Erasmus+

INSTITUT Pasteur

Education
DEPARTMENT

EUGLOH

Projects 2025-2026
MD-PhD program

RESEARCH CENTRE

Legal name: **Institut Pasteur**

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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, 146 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 8 projects for Erasmus internships for medical students as a part of the MD-PhD program, reflecting the Institut Pasteur's engagement in the European University Alliance for Global Health (EUGLOH).
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
- **Additional salary:** additional salary of approximately 600 euros/month (for internships longer than 60 days) is paid by the host lab (4.35 euros/hour, 7 hours/day)

Institut Pasteur, 2025-2026

Title of the work program 1

Lipid Regulation of Lysosomes and Amyloid Beta

Description of the work program

Alzheimer's disease (AD) is a devastating brain disorder that causes memory loss and cognitive decline. Current treatments can only relieve symptoms – they do not stop or slow the disease itself. A key feature of AD is the buildup of harmful protein clumps in the brain, known as amyloid plaques and neurofibrillary tangles. These plaques form when a normal protein, called APP, is broken down in a way that produces toxic fragments known as amyloid beta (AB). These fragments tend to stick together and accumulate between brain cells, damaging them over time.
We still don't fully understand what triggers this toxic process. However, because these events happen in the membrane surrounding brain cells, we believe that changes in the composition of these membranes – especially their fat (lipid) content – may play a key role in either the production of these toxic aggregates, or their internalization and processing by neighboring cells. In this project, we will study how changes in brain cell membranes affect the production of AB. We will also explore whether these changes interfere with the cells' ability to clear toxic proteins, and whether correcting them can help prevent or slow the disease.
By uncovering how brain cell membrane influence AD progression, our work could open the door to new treatments that target the disease at its roots – not just its symptoms.

Tutor/supervisor

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X☐ 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

- Palese F., Rokotobe M., Zurzolo C. Transforming the concept of connectivity: unveiling tunneling nanotube biology and their roles in brain development and neurodegeneration. Physiol Rev, 2025 DOI: 10.1152/physrev.00023.2024
- Palese F., et al. A protective role for N-acylphosphatidylethanolamine phospholipase D in 6-OHDA-induced neurodegeneration. Sci Rep, 2019 DOI: 10.1038/s41598-019-51799-1
- Palese F., et al. NAPE-specific phospholipase D regulates LRRK2 association with neuronal membranes. Adv Pharmacol, 2021 DOI: 10.1016/bs.apha.2020.09.003

Scientific or technical background required for work program

Students are expected to be familiar with cell culture techniques and working under sterile conditions. A solid understanding of wet lab methods such as Western blotting and RT-PCR is highly valued. Experience with immunofluorescence and confocal microscopy is also appreciated.

Institut Pasteur, 2025-2026

Title of the work program 2

Molecular mechanisms underlying craniofacial muscle physiolopathology

Description of the work program

This research project investigates the cellular and genetic mechanisms that endow craniofacial muscles with specialized properties and resilience, particularly in the context of dystrophic and neurodegenerative diseases. Unlike trunk muscles, which primarily specialize in either force generation or endurance, craniofacial muscles perform highly intricate tasks essential for eye movements, feeding, and speech.

In this project, we will employ an integrative approach that combines advanced multiomics, histological and structural analysis of eye muscle resection material from patients, together with the characterisation of new mouse models developed in the lab. By selectively perturbing key gene expression programs during homeostasis and in pathological models, we aim to establish direct links between molecular determinants and muscle physiopathology. Physiological assessments will be done in collaboration with neuroscience and muscle physiology labs in the Parisian region.

Expected Impact: this project has to potential to achieve several conceptual breakthroughs: 1) uncover the molecular and structural features that confer EOMs with exquisite sensory-motor specialisation. These findings will be relevant to the medical fields of ophthalmology and strabismus surgery; 2) link craniofacial muscle contractile properties to physiology and sparing in neuromuscular disease ; 3) provide a framework for developing refined strategies to confer other body muscles with protective mechanisms in disease. Altogether, this project promises to illuminate universal principles of musculoskeletal specialisation, with far reaching implications for regenerative medicine, disease modeling, and yield valuable knowledge on a variety of congenital craniofacial disorders and evolutionary processes.

