Development of a highly specific and sensitive VHH-based sandwich immunoassay for the detection of the SARS-CoV-2 nucleoprotein. *Journal of Biological Chemistry*, 2022, 298 (1), pp.101290.
- Escriou et al., Patent: Measles-vectored COVID-19 immunogenic compositions and vaccines. PCT/EP2021/053540 filed on February 12, 2021.
- Launay et al. Safety and Immunogenicity of a measles-vectored Sars-Cov-2 vaccine candidate, V591 / TMV-083, in healthy adults: results of a randomized, placebo-controlled Phase I study. *Ebiomedicine*, 2022, Jan;75:103810.
- Brunet et al. A measles vectored vaccine candidate expressing prefusion stabilized SARS-CoV-2 spike protein brought to Phase I/II clinical trials: Candidate selection in a preclinical murine model. *J Virol, 2024,* 14;98(5):e0169323.
- Nambulli et al. A measles vectored vaccine candidate expressing prefusion stabilized SARS-CoV-2 spike protein brought to Phase I/II clinical trials: Protection of African green monkeys from COVID-19 disease. J. Virol, 2024, 14;98(5):e0176223.

Scientific or technical background required for work program

Hands-on experience with virology techniques, protein western blotting, immunofluorescence would be an asset. Training to work in BSL3 will be provided for students able to stay more than 6 months.