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INSTITUT PASTEUR
EDUCATION

Projects 2023-2024

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Institut Pasteur, 2023-2024

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 almost 2600 individuals.
Research: priority is given to fight infectious diseases, such as viral, bacterial, and parasitic diseases, as well as certain types of cancer, genetic, neurodegenerative, and allergic diseases.
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 a), b), c) etc:

The laboratories at Pasteur have proposed 26 projects for Erasmus internships (see following pages).
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/).

FACILITIES (not compulsory for the host centre)

- **Accommodation**

a limited number of rooms for rent are reserved for Pasteur at the student residence Cité Universitaire http://www.ciup.fr/

- **Canteen**

partially subsidized canteen is available on the Pasteur Campus

- **Additional salary**

additional salary of approximately 600 euros/month (depending on the number of working days) is paid by the host lab (4.05 euros/hour, 7 hours/ day)

Title of the work program 1

Brain-body interactions in mood disorders

Description of the work program

Summary of the Project:

The purpose of the present program is to promote translational research in the field of mood disorders. We seek to characterize some dimensions of psychiatric disorders by investigating brain circuits plasticity and neuroimmune signaling in order to identify novel therapeutics. **We believe that disentangling the causal links that mediate internal responses to behavior, in the healthy and pathological brain, is a necessary step for innovative therapeutical approaches**. Today, a major obstacle hindering our understanding of brain function is the fragmentation of brain research and the vast collection of data it produces. Understanding brain function with a holistic vision that integrates molecular, cellular and system levels, but also includes systemic brain-body interactions, is a prerequisite to unravel the mechanism of brain disorders. For this reason, the present proposal aims at nurturing a virtuous circle between basic research and the clinic.

Goals of the Project:

The idea that psychiatric disorders could progress in stages, and with age, applied to mood disorders [1]. In recent years, the hippocampus has been identified as central to regulate mood states, and impaired neural stem cell (NSC) function and neurogenesis have been associated to advanced aging [2] and depression [3]. Under altered physiological conditions, NSCs become increasingly unable to self-renew and differentiate, which leads to decreased neurogenesis, yet the underlying mechanisms remain unknown. Based on our preliminary evidence, we postulate that NSCs acquire a state of premature senescence in the context of depression. Given the recent major findings that adult neurogenesis is impacted in neurodegeneration and aging in humans [4], identifying these mechanisms would lead to further understanding and treating neurogenesis impairments in the context of depression (**Aim #1**).

Neurogenesis is regulated by the extrinsic environment, such as blood-borne signals from the periphery and neuronal circuits in the brain [5]. We previously demonstrated that infusion of old blood into a young animal accelerated NSC and brain aging, leading to cognitive decline [6, 7]. However, it is unknown whether specific systemic alterations due to depression could also affect neurogenesis. Based on preliminary findings, we hypothesize that pro-aging blood-borne signals negatively regulate hippocampal neurogenesis in the context of depression. Hence, identifying these signals could allow understanding the pathophysiology of the disease and use of these molecules as potential biomarkers for early detection, prevention and/or treatment (**Aim #2**).

We have previously identified GDF11, a blood factor with anti-aging potential in the brain [6, 8-10]. Our preliminary findings demonstrate that GDF11 exhibits an anti-depressant effect in mice, and levels of circulating GDF11 are lower in major *depressive disorder* (MDD) patients. However, the mechanistic role of GDF11 in depression is widely unknown. Based on our preliminary findings we hypothesize that GDF11 directly acts on hippocampal newborn neurons, linking neurogenesis to depression. Further exploring this novel role for GDF11 as a potential treatment for depression could open new avenues in the treatment of depression

(**Aim #3**). By considering the reciprocal relationships of depression with aging-related processes, we aim to address the above unexplored questions and generate novel hypotheses on affective disorders and treatment targets.

References

1 Ferrari, A. J. *et al.* Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. *Psychol Med* **43**, 471-481, doi:10.1017/S0033291712001511 (2013).
2 Leschik, J., Lutz, B. & Gentile, A. Stress-Related Dysfunction of Adult Hippocampal Neurogenesis-An Attempt for Understanding Resilience? *Int J Mol Sci* **22**, doi:10.3390/ijms22147339 (2021).
3 Mathers, C. D. & Loncar, D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* **3**, e442, doi:10.1371/journal.pmed.0030442 (2006).
4 Krishnan, V. & Nestler, E. J. The molecular neurobiology of depression. *Nature* **455**, 894-902, doi:10.1038/nature07455 (2008).
5 Floresco, S. B., Todd, C. L. & Grace, A. A. Glutamatergic afferents from the hippocampus to the nucleus accumbens regulate activity of ventral tegmental area dopamine neurons. *J Neurosci* **21**, 4915-4922 (2001).
6 O'Donnell, P. & Grace, A. A. Synaptic interactions among excitatory afferents to nucleus accumbens neurons: hippocampal gating of prefrontal cortical input. *J Neurosci* **15**, 3622-3639 (1995).
7 Kempermann, G., Song, H. & Gage, F. H. Neurogenesis in the Adult Hippocampus. *Cold Spring Harb Perspect Biol* **7**, a018812, doi:10.1101/cshperspect.a018812 (2015).
8 Fanselow, M. S. & Dong, H. W. Are the dorsal and ventral hippocampus functionally distinct structures? *Neuron* **65**, 7-19, doi:10.1016/j.neuron.2009.11.031 (2010).
9 Obernier, K. & Alvarez-Buylla, A. Neural stem cells: origin, heterogeneity and regulation in the adult mammalian brain. *Development* **146**, doi:10.1242/dev.156059 (2019).
10 Denoth-Lippuner, A. & Jessberger, S. Formation and integration of new neurons in the adult hippocampus. *Nat Rev Neurosci* **22**, 223-236, doi:10.1038/s41583-021-00433-z (2021).

Tutor/supervisor

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

Team Publications for the last ten years (the name of members of the team underlined and highlighted are the main publications in relation to the project):

1. Siopi E, Galerne M, Rivagorda M, Saha S, Moigneu C, Bigot M, Oury F & Lledo PM (2023). Gut microbiota changes require vagus nerve integrity to promote depressive-like behaviors in mice. *Molecular Psychiatry* (in press).

2. Moigneu C, Abdellaoui S, Pfaffenseller B, Wollenhaupt-Aguiar B, Chiche A, Kuperwasser N, Pedrotti Moreira F, Li H, Oury F, Kapczinski F, Lledo PM* & Katsimpardi L* (2023). Systemic GDF11 attenuates depression-like phenotype in aged mice via stimulation of neuronal autophagy, *Nature Aging* 3: 213–228.

3. Guérinot C, Marcon V, Godard C, Blanc T, Verdier H, Planchon G, Raimondi F, Boddaert N, Alonso M, Sailor K, Lledo PM, Hajj B, El Beheiry M & Masson JB (2022). New approach to accelerated image annotation by leveraging virtual reality and cloud computing. *Front Bioinform* 1: 777101.

4. Mazo C, Nissant A, Saha S, Peroni E, Lledo P-M* & Lepousez G* (2022). Long-range GABAergic projections contribute to cortical feedback control of sensory processing, *Nature Comm.* 13: 6879.

5. Bigot M, Vicq E, Lledo PM, Alonso M & Henry C (2022). Assessing positive and negative valence systems to refine animal models of bipolar disorders: the example of GBR 12909-induced manic phenotype. *Sci Rep.* 12(1): 7364.

6. Lazarini F, Lannuzel A, Cabié A, Michel V, Madec Y, Chaumont H, Calmont I, Favrat M, Montagutelli X, Roze E & Lledo PM. ZikaSmell Working Group (2022). Olfactory outcomes in Zika virus-associated Guillain-Barré syndrome. *Eur J Neurol.* 29(9): 2823-2831.

7. Rei D, Saha S, Haddad M, Rubio AH, Perlaza BL, Berard M, Ungeheuer MN, Sokol H & Lledo PM (2022). Age-associated gut microbiota impair hippocampus-dependent memory in a vagus-dependent manner. *JCI Insight*. 7(15): e147700.

8. Pascal M, Kazakov A, Chevalier G, Dubrule L, Deyrat J, Dupin A, Saha S, Jagot F, Sailor K, Dulauroy S, Moigneu C, Belkaid Y, Lepousez G*, Lledo P-M*, Wilhelm C* & Eberl G* (2022). The neuropeptide VIP potentiates intestinal innate type 2 and type 3 immunity in response to feeding. *Mucosal Immunol.* 15, 629-641.

9. Lazarini F, Levivien S, Madec Y, Taieb F, Mottez E, Buivan TP, Maudoux A, Wiener-Vacher S, Nevoux J, Van Den Abbeele T, Gressens P, Lledo P-M* & Teissier N* (2022). Olfactory function in congenital cytomegalovirus infection: a prospective study. *Eur J Pediatr.* 14: 1-11.

10. Bourhy L, Mazeraud A, Costa LH, Levy J, Rei D, Hecquet E, Gabanyi I, Bozza FA, Chrétien F, Lledo P-M*, Sharshar T* & Lepousez G* (2022). Silencing of amygdala circuits during sepsis prevents the development of anxiety-related behaviors. *Brain* 145: 1391-1409.

11. Gabanyi I, Lepousez G, Wheller R, Renier N, Vieites Prado A, Nissant A, Wagner S, Mognieu C, Dulauroy S, Hicham S, Gomperts Boneca I, Eberl G & Lledo P-M (2022). Bacterial sensing via neuronal Nod2 contributes to appetite and body temperature regulation. *Science* 376: eabj3986.

12. Gransagne M, Aymé G, Brier S, Chauveau-Le Friec G, Meriaux V, Nowakowski M, Dejardin F, Levallois S, Dias de Melo G, Donati F, Prot M, Brûlé S, Raynal B, Bellalou J, Goncalves P, Montagutelli X, Di Santo JP, Lazarini F, England P, Petres S, Escriou N, Lafaye P. Development of a highly specific and sensitive VHH-based sandwich immunoassay for the detection of the SARS-CoV-2 nucleoprotein. *Journal of Biological Chemistry*, 298(1):101290

13. Sailor KA, Agoranos G, Pez-Manzaneda SL, Tada S, Gillet-Legrand B, Guerinot C, Masson JB, Vestergaard CL, Bonner M, Gagnidze K, Veres G, Lledo P-M* & Cartier N* (2022). Hematopoietic stem cell transplantation chemotherapy causes microglia senescence and peripheral macrophage engraftment in the brain. *Nature Med*, 28: 517-527.