Tutor/supervisor

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

- Comai, G. E., 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, N. B., Schweitzer, R., & Tajbakhsh, S. (2020). **Local**

retinoic acid signaling directs emergence of the extraocular muscle functional unit. *PLoS biology*, *18*(11), e3000902. https://doi.org/10.1371/journal.pbio.3000902

- Grimaldi, A., & Tajbakhsh, S. (2021). **Diversity in cranial muscles: Origins and developmental programs.** *Current opinion in cell biology*, *73*, 110–116. https://doi.org/10.1016/j.ceb.2021.06.005
- Girolamo, D. D., Benavente-Diaz, M., Murolo, M., Grimaldi, A., Lopes, P. T., Evano, B., Kuriki, M., Gioftsidi, S., Laville, V., Tinevez, J. Y., Letort, G., Mella, S., Tajbakhsh, S., & Comai, G. (2024). **Extraocular muscle stem cells exhibit distinct cellular properties associated with non-muscle molecular signatures.** *Development (Cambridge, England)*, *151*(4), dev202144. https://doi.org/10.1242/dev.202144
- Korb, A., Tajbakhsh, S., & Comai, G. E. (2024). **Functional specialisation and coordination of myonuclei.** *Biological reviews of the Cambridge Philosophical Society*, 10.1111/brv.13063. Advance online publication. https://doi.org/10.1111/brv.13063

We are collaborating with V. Taglietti and E. Malfatti (Inst de recherche biomedicale Mondor, Créteil), Dr. M. Robert (Hopital Necker, strabismus surgery surgeon) and G. Bouvier (Sensomotion Lab, NeuroPsi, Paris-Saclay, France).

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 project will involve experimental and computational work. The student will become familiar with a number of techniques routinely used in the lab including histology, confocal microscopy and image processing. Prior expertise in cell culture, image analysis and coding would be highly appreciated. Part of the work (Electron microscopy, eye movement testing, contractility) tests will be done in collaboration with specific platforms/partners. The candidate should feel comfortable working in English and be able to critically discuss experimental results and the literature. Students will be fully integrated in the scientific life of the lab and department (seminars, lab retreat, training).

Institut Pasteur, 2025-2026

Title of the work program 3

Manipulation of host lipid metabolism by an intracellular bacterium

Description of the work program

Chlamydia trachomatis causes the most common bacterial sexually transmitted infection worldwide. The bacteria undergo an obligate intracellular developmental cycle in epithelial cells of the genital tract (1). They develop inside a vacuolar compartment and use a virulence associated non-flagellar type 3 secretion system (T3SS) to translocate proteins into the cytoplasm of their host cell. These so-called "effector" proteins manipulate host pathways to the benefit of the bacteria and are often made of several domains, each engaged in a specific function. TaiP is a 68 kDa protein made of two domains of about equal size and we showed this protein was an effector associated to *C. trachomatis* virulence (2). We discovered that its carboxy-terminal domain targeted one host protein called ATG16L1. By binding ATG16L1 we showed that TaiP allowed some vesicular traffic to be re-routed towards the vacuole in which the bacteria develop (3).
The internship will focus on the second domain of TaiP, whose function has not yet been characterized. We recently discovered that it bound a host lipid metabolism enzyme. The intern will use molecular biology and biochemistry tools to delineate the interacting domains within the two proteins. In parallel, the intern will investigate the consequences of this interaction on lipid metabolism in the host and whether it contributes to lipid acquisition by the bacteria.

Tutor/supervisor

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

Publications related to the project:

1. Triboulet, S., and Subtil, A. (2019) Make It a Sweet Home: Responses of Chlamydia trachomatis to the Challenges of an Intravacuolar Lifestyle. *Microbiol Spectr* **7**
2. Cossé, M. M., Barta, M. L., Fisher, D. J., Oesterlin, L. K., Niragire, B., Perrinet, S., Millot, G. A., Hefty, P. S., and Subtil, A. (2018) The Loss of expression of a single type 3 effector (CT622) strongly reduces *Chlamydia trachomatis* infectivity and growth. *Front Cell Inf Microbiol* **8**, 145
3. Hamaoui, D., Cossé, M. M., Mohan, J., Lystad, A. H., Wollert, T., and Subtil, A. (2020) The *Chlamydia* effector CT622/TaiP targets a nonautophagy related function of ATG16L1. *Proc. Natl. Acad. Sci. U. S. A.* **117**, 26784-26794

Scientific or technical background required for work program

Past experience in tissue culture, and in cell biology technics, is recommended.