14. de Melo GD, Lazarini F, Larrous F, Feige L, Kornobis E, Levallois S, Marchio A, Kergoat L, Hardy D, Cokelaer T, Pineau P, Lecuit M, Lledo PM, Changeux JP, Bourhy H (2021). Attenuation of clinical and immunological outcomes during SARS-CoV-2 infection by ivermectin. *EMBO Mol Med*.13(8):e14122.

15. Robinot R, Hubert M, Dias de Melo G, Lazarini F, Bruel T, Smith N, Levallois S, Larrous F, Fernandes J, Gellenoncourt S, Rigaud S, Gorgette O, Thouvenot C, Trébeau C, Mallet A, Duménil G, Gobaa S, Etournay R, Lledo P-M, Lecuit M, Bourhy H, Duffy D, Michel V, Schwartz O & Chakrabarti LA (2021). SARS-CoV-2 infection induces the dedifferentiation of multiciliated cells and impairs mucociliary clearance. *Nature Comm.* 12: 4354.

16. Travier L, Alonso M, Andronico A, Hafner L, Lledo P-M, Cauchemez S & Lecuit M. (2021). Neonatal susceptibility to meningitis results from the immaturity of epithelial barriers and gut microbiota. *Cell Reports* 35: 109319.

17. de Melo GD*, Lazarini F*, Levallois S*, Hautefort C*, Michel V, Larrous F, Verillaud B, Aparicio C, Wagner S, Gheusi G, Kergoat L, Kornobis E, Donati F, Cokelaer T, Hervochon R, Madec Y, Roze E, Salmon D, Bourhy H, Lecuit M & Lledo P-M (2021). COVID-19-related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters. *Science Transl Med*. 13(596): eabf8396.

18. Dargél AA, Mosconi E, Masson M, Plaze M, Taieb F, Von Platen C, Buivan TP, Pouleriguen G, Sanchez M, Fournier S, Lledo P-M & Henry C (2020). Toi Même, a Mobile Health Platform for Measuring Bipolar Illness Activity: Protocol for a Feasibility Study. *JMIR Res Protoc.* 9(8):e18818.

19. Chaumont H, Roze E, Tressières B, Lazarini F & Lannuzel A. Central nervous system infections in a tropical area: Influence of emerging and rare infections. *European Journal of Neurology*, 2020 Nov;27(11):2242-2249.

Scientific or technical background required for work program

Don't be afraid of handling mice

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Institut Pasteur, 2023-2024

Title of the work program 2

Novel pathways in the left-right patterning of the heart

Description of the work program

The acquisition of a specific shape is key for organ function. **Left-right asymmetric morphogenesis** partitions the heart into distinct compartments, driving the systemic and pulmonary blood circulations. Whereas the molecular cascade breaking the bilateral symmetry of the early embryo has been well characterised, how it is sensed by organ-specific precursor cells to generate asymmetric organogenesis remains poorly understood. The rightward looping of the embryonic heart tube provides a striking example of asymmetric morphogenesis, during which the tubular primordium acquires a helical shape, essential to align cardiac chambers and establish the double blood flow [4]. In the recent years, the team of *Heart Morphogenesis* has developed a novel technological and conceptual framework to investigate asymmetric heart morphogenesis [1, 2, 3, 5]. We have dissected the contribution of Nodal signaling to **heart looping** [2] and shown that it is not the only player of asymmetric heart morphogenesis. We have now performed a **transcriptomic screen** to identify novel genes asymmetrically expressed in the heart field. The proposed project aims at validating candidate genes, using advanced technologies in **quantitative imaging** of gene expression and shape in 3D, with a high spatio-temporal resolution. The project will thus contribute to identify novel pathways **patterning** the field of heart progenitors and novel mechanisms of asymmetric organogenesis. Our work in the mouse is relevant to **congenital heart defects** in humans [6], which is explored with our collaborators of the Hospital Necker-Enfants Malades, where the Institut *Imagine* is located. The laboratory is also affiliated to the Department of Stem Cell and **Developmental Biology** of the Institut Pasteur.

Tutor/supervisor

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

1- S. Bernheim et al, 2023 BIORXIV/2023/540418, Torsion of the heart tube by shortage of progenitor cells : identification of *Greb1l* as a genetic determinant of criss-cross heart in mice

2-A. Desgrange et al., 2020 Developmental Cell 55(4):413-431, Transient Nodal signalling in left precursors coordinates opposed asymmetries shaping the heart loop

3-A. Desgrange et al., 2019 Disease Models & Mechanisms, 12(7):dmm038356, Standardised imaging pipeline for phenotyping mouse laterality defects and associated heart malformations, at multiple scales and multiple stages

4-A. Desgrange, J-F. Le Garrec, and S. Meilhac, 2018 Development 145(22):dev162776, Left-right asymmetry in heart development and disease : forming the right loop (Review)

5-J-F. Le Garrec et al., 2017 eLife, 6 :pii: e28951, A predictive model of asymmetric morphogenesis from 3D reconstructions of mouse heart looping dynamics

6- L. Houyel and S. Meilhac, 2021 Annu Rev Genomics Hum Genet 22:257:284, Heart Development and Congenital Structural Heart Defects (Review)

Scientific or technical background required for work program

Strong interest in developmental biology. Previous lab experience. Skills in cellular and molecular biology. Dexterity to manipulate small, precious and fragile samples.

Title of the work program 3

Cell-cell interactions in esophageal development and homeostasis

Description of the work program

Muscles of the trunk originate from the segmented somites, whereas head muscles arise independently from the cardiopharyngeal mesoderm (CPM) located more anteriorly in the early embryo. The specification of head and trunk muscles involves divergent genetic regulatory networks, to activate the bHLH myogenic regulatory factors Myf5, Mrf4, Myod and Myogenin that play crucial roles in governing striated muscle cell fate and differentiation.

In most vertebrates, the upper digestive tract is composed of muscularized jaws linked to the esophagus that permits food ingestion and swallowing. Esophagus striated muscles (ESM) are present in the trunk but share a common CPM origin. ESM are unusual among striated muscles as they are established using smooth muscle as scaffold. The smooth muscle layer is established prior to colonization of the esophageal tube by myogenic progenitors. Yet, the smooth muscle layer disappears in the early postnatal phase. What is the functional role of establishing a complex 3D smooth muscle pattern and then removing it? What are the molecular mechanisms involved? What are the consequences from the striated muscle point of view?

In project, we thus aim at understanding the developmental origin and cellular dynamics of esophagus smooth muscle using a combination of mouse genetics, histological analysis and ex vivo/in vitro culture. Moreover, we aim at uncovering novel signaling pathways that ensure the cross talk among striated muscle, smooth muscle and connective tissues by taking profit of single-nucleus RNAseq already available in the lab and single molecule FISH.

Tutor/supervisor

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

Comai G, Heude E, Mella S, Paisant S, Pala F, Gallardo M, Langa F, Kardon G, Gopalakrishnan S, Tajbakhsh S. A distinct cardiopharyngeal mesoderm genetic hierarchy establishes antero-posterior patterning of esophagus striated muscle. eLife. 2019 Sep 19;8.

Gopalakrishnan S, Comai G, Sambasivan R, Francou A, Kelly RG, Tajbakhsh S. A cranial mesoderm origin for esophagus striated muscle (2015). Developmental Cell. Sep 28;34(6):694-704.

Grimaldi A and Tajbakhsh S. Diversity in cranial muscles: Origins and developmental programs (2021). Curr Op in Cell Biol. 73:110–116

Scientific or technical background required for work program

We are looking for a highly motivated and curious student willing to work on an international environment in the Stem Cells and Development Department. Student should have a background on Developmental Biology, immunostaining, molecular biology, cell culture and image analysis. Previous experience with mouse work and bioinformatic analysis is not required but a constitute a plus. English is the working language of the lab; Report and lab meetings should be written in English. We expect a motivation letter to join the lab and this specific project.

Title of the work program 5

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Institut Pasteur, 2023-2024

Exploring pathogenic mechanisms of chronic inflammatory disease: unresolved issues in IL-23 biology

Description of the work program 4

Chronic inflammatory diseases (CID), such as Axial spondylarthritis (axSpA), inflammatory bowel disease and psoriasis, are a group of clinically heterogeneous diseases that share common pathogenic pathways. The implication of interleukin 23 (IL-23) and its receptor (IL23R) in their pathogenesis has been confirmed by evidence from animal models in which overexpression of IL-23 induces hallmarks of axSpA[1], and from genome wide association studies that have shown a strong association between genetic polymorphisms in the *IL23R* locus with the susceptibility to develop several CIDs[2]. However, the underlying pathological mechanisms are not fully understood. This project asks what are the immune cell populations that express the IL23R (and therefore respond to IL-23) and how is expression of the IL-23 receptor regulated.

To address the molecular mechanisms of IL23R induction, we use ATACseq to identify regions with an open chromatin conformation in the IL23R locus, in T cells stimulated in different conditions and we investigate transcription factors (TF) that may bind to these regions by TF footprinting analysis. To test the role of these TF in the regulation of *IL23R* gene expression, we use self-delivering siRNA pools to silence each TF and measure the effect on *IL23R* expression using nCounter technology (Nanostring). Binding *in vivo* of selected TF will be confirmed by ChIPseq experiments.

To obtain a comprehensive map of IL-23R-expressing and of IL-17A-producing leukocytes in disease tissues, we will isolate immune cells from synovial fluid of psoriatic arthritis patients and define their single-cell transcriptomes and surface protein markers by "Cellular Indexing of transcriptomes and Epitopes by sequencing" (CITE-seq).

1) Sherlock, J. P. *et al.* IL-23 induces spondyloarthropathy by acting on ROR-γt+ CD3+CD4-CD8- entheseal resident T cells. *Nat. Med.* **18**, 1069–1076 (2012).
2) Brown, M. A., Kenna, T. & Wordsworth, B. P. Genetics of ankylosing spondylitis--insights into pathogenesis. *Nat. Rev. Rheumatol.* **12**, 81–91 (2016).

Tutor/supervisor

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

- 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. 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. *Arthritis Rheumatol*. 2022 Nov;74(11):1786-1795. doi: 10.1002/art.42090. Epub 2022 Sep 22. PMID: 35166073
- 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. Immune response profiling of patients with spondyloarthritis reveals signaling networks mediating TNF-blocker function in vivo. *Ann Rheum Dis*. 2020 Dec 2;80(4):475–86. doi:10.1136/annrheumdis-2020-218304. PMID: 33268443; PMCID: PMC7958106.
- Latis E, Michonneau D, Leloup C, Varet H, Peffault de Latour R; CRYOSTEM Consortium, Bianchi E, Socié G, Rogge L. Cellular and molecular profiling of T-cell subsets at the onset of human acute GVHD. *Blood Adv*.

- Yahia-Cherbal, H, Rybczynska M, Lovecchio D, Stephan T, Lescoat C, Placek K, Larghero J, Rogge L, Bianchi E* NFAT primes the human RORC locus for RORgt expression in CD4+ T cells. *Nature Communications*, 2019;10(1):4698.

Review articles

- Bianchi E*, Vecellio M, Rogge L. Editorial: Role of the IL-23/IL-17 Pathway in Chronic Immune-Mediated Inflammatory Diseases: Mechanisms and Targeted Therapies. Front Immunol. 2021 *Front. Immunol*., 23 September 2021 doi.org/10.3389/fimmu.2021.770275
- Mezghiche I, Yahia-Cherbal H, Rogge L, Bianchi E*. Novel approaches to develop biomarkers predicting treatment responses to TNF-blockers. *Expert Rev Clin Immunol*. 2021 Apr;17(4):331-354. doi: 10.1080/1744666X.2021.1894926. PMID: 33622154.
- Bianchi E, Rogge L. The IL-23/IL-17 pathway in human chronic inflammatory diseases-new insight from genetics and targeted therapies. *Genes Immun*. 2019, 20(5):415-425. doi: 10.1038/s41435-019-0067-y.
- Menegatti S, Bianchi E, Rogge L. Anti-TNF Therapy in Spondyloarthritis and Related Diseases, Impact on the Immune System and Prediction of Treatment Responses. *Front Immunol*. 2019 Mar 19;10:382. doi: 10.3389/fimmu.2019.00382.

Scientific or technical background required for work program

Background knowledge in immunology and/or transcription/epigenetics is desirable.
Some lab experience (cell culture or molecular biology) preferred, but the student will be taught the relevant techniques. The student will handle blood samples and synovial fluid samples.

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Title of the work program 5

Exploring pathogenic mechanisms of chronic inflammatory disease: unresolved issues in IL-23 biology

Description of the work program

Chronic inflammatory diseases (CID), such as Axial spondylarthritis (axSpA), inflammatory bowel disease and psoriasis, are a group of clinically heterogeneous diseases that share common pathogenic pathways. The implication of interleukin 23 (IL-23) and its receptor (IL23R) in their pathogenesis has been confirmed by evidence from animal models in which overexpression of IL-23 induces hallmarks of axSpA[1], and from genome wide association studies that have shown a strong association between genetic polymorphisms in the *IL23R* locus with the susceptibility to develop several CIDs[2]. However, the underlying pathological mechanisms are not fully understood. This project asks what are the immune cell populations that express the IL23R (and therefore respond to IL-23) and how is expression of the IL-23 receptor regulated.

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3) Sherlock, J. P. *et al.* IL-23 induces spondyloarthropathy by acting on ROR-γt+ CD3+CD4-CD8- entheseal resident T cells. *Nat. Med.* **18**, 1069–1076 (2012).
4) Brown, M. A., Kenna, T. & Wordsworth, B. P. Genetics of ankylosing spondylitis--insights into pathogenesis. *Nat. Rev. Rheumatol.* **12**, 81–91 (2016).

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

- 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. 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. *Arthritis Rheumatol*. 2022 Nov;74(11):1786-1795. doi: 10.1002/art.42090. Epub 2022 Sep 22. PMID: 35166073
- 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. Immune response profiling of patients with spondyloarthritis reveals signaling networks mediating TNF-blocker function in vivo. *Ann Rheum Dis*. 2020 Dec 2;80(4):475–86. doi:10.1136/annrheumdis-2020-218304. PMID: 33268443; PMCID: PMC7958106.

- Latis E, Michonneau D, Leloup C, Varet H, Peffault de Latour R; CRYOSTEM Consortium, Bianchi E, Socié G, Rogge L. Cellular and molecular profiling of T-cell subsets at the onset of human acute GVHD. *Blood Adv*.
- Yahia-Cherbal, H, Rybczynska M, Lovecchio D, Stephan T, Lescoat C, Placek K, Larghero J, Rogge L, Bianchi E* NFAT primes the human RORC locus for RORgt expression in CD4+ T cells. *Nature Communications*, 2019;10(1):4698.

Review articles

- Bianchi E*, Vecellio M, Rogge L. Editorial: Role of the IL-23/IL-17 Pathway in Chronic Immune-Mediated Inflammatory Diseases: Mechanisms and Targeted Therapies. Front Immunol. 2021 *Front. Immunol*., 23 September 2021 doi.org/10.3389/fimmu.2021.770275
- Mezghiche I, Yahia-Cherbal H, Rogge L, Bianchi E*. Novel approaches to develop biomarkers predicting treatment responses to TNF-blockers. *Expert Rev Clin Immunol*. 2021 Apr;17(4):331-354. doi: 10.1080/1744666X.2021.1894926. PMID: 33622154.
- Bianchi E, Rogge L. The IL-23/IL-17 pathway in human chronic inflammatory diseases-new insight from genetics and targeted therapies. *Genes Immun*. 2019, 20(5):415-425. doi: 10.1038/s41435-019-0067-y.
- Menegatti S, Bianchi E, Rogge L. Anti-TNF Therapy in Spondyloarthritis and Related Diseases, Impact on the Immune System and Prediction of Treatment Responses. *Front Immunol*. 2019 Mar 19;10:382. doi: 10.3389/fimmu.2019.00382.

Scientific or technical background required for work program

Background knowledge in immunology and/or transcription/epigenetics is desirable.
Some lab experience (cell culture or molecular biology) preferred, but the student will be taught the relevant techniques. The student will handle blood samples and synovial fluid samples.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 6

Simulated body approach to drosophila larva motion strategies

Description of the work program

Embodiment matters[1]. Animals, humans, and robots are not merely autonomous neural networks[2] tasked solely with resolving learning, representation, or classification challenges. The body, through its physical and biological 'hardware' constraints, the temporal continuity necessitated by real-world action, and the limitations and complexities imposed by internal states, plays a crucial role in shaping the central nervous system and the algorithms it deploys. Additionally, the representation of the body and its interactions with its immediate environments through proprioception can vary significantly depending on whether the body is rigid, possessing joints, muscles, and a skeleton (such as a mouse), or if it is fully deformable like the larva of Drosophila[3]. Embodiment is a key factor explaining why biological neural networks exhibit differences in design and functionality compared to artificial ones.

Deformable bodies, spanning from animals to 'soft robotics[4,5], constitute a topic of profound interest. They introduce high-dimensional challenges in control due to the extensive degrees of freedom associated with possible movements. Despite this, numerous animals, ranging from larvae to octopi, successfully manage their highly deformable bodies to navigate through various challenges, utilising both local and global computation. In the context of insect larvae, these computations can be executed with a notably limited number of neurons. This implies the existence of a constrained, low-dimensional latent space where the body's complex dynamics can be encoded, as well as an evolutionary strategy to encapsulate muscle control within a minimal neural population.

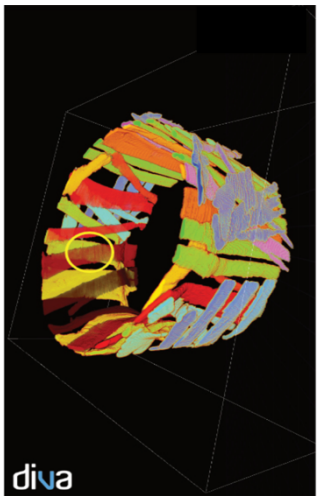

Fig 1. Volumetric representation (in DIVA[6]) of the segmented muscle of one segment of the *Drosophila* larva. The yellow circle on the left highlights overlapping muscle

The primary objective of this internship is to contribute to the development of a robust, simple 3D simulation platform that can accurately replicate the motor control dynamics observed in a Drosophila larva and capture the essential physics of larva body deformation and local motion dynamics. Leveraging the rich repository of data on the larva's behavioural data we will attempt at inferring parameters used in the simulations

Tutors/supervisors

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Selected publications

1. Kiverstein, J. & Miller, M. The embodied brain: towards a radical embodied cognitive neuroscience. *Frontiers in Human Neuroscience* **9**, (2015).
2. Goodfellow, I. *Deep learning*. (The MIT Press, 2016).
3. Winding, M. *et al.* The connectome of an insect brain. 2022.11.28.516756 Preprint at https://doi.org/10.1101/2022.11.28.516756 (2022).
4. Laschi, C., Mazzolai, B. & Cianchetti, M. Soft robotics: Technologies and systems pushing the boundaries of robot abilities. *Science Robotics* **1**, eaah3690 (2016).
5. Kim, S., Laschi, C. & Trimmer, B. Soft robotics: a bioinspired evolution in robotics. *Trends in Biotechnology* **31**, 287–294 (2013).
6. El Beheiry, M. *et al.* DIVA: Natural Navigation Inside 3D Images Using Virtual Reality. *Journal of Molecular Biology* **432**, 4745–4749 (2020).