Institut Pasteur, 2025-2026

Title of the work program 4

Emotional processing in mood disorders

Description of the work program

Understanding the neural circuits that link internal and external stimuli with positive or negative emotional value to guide behavior is one of the central questions in contemporary neuroscience. Emotional expressions are considered windows into the affective state of an individual across species—from insects to humans. Notably, emotional processing is a core domain disrupted in mood disorders.

Human and animal studies have shown that the olfactory and emotional systems are closely interconnected, sharing common neural substrates. Disruption of the olfactory system can lead to significant behavioral changes in animals, and in humans, there is a strong, reciprocal link between impaired olfaction and various psychiatric disorders.

This project aims to uncover how the mammalian brain assigns emotional value to stimuli under both normal and pathological conditions. We are particularly interested in olfactory perception and its connection to emotional states. By combining behavioral analyses in mice, animal models of mood disorders, intersectional viral vector strategies, neuroanatomy, in vivo imaging, and optogenetic/chemogenetic tools, our research seeks to establish causal links between the activity of defined neural circuits, full-body physiological responses, and behavior.

Tutor/supervisor

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Institut Pasteur, 2025-2026

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

Bigot M, Vicq E, Lledo PM, **Alonso M*,** Henry C*. Assessing positive and negative valence systems to refine animal models of bipolar disorders: the example of GBR 12909-induced manic phenotype. Sci Rep 2022, 12: 7364. *Last coauthors

Grelat A, Benoit L, Wagner S, Moigneu C, Lledo P-M*, **Alonso M*.** Adult-born neurons boost odor-reward association. PNAS 2018 115, 2514-2519. *Last coauthors

Alonso M, Lepousez G, Wagner S, Bardy C, Gabellec M-M, Torquet N, Lledo P-M. Activation of adult-born neurons facilitates learning and memory. Nat. Neurosci. 2012 15, 897–904.

Alonso M, Ortega I, Grubb M, Bourgeois JP, Chaneau P, Lledo PM. Turning astrocytes from the rostral migratory stream into neurons: a role for the olfactory sensory organ. J Neurosci 2008 28:11089-102.

Scientific or technical background required for work program

We are seeking a motivated MD student to join our research project focused on deciphering emotional circuits in the rodent brain. Candidates should have a solid background in neuroscience, including knowledge of neuroanatomy, behavioral neuroscience, and neurophysiology. Prior experience with rodent handling and behavioral assays is highly desirable. Familiarity with experimental techniques such as immunohistochemistry, viral tracing, or in vivo imaging is a strong plus. Basic data analysis skills (e.g., Python, MATLAB, or R) and understanding of statistical methods are required. For MD candidates, prior knowledge of psychiatric disorders (e.g., depression, bipolar disorder, anxiety disorders) is particularly valuable and will be considered an asset.

Institut Pasteur, 2025-2026

Title of the work program 5

Identification and characterisation of *Leishmania infantum* "persisters" causing amphotericin B-unresponsive relapses of visceral leishmaniasis in immunocompromised patients using hybridization ('selfing') as a tool to identify the resistance gene by investigating the phenotype and genetic composition of the F1 hybrids

Description of the work program

Step 1. Identification and characterization of *L. infantum* « persisters ».
Identification and amplification *in vitro* of the subpopulation of *L. infantum* "persisters" after repeated exposure to amphotericin B (AmB), mimicking the drug pressure applied in immunocompromised patients (ongoing)

Step 2. Proteomic and genotypic characterization of the « persister strains » will be performed.
We will perform proteomic and RNA-seq analysis of "persisters" and control parasite subpopulations to identify a specific molecular signature of these parasites able to persist. Depending on the efficacy of our ongoing enrichment process we will apply conventional or single-cell methods.

Step 3. Identification of the resistance gene by in vitro generation of genetic hybrids ('selfing') between AmB "persisters" and "non-peristers" and investigation of phenotype and genetic composition of the F1 hybrids.

Step 4. Comparative phenotypic and genomic analyses of the F1 hybrids to identify the genes underlying the "persister" phenotype.