Scientific or technical background required for work program

The successful intern should have one of the following backgrounds:

- Statistical or condensed matter physics, applied mathematics,
- Software engineer

Some fluency in Python and large-scale simulations is expected.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 7

Development of multistage vaccines for *Plasmodium vivax* malaria

Description of the work program

Plasmodium vivax remains a major public health problem in many parts of the tropical world. Standard malaria control efforts are less effective against *P. vivax* due to its unique biology including the ability to form latent hypnozoites in the liver that can emerge months or even years later to cause infection. An effective vaccine that can protect individuals against *P. vivax* could be a valuable tool to help elimination efforts. We propose to develop a multi-stage vaccine based on the *P. vivax* circumsporozoite protein (PvCSP) and receptor-binding domain, region II, of *P. vivax* Duffy binding protein (PvDBPII). We will use Spy Catcher-Tag technology to crosslink PvCSP and PvDBPII to AP205 bacteriophage surface protein to produce chimeric virus-like-particles (cVLPs). The immunogenicity of the cVLPs will be tested in C57BL/6 mice individually and in combination. Mice immunized with PvCSP-cVLPs will be challenged with transgenic *P. berghei* sporozoites expressing PvCSP to evaluate their protective efficacy. Sera from mice immunized with PvDBPII-cVLPs will be tested for inhibition of PvDBPII-DARC binding. Mice immunized with combination of PvCSP-cVLPs and PvDBPII-cVLPs will be tested both for protection against infection by *P. berghei* sporozoites expressing PvCSP and for inhibition of PvDBPII-DARC binding. Adjuvants including alhydrogel and Matrix M will be evaluated for optimal antibody responses. Constructs and adjuvants that yield high levels of protection (> 80%) against transgenic *P. berghei/*PvCSP infection and efficient inhibition of PvDBPII-DARC binding (IC50 > 1:100) will be selected as a vaccine candidate for *P. vivax* malaria.

Tutor/supervisor

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

1.

2. Hou MM, Barrett JR, Themistocleous Y, Rawlinson TA, Diouf A, Martinez FJ, Nielsen CM, Lias AM, King LDW, Edwards NJ, Greenwood NM, Kingham L, Poulton ID, Khozoee B, Goh C, Mac Lochlainn DJ, Salkeld J, Guilotte-Blisnick M, Huon C, Mohring F, Reimer JM, Chauhan VS, Mukherjee P, Biswas S, Taylor IJ, Lawrie AM, Cho JS, Nugent FL, Long CA, Moon RW, Miura K, Silk SE, **Chitnis CE***, Minassian AM*, Draper SJ*. 2023. Vaccination with *Plasmodium vivax* Duffy-binding protein inhibits parasite growth during Controlled Human Malaria Infection. **Sc. Trans. Med.** 15(704):eadf1782. doi: 10.1126/scitranslmed.adf1782. *Corresponding authors.

3. Martinez FJ, Guillotte-Blisnick M, Huon C, England P, Popovici J, Laude H, Arowas L, Ungeheuer MN, Reimer JM, Carter D, Reed S, Mukherjee P, Chauhan VS & **Chitnis CE**. 2023. Immunogenicity of a *Plasmodium vivax* vaccine based on the duffy binding protein formulated using adjuvants compatible for use in humans. **Sci Rep.** 13:13904. doi:.org/10.1038/s41598-023-40043-6.

4. Wagner MP, Formaglio P, Gorgette O, Dziekan JM, Huon C, Berneburg I, Rahlfs S, Barale JC, Feinstein SI, Fisher AB, Ménard D, Bozdech Z, Amino R, Touqui L, **Chitnis CE**. 2022. Human peroxiredoxin 6 is essential for malaria parasites and provides a host-based drug target. **Cell Reports.** 39(11):110923. doi:10.1016/j.celrep.2022.110923.

Scientific or technical background required for work program

The candidate should have studied modern biology and have a strong background in Biochemistry / Molecular Biology / Cell Biology / Microbiology. Students with laboratory experience and/or practical course work in at least one of these areas are encouraged to apply.

Title of the work program 8

Metabolism and Patterning Speed

Description of the work program

The time it takes for a fertilized egg to produce a feeding and sexually mature multicellular organism is both species-specific and variable between animal species. While differences in developmental speed across species are in part encoded in the genome, the genetic basis of developmental speed remains to be discovered. Here, we propose to use the fly eye to decipher the genetic basis of developmental speed in Drosophila.

The compound eye of adult Drosophila flies comprises ~750 light-receiving ommatidia that are arranged in a crystal-like pattern. These ommatidia form sequentially in the developing retina, with one new row of ommatidia appearing every 2 hours posterior to a moving differentiation front sweeping through the eye neuroepithelium. The molecular logic of the progression of the differentiation front is relatively well understood, with Hedgehog (Hh) signaling playing a critical role in moving the front forward (2). By contrast, the mechanisms that regulate the progression speed of the front are unknown.

We recently found that energy metabolism plays a key role in regulating the progression speed of this differentiation front (our unpublished results), consistent with recent findings showing that energy metabolism contributes to developmental speed in mammalian embryos (3). Thus, changes in metabolic activity appear to underlie differences in development speed across animal species. Additionally, we recently observed that lowering Hh signaling slows down the progression speed of the front (unpublished). Therefore, we now propose to investigate whether and how Hh signaling collaborates with metabolism to modulate the speed of the moving front in the developing fly eye.

This project will address two main questions:
• what is the impact of low Hh signaling and altered metabolism on the dynamics of fate decision in the eye?
• what is the impact of low Hh signaling on energy metabolism? Conversely, what is the impact of altered metabolism on Hh signaling?

These questions will be addressed using genetical and imaging approaches, making use of the unique tools that we have recently developed to study energy metabolism and fate dynamics in the developing fly eye.

References :
1. Esibuya and Briscoe 2017 Development PMID:29945985
2. Roignant and Treisman 2009 Int J Dev Biol 53:595-604
3. Diaz-Cuadros et al. 2021 bioRxiv https://doi.org/10.1101/2021.08.27.457974

Tutor/supervisor

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

C. Shard, J. Luna-Escalante, **F. Schweisguth** (2020) Neuralized regulates a traveling wave of Epithelium-to neural stem cell morphogenesis in *Drosophila*. **The Journal of Cell Biology**, 219, e202005035
Spotlight in JCB (2020) 219, e202009040

F. Schweisguth and F. Corson (2019) Self-organization in pattern formation. **Developmental Cell,** 49, 659-677 doi: 10.1016/j.devcel.2019.05.019

L. Couturier, K. Mazouni, F. Corson, **F. Schweisguth** (2019) Regulation of specific *E(spl)-HLH* genes by proneural factors shape output dynamics during bristle patterning in *Drosophila*. **Nature Communications**, 10, 3486

F. Corson, L. Couturier, H. Rouault, K. Mazouni and **F. Schweisguth** (2017) Self-organized Notch dynamics generate stereotyped sensory organ patterns in *Drosophila*. **Science** 356, 501, eaai7407

Scientific or technical background required for work program

Genetics and/or Cell and Developmental Biology

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 9

Actinobacterial cell division: understanding the molecular architecture of the divisome

Description of the work program

Understanding how one cell becomes two has always been a key question in cellular biology. Major differences exist between Archaea, Eukarya and Bacteria and even within the latter, the richness of cell shapes and cell wall compositions implies many specificities. Cell division has been a major target of antibiotics since the discovery of penicillin by Alexander Fleming in 1928. With the rise of antimicrobial resistance, which WHO deemed one of the ten utmost threats to global health in 2019, it is more crucial than ever to understand how cell division occurs in Bacteria.

Bacterial cell division requires the timely recruitment at the site of septation of a cell wall remodelling complex called the *divisome*, regulated both spatially and temporally to ensure the viability of the two daughter cells. characterising the molecular details of cell division has remained highly challenging due to the dynamic and membrane bound nature of these complexes. However, the recent technological developments in high-resolution cryo-microscopy, cutting-edge membrane technology and genetic tools has given a new impulse in the race towards unravelling the secrets of cell division in Bacteria at the molecular level.

In the lab, we use an integrative approach to study the detailed mechanisms of cell division: from *in vitro* biochemical characterisation and structure determination by crystallography and cryo-electron microscopy, to *in vivo* cell imaging and genetic engineering. We are especially interested in the medically relevant, human pathogen *Mycobacterium tuberculosis*, whose complex cell wall still remains mysterious. For our cellular studies we work with the non-pathogenic actinobacterial model organism *Corynebacterium glutamicum*. Our multidisciplinary perspective has recently been proven successful in gaining new insights in corynebacterial cell division [Martinez, et al., 2023; Sogues *et al.*, 2020].

The scientific outcomes will shed light on the regulation of a fundamental and cardinal process of bacterial cell biology. The benefits are diverse and range from an immediate knowledge of cell division to the opening of new concepts concerning the inner-workings of a living cell. Furthermore, since cell division is fundamental to all forms of life, a better understanding of how bacteria grow and divide at the molecular level is not only important for cell biology, but it is also expected to have a strong impact on biomedical research.

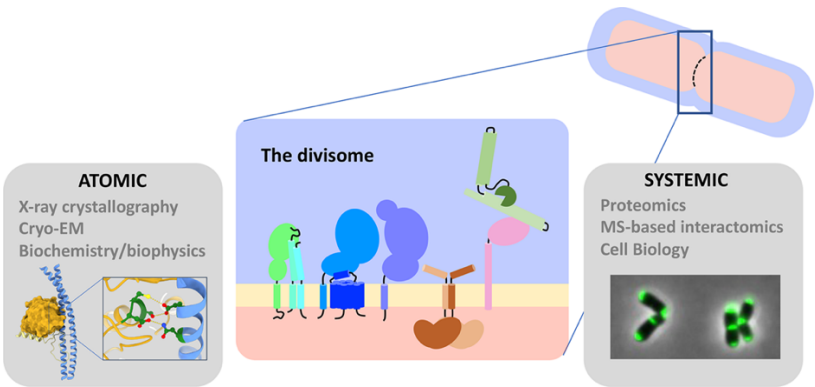

Figure 1: an integrative approach to understand corynebacterial cell division.

Tutor/supervisor

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

1. Martinez M, Petit J, Leyva A, Sogues A, Megrian D, Rodriguez A, Gaday Q, Ben Assaya M, Portela M, Haouz A, Ducret A, Grangeasse C, Alzari PM, Durán R#, Wehenkel A# (2023). Eukaryotic-like gephyrin and cognate membrane receptor coordinate corynebacterial cell division and polar elongation. 2023. Nature Microbiology 8, 1896–1910. # Corresponding author

2. Gaday Q, Megrian D, Carloni G, Martinez M, Sokolova B, Ben Assaya M, Legrand P, Brûlé S, Haouz A, Wehenkel A#, Alzari PM# (2022). Structural basis of FtsEX-independent RipA-mediated cell separation in Corynebacteriales. Proc Natl Assoc Sci USA, 119, e2214599119. #Corresponding author

3. Sogues, A., Martinez, M., Gaday, Q., Ben-Assaya, M., Graña, M., Voegele, A., VanNieuwenhze, M., England, P., Haouz, A., Chenal, A., Trepout, S., Duran, R., Wehenkel#, A. & Alzari#, PM. Essential dynamic interdependence of FtsZ and SepF for Z-ring and septum formation in Corynebacterium glutamicum. Nat Commun 11, 1–14 (2020). # Corresponding author.

Scientific or technical background required for work program

We are looking for a curious, motivated student, preferably studying for a University degree that provides her/him with general knowledge in either microbiology, molecular biology, biochemistry, biophysics or cell imaging. Previous lab experience would be beneficial. This internship represents an opportunity to be acquainted with a large range of techniques, and help us answer fundamentally and therapeutically important questions.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 10

Identifying the molecular composition and architecture of the Leptospira endoflagellum

Description of the work program

Spirochetes which include the agents of leptospirosis (*Leptospira interrogans*), syphilis (*Treponema pallidum*) and Lyme disease (*Borrelia burgdorferi*) have spiral-shaped cells and they evolved characteristically powerful swimming capabilities that enable them to rapidly disseminate through connective tissue, blood, and all organs. The motility of spirochetes is unique in that it is conferred by flagella (called endoflagella or periplasmic flagella) inserted at both poles of the cells and extended within the periplasm between the outer and inner membranes. The endoflagellum of spirochetes is more complex in terms of protein composition as compared to bacteria with extracellular appendages and our understanding of the function and architecture of spirochetal flagella remain poorly characterized. We propose to characterize the components of the endoflagellum and determine how these features facilitate Leptospira motility. We will generate mutants of genes encoding flagellar-associated proteins by using the allelic exchange and dcas9 approaches. We will test if deletion of each protein has an effect on cell morphology, motility (measurement of velocity), and filament geometry/morphology. Genes of interest will include genes encoding new putative flagellar-associated proteins identified by proteomic analysis of purified filaments from Leptospira spp. as well as genes encoding flagellar proteins showing apparent redundancy in the form of several paralogous isoforms. Characterizing the molecular determinants of the spirochete flagella and defining the mechanisms by which these bacteria move, shall uncover paradigm-shifting mechanisms of bacterial motility. Leptospira shall serve as a new paradigm for bacterial flagella and as an instrumental model to understand spirochete motility with high impact for serious public health issues including syphilis and Lyme disease

Tutor/supervisor

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

Diving into the complexity of the spirochetal endoflagellum. San Martin F, Fule L, Iraola G, Buschiazzo A, Picardeau M. Trends Microbiol. 2023 Mar;31(3):294-307. doi: 10.1016/j.tim.2022.09.010.

Role of the major determinant of polar flagellation FlhG in the endoflagella-containing spirochete Leptospira. Fule L, Halifa R, Fontana C, Sismeiro O, Legendre R, Varet H, Coppée JY, Murray GL, Adler B, Hendrixson DR, Buschiazzo A, Guo S, Liu J, Picardeau M. Mol Microbiol. 2021 Nov;116(5):1392-1406. doi: 10.1111/mmi.14831. Epub 2021 Oct 30. PMID: 34657338

An asymmetric sheath controls flagellar supercoiling and motility in the leptospira spirochete. Gibson KH, Trajtenberg F, Wunder EA, Brady MR, San Martin F, Mechaly A, Shang Z, Liu J, Picardeau M, Ko A, Buschiazzo A, Sindelar CV. Elife. 2020 Mar 11;9:e53672. doi: 10.7554/eLife.53672. PMID: 32157997

FcpB Is a Surface Filament Protein of the Endoflagellum Required for the Motility of the Spirochete Leptospira.Wunder EA Jr, Slamti L, Suwondo DN, Gibson KH, Shang Z, Sindelar CV, Trajtenberg F, Buschiazzo A, Ko AI, Picardeau M. Front Cell Infect Microbiol. 2018 May 8;8:130. doi: 10.3389/fcimb.2018.00130. eCollection 2018. PMID: 29868490

Gene silencing based on RNA-guided catalytically inactive Cas9 (dCas9): a new tool for genetic engineering in Leptospira. Fernandes LGV, Guaman LP, Vasconcellos SA, Heinemann MB, Picardeau M, Nascimento ALTO. Sci Rep. 2019 Feb 12;9(1):1839. doi: 10.1038/s41598-018-37949-x.

Scientific or technical background required for work program

Experience with molecular biology techniques such as PCR, molecular cloning, etc

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 11

Characterization of candidate proteins for their roles in DNA double-strand break repair and antigen receptor gene diversification.

Description of the work program

DNA double-strand breaks (DSBs) are toxic cellular lesions that must be efficiently repaired to maintain genome integrity and prevent the onset of pathological somatic mutations. The two main DSB repair pathways are non-homologous end joining (NHEJ) and homologous recombination (HR), with pathway choice and regulation being critical to preserve DNA integrity upon breakage.

In lymphocytes, antigen receptor diversity is generated through a unique cut-and-paste recombination mechanism termed V(D)J recombination, which shuffles pre-existing V-(D)-J DNA elements to create an almost unlimited repertoire of functional genes encoding for antigen receptor molecules. This process relies on the complex interplay of proteins that sense, signal and repair DNA DSBs and, as such, represent a unique paradigm to study the mechanisms of DSB repair.

We recently used mass spectrometry-based proteomics and CRISPR-Cas9 screening in recombining B lymphocytes to analyze the cellular response to DNA breaks generated during V(D)J recombination. In this project, we will use a combination of gene editing techniques and molecular and cellular assays to characterize candidate proteins for their roles in V(D)J recombination and DSB response and repair.

Tutor/supervisor

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

Lescale C and Deriano L (2023) V(D)J Recombination: Orchestrating Diversity Without Damage. In: Bradshaw Ralph A., Hart Gerald W. and Stahl Philip D. (eds.) *Encyclopedia of Cell Biology,* Second Edition, vol. 5, pp. 372-397. Oxford: Elsevier.

Libri A, et al. The (Lack of) DNA Double-Strand Break Repair Pathway Choice During V(D)J Recombination. *Front Genet.* 2022 Jan 5;12:823943. doi: 10.3389/fgene.2021.823943.

Vincendeau E, et al. SHLD1 is dispensable for 53BP1-dependent V(D)J recombination but critical for productive class switch recombination. *Nat Commun*. 2022 Jun 28;13(1):3707. doi: 10.1038/s41467-022-31287-3.

Rogier M, et al. Fam72a enforces error-prone DNA repair during antibody diversification. *Nature*. 2021 Dec;600(7888):329-333. doi: 10.1038/s41586-021-04093-y.

Yu W, Repair of G1 induced DNA double-strand breaks in S-G2/M by alternative NHEJ. *Nat Commun*. 2020 Oct 16;11(1):5239. doi: 10.1038/s41467-020-19060-w.

Scientific or technical background required for work program

Knowledge in genetics, genome integrity and molecular and cellular biology fields are highly desirable. Experience in cell culture, molecular biology, gene editing and genetic screen techniques would be beneficial.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 12

CRISPR-based regulation circuits for host-considerate protein bioproduction

Description of the work program

- Context

Bioproduction of chemicals and proteins is a key area in the era of the fourth industrial revolution. Resources (precursors, energy, enzymes) normally used by host cells for growth are diverted towards the production of desired molecules. Achieving maximal resource diversion without compromising the essential functions of the host is of critical importance but is also particularly challenging. **Synthetic biology** holds great potential to tackle this challenge. **Host-aware circuit design strategies** are needed.

The **secretion of heterologous proteins in yeast** perfectly illustrates the need for host-aware circuit design. Making yeast produce and secrete heterologous proteins is generally burdensome to the cell because the capacities of the secretory pathway are often exceeded.

- Problem

In recent works, using **cybergenetics approaches**, we have identified a **sweet spot for bioproduction**: the induction level should match exactly the maximal secretion capacities of the cells [1]. This level is specific to the heterologous protein produced.

Our goal is to engineer a self-tuning regulation system that maintains cells in their sweet spots. More precisely, we aim to build a CRISPR-based negative feedback regulation circuit that decreases the responsiveness of the cell to the external demand when stress is excessive.

- Approach

The self-tuning regulation system we designed is a complex gene circuit hence our strategy consists in characterizing parts separately before assembling them. Part characterization is essentially done.

The first task of the internship will be to better define the full circuit from selected parts using data of their characterizations.

Then, circuits will constructed using modular cloning (Yeast Tool Kit) and integrated in yeast strains secreting a range of proteins with different secretion bottlenecks. These strains will be tested using the **automated bioreactor platform** we recently pubblished [2] and the effectiveness of the embedded controller will be quantitatively evaluated by measuring the amount of secreted proteins in different conditions. Several iterations of the design, build and test steps might be needed to obtain effective and robust solutions.