Tutor/supervisor

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

Antimony Used as Rescue Therapy in a Kidney Transplant Recipient Unresponsive to Liposomal Amphotericin B for Chronic Visceral Leishmaniasis ; Mrozek, Natacha; Philipponnet, Carole; Zaghdoudi, Aida; Ravel, Christophe; Moniot, Maxime; Garrouste, Cyril; Rouges, Celia; Buffet, Pierre; MELENOTTE, Cléa ; Accepted, Journal Antimicrobial Chemotherapy, 2025 ; DOI: 10.1093/jac/dkaf158

Morizot G, Jouffroy R, Faye A, Chabert P, Belhouari K, Calin R, et al. Antimony to Cure Visceral Leishmaniasis Unresponsive to Liposomal Amphotericin B. PLoS Negl Trop Dis. 2016 Jan;10(1):e0004304.

Cojean S, Houzé S, Haouchine D, Huteau F, Lariven S, Hubert V, et al. Leishmania resistance to miltefosine associated with genetic marker. Emerg Infect Dis. 2012 Apr;18(4):704–6.

Morizot G, Jouffroy R, Faye A, Chabert P, Belhouari K, Calin R, et al. Antimony to Cure Visceral Leishmaniasis Unresponsive to Liposomal Amphotericin B. PLoS Negl Trop Dis. 2016 Jan;10(1):e0004304.

Späth GF, Piel L, Pescher P. Leishmania genomic adaptation: more than just a 36-body problem. Trends Parasitol. 2025 May 1;S1471-4922(25)00096-0.

Bussotti G, Benkahla A, Jeddi F, Souiaï O, Aoun K, Späth GF, et al. Nuclear and mitochondrial genome sequencing of North-African Leishmania infantum isolates from cured and relapsed visceral leishmaniasis patients reveals variations correlating with geography and phenotype. Microbial Genomics [Internet]. 2020 Oct 1 [cited 2023 Jun 20];6(10). Available from:
https://www.microbiologyresearch.org/content/journal/mgen/10.1099/mgen.0.000444

Prieto Barja P, Pescher P, Bussotti G, Dumetz F, Imamura H, Kedra D, et al. Haplotype selection as an adaptive mechanism in the protozoan pathogen Leishmania donovani. Nat Ecol Evol. 2017 Dec;1(12):1961–9.

Yau WL, Lambertz U, Colineau L, Pescher P, MacDonald A, Zander D, et al. Phenotypic Characterization of a Leishmania donovani Cyclophilin 40 Null Mutant. J Eukaryot Microbiol. 2016 Nov;63(6):823–33.

Cross-subgenus hybridization between Leishmania and Sauroleishmania informs on parasite genomic compatibility and transcriptomic adaptation Viviane Noll Louzada-Flores1, Pascale Pescher2, Thomas Cokelaer2, Tiago Rodrigues Ferreira3, Maria Stefania Latrofa1, Jairo Alfonso Mendoza-Roldan1, Domenico Otranto1,4, Gerald F Späth2, and Isabelle Louradour

Genomic and epidemiological evidence for the emergence of a L. infantum/L. donovani hybrid with unusual epidemiology in northern Italy. F Bruno # 1, G Castelli # 1, B Li 2, S Reale 1, E Carra 3, F Vitale 1, S Scibetta 1, M Calzolari 3, S Varani 4, M Ortalli 4 5, E Franceschini 6, W Gennari 7, G Rugna 3, G F Späth 8, Affiliations Expand, PMID: 38832792

Scientific or technical background required for work program

Comprehension of medical language
Comprehension of scientific language
Comprehension of English
Article analysis and bibliography
Master 2 in biology: in vitro experimentation: microbiology and cell culture
Basic pharmacology: IC50 measurement
GraphPad

Institut Pasteur, 2025-2026

Title of the work program 6

Analysis of mucosal-associated invariant T (MAIT) cells in synovial fluid from psoriatic arthritis patients

Description of the work program

Immune-mediated inflammatory diseases (IMID) such as psoriasis (Pso), Crohn's disease (CD), rheumatoid arthritis, and spondyloarthritis (SpA) are a family of common and highly disabling chronic conditions. These diseases constitute a considerable burden to patients because of physical pain, reduced quality of life and increased mortality, and to society because of the associated high health care costs and reduced productivity. There are no curative treatments, and currently available therapies alleviate symptoms in many but not all patients. Our limited understanding of the pathogenic mechanisms is a major bottleneck that hampers the development of more specific and effective therapies for these devastating diseases.