Tutor/supervisor

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

1. Sosa-Carrillo S, Galez H, Napolitano S, Bertaux F, Batt G. Maximizing protein production by keeping cells at optimal secretory stress levels using real-time control approaches. Nat Commun. 2023 May 25;14(1):3028.
2. Bertaux F, Sosa-Carrillo S, Gross V, Fraisse A, Aditya C, Furstenheim M, et al. Enhancing bioreactor arrays for automated measurements and reactive control with ReacSight. Nat Commun. 2022; 13(1):3363.
3. Fox ZR, Fletcher S, Fraisse A, Aditya C, Sosa-Carrillo S, Petit J, Gilles S, Bertaux F, Ruess J and Batt G. Enabling reactive microscopy with MicroMator. Nat Commun. 2022; 13:2199

Scientific or technical background required for work program

Our program is composed of both experimental biology and computational biology. While looking for students having knowledge and skills in both fields, we will also consider applicants with strong background in one field and an appetence to learn about the other.

Recommended

- Knowledge in molecular biology
- Skills in programming, being able to understand a script

Bonus

- Past experience in a laboratory
- Programming in python, the main programming language used by lab
- Knowledge in modeling
- Notions of synthetic biology

Title of the work program 13

Lipid metabolism and ion homeostasis during progressive hearing loss: insights from clarin tetraspan proteins

Description of the work program

Hearing impairment stands as the most prevalent sensory deficit affecting individuals across all age groups. Over 50% of congenital deafness cases stem from hereditary factors. Additionally, hearing loss, which may also have genetic predisposition, can be attributed to other factors such as aging, acoustic trauma, ototoxic drugs like aminoglycosides, and noise exposure. Our research team has been dedicated to unraveling the intricate molecular mechanisms responsible for the progression of hearing impairment. Specifically, we have utilized two mouse models carrying human deafness genes, CLRN1 and CLRN2, to shed light on the critical role these genes play in normal sound-induced transduction within auditory hair bundles and synaptic transmission. These genes, known as Clarins, belong to the tetraspan-like protein family, which are known to directly interact with lipids to modulate their function and orchestrate cell membrane organization.

To identify a distinct signature associated with Clarin-related hearing disorders, we conducted RNAseq profiling on hearing organs from various Clarin mouse models. Ongoing analyses have pinpointed key proteins showing significant up- and down-regulation, identifying some key dysregulated pathways. Notably, lipid metabolism and ionic homeostasis have emerged as two of the top five pathways displaying dysregulation. From this wealth of information, we have carefully selected several candidate proteins originating from these disrupted pathways. These candidates are slated for testing through fluorescence biomolecular complementation (BiFC) assays to explore possible direct interactions with Clarins. Validated hits will be analyzed further in mutated in vivo conditions to substantiate their critical involvement in hearing.

Together, expected findings will help provide a comprehensive understanding of the precise mechanisms underpinning Clarin-mediated hearing loss. In doing so, we hope to pave the way for the development of therapeutic strategies designed to either prevent or decelerate the progression of hearing loss.

Tutor/supervisor

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Profile on http://www.researchgate.net/: Dr El-Amraoui A, head of the team	https://www.researchgate.net/profile/Aziz_El-Amraoui Team website: https://research.pasteur.fr/en/team/progressive-sensory-disorders-pathophysiology-and-therapy/

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

- Dulon, D., et al., *Clarin-1 gene transfer rescues auditory synaptopathy in model of Usher syndrom*e. Journal of Clinical Investigation, 2018. 128(8): p. 3382-3401.
- Dunbar, L.A., et al., *Clarin-2 is essential for hearing by maintaining stereocilia integrity and function.* EMBO Molecular Medicine, 2019. **11**(9).
- Delmaghani, S. and A. El-Amraoui, *Inner Ear Gene Therapies Take Off: Current Promises and Future Challenges.* Journal of Clinical Medicine, 2020. 9(7): p. 2309.

Scientific or technical background required for work program

Biochemistry, Western Blot, Protein-protein interactions, Mammalian cell culture, Fluorescence microscopy, Animal models

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 14

Stromal regulation of tissue homeostasis and inflammation

Description of the work program

The skin is a barrier tissue constantly exposed to the external environment. To respond adequately to infections and injuries, the skin is equipped with various populations to ensure protection from pathogens and promote repair upon injury. Dysregulation of these processes lead to an array of skin diseases associated with chronic inflammation or autoimmunity. The stromal microenvironment is highly heterogeneous and has been involved in skin disease pathogenesis, however the mechanisms remain poorly understood. In this project, we will investigate the stromal populations and signals involved in regulation of skin homeostasis /immunity, and dissect the underlying cellular and molecular mechanisms. Using mice models of skin pathologies (such as injury, psoriasis, scleroderma), we will decipher how dysregulation of these fundamental tissue signals lead to development of an "pathological tissue memory" leading to chronic inflammatory diseases. To that aim, we will use different experimental approaches including transcriptomics, genetic lineage tracing, flow cytometry, or confocal imaging, to investigate the stroma-immune cells-stem cells crosstalk.

Tutor/supervisor

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

- Di Carlo SE, Raffenne J, Varet H, Ode A, Cabrerizo Granados D, Stein M, Legendre R, Tuckermann J, Bousquet C, Peduto L. 2023. Depletion of slow-cycling PDGFRa^{+}ADAM12^{+} mesenchymal cells promotes antitumor immunity by restricting macrophage efferocytosis. **Nature Immunology** (Oct 5). 10.1038/s41590-023-01642-7. Online ahead of print.
- Jacob JM, Di Carlo SE, Stzepourginski I, Lepelletier A, Ndiaye PD, Varet H, Legendre R, Kornobis E, Benabid A, Nigro G, Peduto L. 2022. PDGFRα-induced stromal maturation is required to restrain postnatal intestinal epithelial stemness and promote defense mechanisms. **Cell Stem Cell**, 29(5): 856-868.

Scientific or technical background required for work program

Previous experience/ interest with mice models in vivo (if possible authorization)
Expertise with flow cytometry, fluorescence microscopy and/or transcriptomics (RNAseq)

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 15

Control of the innate immune response of epithelial cells 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. These cells are equipped with several sensing molecules capable of detecting pathogen associated molecular patterns (PAMPs) and to initiate an innate immune response to an infection. However, these cytokines are detected only in a minority of cells infected by *C. trachomatis*, and the inflammation remains globally low, indicating that the bacterial exert a control on the innate response of epithelial cells to infection.

C. trachomatis develop exclusively inside a vacuolar compartment and use a virulence associated non-flagellar type 3 secretion system (T3SS) to translocate a variety of chlamydial proteins into the cytoplasm of their host cell. Some of these so-called "effector" proteins are likely involved in the dampening of the host response to infection, but their identification has remained elusive. The host lab has identified a dozen of chlamydial proteins whose amino-terminal sequence is compatible with the T3SS. The aim of this internship is to identify, among these candidates, effectors that modulate the innate response to infection.

The intern will get training in molecular biology (cloning, RT-qPCR), tissue culture and cell biology technics (transfection, microscopy).

Tutor/supervisor

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

Stelzner, K., N. Vollmuth, and T. Rudel, Intracellular lifestyle of *Chlamydia trachomatis* and host–pathogen interactions. Nature Rev. Microbiol., 2023. 21(7): p. 448-462. doi:10.1038/s41579-023-00860-y

Ouellette SP, Blay EA, Hatch ND, Fisher-Marvin LA. CRISPR Interference To Inducibly Repress Gene Expression in *Chlamydia trachomatis.* Infec Immun. 2021;89(7):e0010821. doi:10.1128/IAI.00108-21

Tang, C., C. Liu, B. Maffei, B. Niragire, H. Cohen, A. Kane, A.C. Donnadieu, Y. Levy-Zauberman, T. Vernay, J. Hugueny, E. Vincens, C. Louis-Sylvestre, A. Subtil, and Y. Wu, Primary ectocervical epithelial cells display lower permissivity to Chlamydia trachomatis than HeLa cells and a globally higher pro-inflammatory profile. Sci Rep, 2021. 11(1): p. 5848.doi:10.1038/s41598-021-85123-7

Hamaoui, D, Cossé, M.M., Mohan, J. Lystad, A.H., Wollert, T. and Subtil, A (2020). The Chlamydia effector CT622/TaiP targets a non-autophagy related function of ATG16L1 PNAS 117(43):26784-26794 doi:10.1073/pnas.2005389117

Subtil A, Delevoye C, Balañá ME, Tastevin L, Perrinet S, Dautry-Varsat A. A directed screen for chlamydial proteins secreted by a type III mechanism identifies a translocated protein and numerous other new candidates. Mol Microbiol. 2005 Jun;56(6):1636-47. PMID: 15916612

Scientific or technical background required for work program

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

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 16

HIV nuclear mechanodynamics trigger viral fate

Description of the work program

Since the beginning of life on Earth, viruses have been at the origin of numerous pandemics that have threatened the lives of thousands of people. The study of how viruses and their hosts have co-evolved has been fertile ground for providing molecular insights into living systems broadly. Many of these studies have explored the biochemical and molecular interactions between viral and host factors in a cell-free context. However, such approaches do not address how the physical microenvironment created by viruses during infection impacts the host. Similarly, we know little about how the mechanical environment of the host cell impacts the viral life cycle. In order to further leverage the power of the virus-host relationship as a conduit for scientific discovery at the molecular, subcellular and cellular scales, here we propose a multidisciplinary strategy that combines quantitative biophysical approaches and cutting-edge techniques capable of dynamically interrogating steps of the viral life cycle. The overarching hypothesis of this proposal is that replication of viruses in the host nucleus applies mechanical forces within the compartment that remodel the chromatin landscape, thereby impacting both functional (e.g. gene expression and genome integrity) and physical (e.g. mechanical stiffness) properties of the nucleus.

Patent Pasteur & NeoVirTech: HIV-ANCHOR

Tutor/supervisor

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

1. pasteur-02548457v1 Blanco-Rodriguez G., Gazi A., B. Monel, Frabetti S., Scoca V., Mueller F., Schwartz O., Krijnse-Locker J., Charneau P., Di Nunzio F Remodeling of the core leads HIV-1 pre-integration complex in the nucleus of human lymphocytes. **J Virol.** 2020 **(Cover JVI 2020)**. doi: 10.1128/JVI.00135-20. Open Access
2. pasteur-03088393v1 Rensen E., Mueller F., Scoca V., Parmar J., Souque P., Zimmer C, Di Nunzio F.Clustering and reverse transcription of HIV-1 genomes in nuclear niches of macrophages, **EMBO J** doi.org/10.1101/2020.04.12.038067 Open Access 2021.
3. pasteur-03214327v1 Scoca V. & Di Nunzio F. The HIV-1 capsid: from structural component to key factor for host nuclear invasion. Review **Viruses**, MDPI, 2021, 13 (2), pp.273. ⟨10.3390/v13020273⟩.
4. pasteur-03214326v1 Scoca V. & Di Nunzio F Membraneless organelles restructured and built by pandemic viruses: HIV-1 and SARS-CoV-2. Review **JMCB**, Oxford UP, 2021, ⟨10.1093/jmcb/mjab020⟩

5. pasteur-03344209, v1 Guillermo Blanco-Rodriguez, Francesca Di Nunzio. The Viral Capsid: A Master Key to Access the Host Nucleus. **Viruses**, MDPI, 2021, 13 (6), pp.1178. ⟨10.3390/v13061178⟩. ⟨pasteur-03344209⟩ 2021-09-14
6. pasteur-04264224v1 Viviana Scoca , Renaud Morin , Maxence Collard , Jean-Yves Tinevez , Francesca Di Nunzio. HIV-induced membraneless organelles orchestrate post-nuclear entry steps. **JMCB**, 2022, 14 (11), ⟨10.1093/jmcb/mjac060⟩
7. pasteur-04126658v1 Francesca Di Nunzio. Stress-induced condensate switch awakens sleeping viruses **Cell Host & Microbe**, 2023, 31 (5), pp.679-680. ⟨10.1016/j.chom.2023.04.008⟩

Scientific or technical background required for work program

We are looking for highly motivated and team player individuals with a strong motivation in the following fields:

- virology
- biochemistry
- cell biology
- molecular biology
- image and signal processing
- biophysics

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 17

HIV nuclear mechanodynamics trigger viral fate

Description of the work program

Since the beginning of life on Earth, viruses have been at the origin of numerous pandemics that have threatened the lives of thousands of people. The study of how viruses and their hosts have co-evolved has been fertile ground for providing molecular insights into living systems broadly. Many of these studies have explored the biochemical and molecular interactions between viral and host factors in a cell-free context. However, such approaches do not address how the physical microenvironment created by viruses during infection impacts the host. Similarly, we know little about how the mechanical environment of the host cell impacts the viral life cycle. In order to further leverage the power of the virus-host relationship as a conduit for scientific discovery at the molecular, subcellular and cellular scales, here we propose a multidisciplinary strategy that combines quantitative biophysical approaches and cutting-edge techniques capable of dynamically interrogating steps of the viral life cycle. The overarching hypothesis of this proposal is that replication of viruses in the host nucleus applies mechanical forces within the compartment that remodel the chromatin landscape, thereby impacting both functional (e.g. gene expression and genome integrity) and physical (e.g. mechanical stiffness) properties of the nucleus.

Patent Pasteur & NeoVirTech: HIV-ANCHOR

Tutor/supervisor

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

8. pasteur-02548457v1 Blanco-Rodriguez G., Gazi A., B. Monel, Frabetti S., Scoca V., Mueller F., Schwartz O., Krijnse-Locker J., Charneau P., Di Nunzio F Remodeling of the core leads HIV-1 pre-integration complex in the nucleus of human lymphocytes. **J Virol.** 2020 **(Cover JVI 2020)**. doi: 10.1128/JVI.00135-20. Open Access
9. pasteur-03088393v1 Rensen E., Mueller F., Scoca V., Parmar J., Souque P., Zimmer C, Di Nunzio F.Clustering and reverse transcription of HIV-1 genomes in nuclear niches of macrophages, **EMBO J** doi.org/10.1101/2020.04.12.038067 Open Access 2021.
10. pasteur-03214327v1 Scoca V. & Di Nunzio F. The HIV-1 capsid: from structural component to key factor for host nuclear invasion. Review **Viruses**, MDPI, 2021, 13 (2), pp.273. ⟨10.3390/v13020273⟩.
11. pasteur-03214326v1 Scoca V. & Di Nunzio F Membraneless organelles restructured and built by pandemic viruses: HIV-1 and SARS-CoV-2. Review **JMCB**, Oxford UP, 2021, ⟨10.1093/jmcb/mjab020⟩

12. pasteur-03344209, v1 Guillermo Blanco-Rodriguez, Francesca Di Nunzio. The Viral Capsid: A Master Key to Access the Host Nucleus. **Viruses**, MDPI, 2021, 13 (6), pp.1178. ⟨10.3390/v13061178⟩. ⟨pasteur-03344209⟩ 2021-09-14
13. pasteur-04264224v1 Viviana Scoca , Renaud Morin , Maxence Collard , Jean-Yves Tinevez , Francesca Di Nunzio. HIV-induced membraneless organelles orchestrate post-nuclear entry steps. **JMCB**, 2022, 14 (11), ⟨10.1093/jmcb/mjac060⟩
14. pasteur-04126658v1 Francesca Di Nunzio. Stress-induced condensate switch awakens sleeping viruses **Cell Host & Microbe**, 2023, 31 (5), pp.679-680. ⟨10.1016/j.chom.2023.04.008⟩

Scientific or technical background required for work program

We are looking for highly motivated and team player individuals with a strong motivation in the following fields:

- virology
- biochemistry
- cell biology
- molecular biology
- image and signal processing
- biophysics

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 18

Development of a new immunotherapeutic approach against solid tumors to reverse T cell exhaustion and spark anti-tumor immunity (6-12 months).

Description of the work program

Background: Immunotherapy by immune checkpoint blockade (ICB, aPD1, aPDL1, e.g.) provides outstanding clinical benefits in some patients, however these successes are limited by the onset of primary and secondary resistances. Our project aims at proposing innovative immunotherapeutic approaches circumventing resistance to ICB. Specifically, we are developing interventions purposed to increase the infiltration of immune cells and optimize their fitness and functionality within tumors. To this end, we are developing a new approach based on the engineering of stromal cells (fibroblast) ex vivo to activate the secretion of one or multiple factors supporting intra-tumoral populations. These engineered stromal cells are then engrafted within solid tumors where they act as factories for the sustained and local production of immune factors. There is wide evidence that the onset of exhaustion in solid tumors is curtailing the aegis of anti-tumor T cells. Conversely, poorly differentiated stem-cell like T cell populations represent a good prognosis and their density correlates with the clinical responses to immunotherapy by ICB.

Aim: This project specifically addresses the screening of relevant cocktail of factors enabling the recruitment and expansion of the stem cell like compartment of tumor-infiltrating lymphocytes. We will focus on the selection of chemokines (CCL19, CXCL9, e.g.), growth factors (IL15, IL21, e.g.) and differentiation cues (costimulatory molecules, 41BB and DNAM ligands e.g.) that altogether enable to recruit, expand and differentiate immune populations.

Objectives and methods: The internship will consist in:

- producing retroviruses encoding key molecules to be tested,
- the production of engineered stromal cells over-expressing these factors upon retroviral transduction
- the engraftment of those engineered MSC within growing tumors in mice
- immunological evaluation of the fate of tumor-infiltrating lymphocytes by imaging and flow cytometry and also single cell RNAseq.

These experiments will necessitate a strong interest for cancer immunology and immunotherapy and enthusiasm with working with pre-clinical murine models of cancer. Longer internships (6 to 12 months) are preferred.

Tutor/supervisor

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

Engineered niches support the development of human dendritic cells in humanized mice.

Anselmi G, Vaivode K, Dutertre CA, Bourdely P, Missolo-Koussou Y, Newell E, Hickman O, Wood K, Saxena A, Helft J, Ginhoux F, **Guermonprez P**.
Nat Commun. 2020 Apr 28;11(1):2054.

Harnessing Mesenchymal Stromal Cells for the Engineering of Human Hematopoietic Niches.
Pievani A, Savoldelli R, Poelchen J, Mattioli E, Anselmi G, Girardot A, Utikal J, Bourdely P, Serafini M, **Guermonprez P.**
Front Immunol. 2021 Mar 15;12:631279. doi: 10.3389/fimmu.2021.631279.

Dendritic Cells.
Tussiwand R.*, Guermonprez P.*, Yona S.*, *: equal contribution
Book chapter In "William Paul's Fundamental Immunology" Edition 2022, M. Flajnik Editor. In press.

Tissue-resident FOLR2^{+} macrophages associate with CD8^{+} T cell infiltration in human breast cancer.
Nalio Ramos R, Missolo-Koussou Y, Gerber-Ferder Y, Bromley CP, Bugatti M, Núñez NG, Tosello Boari J, Richer W, Menger L, Denizeau J, Sedlik C, Caudana P, Kotsias F, Niborski LL, Viel S, Bohec M, Lameiras S, Baulande S, Lesage L, Nicolas A, Meseure D, Vincent-Salomon A, Reyal F, Dutertre CA, Ginhoux F, Vimeux L, Donnadieu E, Buttard B, Galon J, Zelenay S, Vermi W, **Guermonprez P**, Piaggio E, Helft J.
Cell. 2022 Mar 31;185(7):1189-1207.e25. doi: 10.1016/j.cell.2022.02.021.
2012

Transcriptional and Functional Analysis of CD1c^{+} Human Dendritic Cells Identifies a CD163^{+} Subset Priming CD8^{+}CD103^{+} T Cells.
Bourdely P, Anselmi G, Vaivode K, Ramos RN, Missolo-Koussou Y, Hidalgo S, Tosselo J, Nuñez N, Richer W, Vincent-Salomon A, Saxena A, Wood K, Lladser A, Piaggio E, Helft J, **Guermonprez P**.
Immunity. 2020 Aug 18;53(2):335-352.e8.