Although clinically heterogeneous, IMID share common inflammatory pathways, deriving from aberrant immune responses. Genome-wide association studies, together with experimental mouse models revealed that signaling by the heterodimeric cytokine interleukin 23 (IL-23) plays a pivotal role in the initiation of several IMID. Recent studies have pointed to important roles of different immune cell populations expressing the IL-23 receptor (IL-23R) in the pathogenesis of IMID, building the foundation for the subsequent development of new strategies to treat human disorders in which the IL-23 pathway plays a key role.

The clinical relevance of IL-23 has been validated by the successful treatment of Pso, psoriatic arthritis (PsA), CD and ulcerative colitis (UC) with IL-23 inhibitors. However, a subset of patients do not respond to anti-IL-23 therapy, and IL-23 blockade failed in the treatment of axial SpA, despite the strong genetic association of the IL-23 receptor gene with this disease. These data underline our limited understanding of the pathways and the cellular targets affected by IL-23 signaling, and its role in selected patients and specific human diseases.

Our preliminary analysis of single-cell data from IL-23R-positive and negative T cells from synovial fluid of PsA patients revealed a remarkable expansion of specific MAIT cell clones (characterized by identical TCRα and TCRβ chains). MAIT cells recognize microbial-derived riboflavin (vitamin B2) metabolites, such as 5-OP-RU, presented by the MHC class I-related protein 1 (MR1) [1,2]. The expansion of MAIT cell clones in synovial fluid of PsA patients is novel and somewhat unexpected because microbial metabolites and MAIT cells have not previously been associated with PsA pathogenesis. In general, the role of MAIT cells in IMID is debated; we have recently shown that IL-23 signaling may increase pathogenic functions of human MAIT cells isolated from peripheral blood [3], while data from experimental mouse models have demonstrated tissue repair and homeostatic roles of MAIT cells [4,5]. We aim to: (1) Determine whether synovial MAIT cell expansion is a general feature of PsA patients, and (2) characterize the functions of the expanded MAIT cells. We will perform a multiparameter analysis of IL-23R-positive and negative cells isolated from paired samples of synovial fluid and peripheral blood from PsA patients by performing "Cellular Indexing of transcriptomes and Epitopes by sequencing" (CITE-seq) [6] combined with TCR sequencing from a cohort of 20 PsA patients. We will compare frequencies of specific MAIT cell clones in peripheral blood and synovial fluid. To determine the function of synovial fluid MAIT cells we will stimulate them with MR1/5-OP-RU tetramers or cytokines and analyze gene expression and secreted molecules using Luminex technology.

1. Kjer-Nielsen, L., et al. (2012). Nature 491, 717-723. 10.1038/nature11605.
2. Treiner, E., et al. (2003). Nature 422, 164-169. 10.1038/nature01433.
3. Camard, L., et al. (2025). iScience *28*, 111898. 10.1016/j.isci.2025.111898.

4. Constantinides, M.G., et al. (2019). Science 366. 10.1126/science.aax6624.
5. du Halgouet, A., et al. (2023). Immunity 56, 78-92 e76. 10.1016/j.immuni.2022.12.004.
6. Stoeckius, M., et al. (2017). Nat Methods 14, 865-868. 10.1038/nmeth.4380.

Tutor/supervisor

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

IL-23 tunes inflammatory functions of human mucosal-associated invariant T cells.
Camard L, Stephen T, Yahia-Cherbal H, Guillemot V, Mella S, Baillet V, Lopez-Maestre H, Capocefalo D, Cantini L, Leloup C, Marsande J, Garro K, Sienes Bailo J, Dangien A, Pietrosemoli N, Hasan M, Wang H, Eckle SBG, Fourie AM, Greving C, Joyce-Shaikh B, Parker R, Cua DJ, Bianchi E, Rogge L. *iScience*. 2025 Jan 25;28(2):111898. doi: 10.1016/j.isci.2025.111898.

Interleukin 23 receptor: Expression and regulation in immune cells.
Mezghiche I, Yahia-Cherbal H, Rogge L, Bianchi E. *Eur J Immunol*. 2024 Jan;54(1):e2250348. doi: 10.1002/eji.202250348.

Characterization of Blood Mucosal-Associated Invariant T Cells in Patients With Axial Spondyloarthritis and of Resident Mucosal-Associated Invariant T Cells From the Axial Entheses of Non-Axial Spondyloarthritis Control Patients.
Rosine N, Rowe H, Koturan S, Yahia-Cherbal H, Leloup C, Watad A, Berenbaum F, Sellam J, Dougados M, Aimanianda V, Cuthbert R, Bridgewood C, Newton D, Bianchi E, Rogge L*, McGonagle D*, Miceli-Richard C*. *Arthritis Rheumatol*. 2022 Nov;74(11):1786-1795. doi: 10.1002/art.42090. Epub 2022 Sep 22. PMID: 35166073
[* Equal contribution]

Immune response profiling of patients with spondyloarthritis reveals signalling networks mediating TNF-blocker function in vivo.
Menegatti S, Guillemot V, Latis E, Yahia-Cherbal H, Mittermüller D, Rouilly V, Mascia E, Rosine N, Koturan S, Millot GA, Leloup C, Duffy D, Gleizes A, Hacein-Bey-Abina S; Milieu Intérieur Consortium; Sellam J, Berenbaum F, Miceli-Richard C, Dougados M, Bianchi E, Rogge L. *Ann Rheum Dis*. 2021 Apr;80(4):475-486. doi: 10.1136/annrheumdis-2020-218304.

NFAT primes the human RORC locus for RORγt expression in CD4+ T cells.
Yahia-Cherbal H, Rybczynska M, Lovecchio D, Stephen T, Lescale C, Placek K, Larghero J, Rogge L, Bianchi E. *Nat Commun*. 2019 Oct 16;10(1):4698. doi: 10.1038/s41467-019-12680-x. PMID: 31619674

Scientific or technical background required for work program

We are looking for a highly motivated student with a solid knowledge of immunology. Previous experience in cell culture, flow cytometry and molecular biology techniques such as western blots would be very helpful but is not mandatory. The student will be hosted in a multidisciplinary lab, where they will receive training in fundamental immunological methods routinely applied in the field.

Institut Pasteur, 2025-2026

Title of the work program 7

Shaping Stimulation for Hearing Implants

Description of the work program

Some people with severe deafness receive a medical device called a *cochlear implant* that recreates a sensation of sound by stimulating the hearing nerve with electrical currents. The processor of the implant executes a sound coding algorithm that performs the conversion of sound into a spatio-temporal sequence of electrical pulses, replacing the natural mechano-transduction of sound that occurs naturally in a healthy ear. Although the recovered experience of sound is life-changing for the recipient, the outcomes are far from restoring the equivalent of natural, healthy hearing. Part of the limitations might arise from an inaccurate representation of the sound for the hearing nerve, due to suboptimality of the sound coding algorithm or to the specific physiology and hearing pathology of the recipient. Our aim is to build, refine, and exploit models that predict the neural representation of cochlear implant stimulation, capturing both physical and physiological phenomena. In order to determine physiological model parameters, we will develop a new experimental technique to perform and analyse electrophysiological measurements from human implant recipients. By exploiting universal and personalized models, we will propose new principles and algorithms for sound coding that achieve a more useful and naturalistic neural representation, as well as strategies for fitting stimulation parameters to the physiology of individual recipients.

Tutor/supervisor

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

Arzounian, D., Guérit, F., Deeks, J. M., Garcia, C., de Groote, E., Bance, M., & Carlyon, R. P. (2025). Measurement of phase-locked neural responses to cochlear-implant stimulation from multiple stages of the auditory system. Hearing Research, 109338. https://doi.org/10.1016/j.heares.2025.109338

Gaultier, C., & Goehring, T. (2024). Recovering speech intelligibility with deep learning and multiple microphones in noisy-reverberant situations for people using cochlear implants. The Journal of the Acoustical Society of America, 155(6), 3833–3847. https://doi.org/10.1121/10.0026218

Institut Pasteur, 2025-2026

Prof. Paul Avan, Center for Research and Innovation in Human Audiology, Real-time artificial intelligence-based speech enhancement methods for hearing aid improvement: https://research.pasteur.fr/en/project/refined/

Scientific or technical background required for work program

The project may be suitable for a wide range of scientific profiles training in medicine, engineering, physics, computer science, mathematics, computational biology, neuroscience, or audiology. Specific project aims may be adapted to the profile and skills of the candidate. Programming skills will be essential in all cases.

Institut Pasteur, 2025-2026

Title of the work program 8

Characterization and functional consequences of anti-Caspr2 antibodies in autoimmune encephalitis patients

Description of the work program

Contactin-associated protein-like 2 (Caspr2) encephalitis is a rare antibody (Ab)-mediated autoimmune encephalitides (AE). Caspr2-antibodies are associated with a spectrum of neurological core symptom sand signs. The mechanisms by which Caspr2-specific Abs mediate pathology and how Ab-mediated effector functions translate into clinical syndromes and disease progression remain incompletely understood. In this project, we aim to dissect the relationship between anti-Caspr2 antibody characteristics, disease progression and treatment responses.

To this aim we will:

i) identify and analyze anti-Contactin-associated protein-like 2 (Caspr2) specific B cells in patients with autoimmune Contactin-associated encephalitis,
ii) obtain sequences from these B cell antibody heavy and light chain variable regions to determine the antibody repertoire in these patients,
iii) recombinantly express selected antibody candidates,
iv) perform detailed in vitro antibody characterization (specificity, affinity, activity), and
v) determine in vivo pathogenicity through antibody transfer experiments in preclinical humanized mouse models of Caspr2-AE.

N.B.: This project, which largely exceeds the time frame of 6-months, will start upon arrival of the clinical samples. The selected candidate will work on some of the aforementioned tasks depending on the project's progression.

To date, the functional properties and pathogenic mechanisms of Caspr2-specific Abs remain elusive. Furthermore, no biomarkers are available that predict or define phenotype, severity, clinical course and treatment response in patients with Caspr2-Ab associated AE. With this project, we aim to provide novel fundamental insights into effector and regulatory mechanisms of encephalitogenic Abs and how these translate into clinical phenotypes, but also aid the development of personalized medicine for the benefit of patients with Caspr2-Ab associated disease.

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

Institut Pasteur, 2025-2026

Antibody-secreting cell repertoires hold high-affinity anti-rocuronium specificities that can induce anaphylaxis in vivo.
Dejoux A, Zhu Q, Woolfe A, Godon O, Ellouze S, Mottet G, Castrillon C, Gillis C, Pecalvel C, Ganneau C, Iannascoli B, Lemoine F, Saul F, England P, Reber LL, Gouel-Chéron A, de Chaisemartin L, Haouz A, Millot GA, Bay S, Gérard A, Jönsson F, Chollet-Martin S, Bruhns P. J Allergy Clin Immunol. 2025 May;155(5):1557-1574. doi: 10.1016/j.jaci.2025.01.025

Humoral signatures of Caspr2-antibody spectrum disorder track with clinical phenotypes and outcomes.
Terroba-Navajas P, Spatola M, Chuquisana O, Joubert B, de Vries JM, Dik A, Marmolejo L, Jönsson F, Lauc G, Kovac S, Prüss H, Wiendl H, Titulaer MJ, Honnorat J, Lünemann JD. Med. 2025 Feb 14;6(2):100515. doi: 10.1016/j.medj.2024.09.004.

Rocuronium-specific antibodies drive perioperative anaphylaxis but can also function as reversal agents in preclinical models.
Dejoux A, Zhu Q, Ganneau C, Goff OR, Godon O, Lemaitre J, Relouzat F, Huetz F, Sokal A, Vandenberghe A, Pecalvel C, Hunault L, Derenne T, Gillis CM, Iannascoli B, Wang Y, Rose T, Mertens C, Nicaise-Roland P; NASA Study Group; England P, Mahévas M, de Chaisemartin L, Le Grand R, Letscher H, Saul F, Pissis C, Haouz A, Reber LL, Chappert P, Jönsson F, Ebo DG, Millot GA, Bay S, Chollet-Martin S, Gouel-Chéron A, Bruhns P. Sci Transl Med. 2024 Sep 11;16(764):eado4463. doi: 10.1126/scitranslmed.ado4463

Scientific or technical background required for work program

We are seeking an enthusiastic and motivated candidate who works well in a team and is eager to drive this translational project forward. Candidates should have a strong background in immunology and/or neurobiology. Prior laboratory experience with primary human cell cultures, flow cytometry, and general biochemistry and molecular approaches is required. Good communication skills and fluency in English are essential.