Scientific or technical background required for work program

The successful candidate is expected to have an academic background in:

- Cellular Immunology: understanding of major cells and processes of the immune system (antigen recoginition, T lymphocytes, dendritic cells…)
- Interest for immuno-oncology
- A strong motivation to develop new approaches in immunotherapy

A practical lab experience would be a plus, including in those technical areas:

- Basic cell culture of mammalian cells
- Lenti/retro virus design and production
- Murine models of tumors
- Flow cytometry
- Cellular imaging on frozen tissue section by confocal microscopy.
- Analysis of T lymphocyte activation and differentiation
- Single cell RNAseq and R-based analysis with seurat and relevant packages

Long internship (6-12 months) are much preferred.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 19

Human inner ear organoids production

Description of the work program

The developpement of new terapies is one of the main goals of our institute. In this sense, human organoids have become essential for modeling hearing damage. Organoids are a complement to animal models and open the way to molecular screenings that the Institute sets up with a view to precision medicine. For this raison, the cell culture facility wish to developped the activity of inner hear human organoides production to contribute to meeting new scientific challenges with therapeutic aims.

The aim of this project is the characterization of organoids of the audio-vestibular nervous and sensory system by dynamic, super-resolution imaging and imaging after tissue transparency. Through different methods of image analysis, the goal is to achieve a reproctibity and standarization in the production of human organoids.

Tutor/supervisor

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

- Koehler, K. R. & Hashino, E. 3D mouse embryonic stem cell culture for generating inner ear organoids. Nat Protoc 9, 1229–1244 (2014).
- Koehler, K. R. et al. Generation of inner ear organoids containing functional hair cells from human pluripotent stem cells. Nat Biotechnol 35, 583–589 (2017).
- Moore, S. T. et al. Generating High-Fidelity Cochlear Organoids from Human Pluripotent Stem Cells. SSRN Journal (2022) doi:10.2139/ssrn.4170188.
- Hocevar, S. E., Liu, L. & Duncan, R. K. Matrigel is required for efficient differentiation of isolated, stem cell-derived otic vesicles into inner ear organoids. Stem Cell Research 53, 102295 (2021).

Scientific or technical background required for work program

The student should have a background in biology and if possible an experience in cell culture.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 20

Versatile two-photon microscope with photo- stimulation for the study of the hearing system

Description of the work program

The institute…

The Hearing Institute (Institut de l'Audition, IdA) 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. The Institute is therefore setting up, a state-of-the-art imaging facility, which is now equipped with modern confocal microscopes for structural investigation of ear and brain tissues in vitro. However, the facility does not provide any equipment for imaging deep tissues *in vivo,* which is necessary to bridge the molecular and system scales and understand how cellular assemblies, in the ear and in the brain, construct the hearing function. To cope with this major issue, this project aims at building a versatile shared two-photon microscope for measurements and manipulations of the neural networks of the central auditory system and for optical investigation of 3D cochlear organoids.

The project…

The aim of the project is to build a completely homemade two-photon laser microscopy system featuring patterned illumination for photostimulation and free rotations around the sample. The system will be custom-built at low cost and tailored to the needs of five core teams in the institute. The majority of the elements has been bought and the construction of the two photon imaging part has started. The student will mount, align and characterize mostly the photo-stimulation part of the system.

This unique instrument will be used in particular for the observation of neural network activity through thousands of neurons and for the design of stimulation patterns allowing to reproduce artificially observed activity patterns. The combination of these two features will allow investigating the causality of specific neuronal activity patterns for auditory perception, and thereby identify the neural substrate of perception, but also provide new avenue for cochlear electrophysiology and development studies. It will, as well, open new opportunities to investigate high level properties of the auditory system such as its lateralization and plasticity in the context of hearing restoration.

Tutor/supervisor

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

Filipchuk A, Schwenkgrub J., Destexhe A, **Bathellier B**, Awake perception is associated with dedicated neuronal assemblies in cerebral cortex, Nature Neuroscience, 2022, 25(10):1327-1338.

Ducros, M., **Goulam Houssen, Y**., Bradley, J., Sars, V. de & Charpak, S. Encoded multisite two-photon microscopy. Proceedings of the National Academy of Sciences of the United States of America 110, 13138–43 (2013). doi:10.1073/pnas.1307818110

Scientific or technical background required for work program

The student should have a background in optics and if possible in biology.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 21

Importance of glycerol in the development of African trypanosomes in the tsetse fly

Description of the work program

African trypanosomes are flagellated protist parasites responsible for human African trypanosomiasis or sleeping sickness. They are transmitted by the bite of the tsetse fly. Their development in the insect is long (> 3 weeks) and complex, with several phases of adaptation in the midgut, proventriculus and salivary glands (> 8 stages). During their development, trypanosomes adapt their central metabolism according to the different carbon sources available (glucose and proline). On the other hand, the presence of certain metabolites in the digestive tract of the fly could also be involved in the regulation of the parasite development program. Our recent data show that glycerol could play a crucial role in these two functions. The aim of the project is to verify the importance of glycerol in the metabolism and differentiation of the early stages of the parasite in the tsetse fly. The development of some mutant trypanosomes lacking certain key enzymes involved in central metabolism (HK and GK for glycolysis/gluconeogenesis) or in sensory perception (AQP and PKA for signal reception and transduction) of glycerol (already engineered) will be studied and compared *in vivo* through experimental infections of tsetse flies (available in the laboratory). The student will therefore use different techniques of cellular and molecular biology, entomology and microscope imaging.

Tutor/supervisor

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

1. Stumpy forms are the predominant transmissible forms of *Trypanosoma brucei*. Jean Marc Tsagmo Ngoune, Parul Sharma, Aline Crouzols, Brice Rotureau. bioRxiv 2023.08.30.555461; doi: https://doi.org/10.1101/2023.08.30.555461 (In revision for **eLife**).
2. A multi-adenylate cyclase regulator at the flagellar tip controls African trypanosome transmission. Bachmaier S, Giacomelli G, Calvo-Alvarez E, Vieira LR, Van Den Abbeele J, Aristodemou A, Lorentzen E, Gould MK, Brennand A, Dupuy JW, Forné I, Imhof A, Bramkamp M, Salmon D, Rotureau B, Boshart M. **Nat Commun**. 2022 Sep 16;13(1):5445. doi: 10.1038/s41467-022-33108-z. PMID: 36114198.
3. Oxidative Phosphorylation Is Required for Powering Motility and Development of the Sleeping Sickness Parasite Trypanosoma brucei in the Tsetse Fly Vector. Dewar CE, Casas-Sanchez A, Dieme C, Crouzols A, Haines LR, Acosta-Serrano Á, Rotureau B, Schnaufer A. **mBio**. 2022 Feb 22;13(1):e0235721. doi: 10.1128/mbio.02357-21. Epub 2022 Jan 11. PMID: 35012336.
4. Redistribution of FLAgellar Member 8 during the trypanosome life cycle: Consequences for cell fate prediction. Calvo-Álvarez E, Bonnefoy S, Salles A, Benson FE, McKean PG, Bastin P, Rotureau B. **Cell Microbiol**. 2021 Sep;23(9):e13347. doi: 10.1111/cmi.13347. Epub 2021 May 14. PMID: 33896083.
5. Gluconeogenesis is essential for trypanosome development in the tsetse fly vector. Wargnies M, Bertiaux E, Cahoreau E, Ziebart N, Crouzols A, Morand P, Biran M, Allmann S, Hubert J, Villafraz O, Millerioux Y, Plazolles N, Asencio C, Rivière L, Rotureau B, Boshart M, Portais JC, Bringaud F. **PLoS**

Pathog. 2018 Dec 17;14(12):e1007502. doi: 10.1371/journal.ppat.1007502. eCollection 2018 Dec. PMID: 30557412.

6. Glycerol supports growth of the Trypanosoma brucei bloodstream forms in the absence of glucose: Analysis of metabolic adaptations on glycerol-rich conditions. Pineda E, Thonnus M, Mazet M, Mourier A, Cahoreau E, Kulyk H, Dupuy JW, Biran M, Masante C, Allmann S, Rivière L, Rotureau B, Portais JC, Bringaud F. **PLoS Pathog**. 2018 Nov 1;14(11):e1007412. doi: 10.1371/journal.ppat.1007412. eCollection 2018 Nov. PMID: 30383867.

Scientific or technical background required for work program

Experience in at least 2 of the following disciplines would be greatly appreciated:

- Parasitology
- Cellular biology
- Molecular biology
- Entomology
- Microscope imaging

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 22

Development of a high-dimensional flow cytometry panel applied to cryopreserved blood samples

Description of the work program

Flow cytometry is the method of choice for immunophenotyping in the context of clinical, translational, and systems immunology studies. New-generation spectral cytometers enable high-dimensional immune cell characterization from small sample volumes. For certain clinical trials/studies, it is often impossible to perform analysis of fresh peripheral blood at the time being, since frequently the recruitment centres and laboratories that perform analysis, are geographically very distant. In this case, blood could be preserved (fixed and frozen) before transportation to the laboratory of interest for the subsequent immune analysis. Another advantage of this approach is that all samples could be stored for a prolonged time and analysed simultaneously. Thus, the batch effect could be avoided or at least reduced. To this end, we plan to modify two antibody panels (for characterisation of adaptive and innate immune cell populations) previously developed to analyse fresh blood samples and develop a unique panel. This panel will be validated in both fresh and cryopreserved blood samples.

The selected candidate will have the opportunity to:

- Design a new panel using the available high-performant online tool
- Work in P2 laboratory with blood samples
- Use ID7000 (Sony BioTecnology) spectral cytometer
- Analyse high-dimensional flow cytometry data

Tutor/supervisor

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

Standardized high-dimensional spectral cytometry protocol and panels for whole blood immune phenotyping in clinical and translational studies.

Dott T, **Culina S**, Chemali R, Mansour CA, Dubois F, Jagla B, Doisne JM, Rogge L, Huetz F, Jönsson F, Commere PH, Di Santo J, Terrier B, Quintana-Murci L, Duffy D, Hasan M; Milieu Intérieur Consortium. Cytometry A. 2023 Sep 26. doi: 10.1002/cyto.a.24801. Online ahead of print. PMID: 37751141

Scientific or technical background required for work program

- Basic knowledge of immunology
- Basic flow cytometry training

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 23

Host-based approaches to improve tuberculosis treatment

Description of the work program

Tuberculosis (TB), which is caused by *Mycobacterium tuberculosis* (MTB), is the deadliest disease due to a single infectious agent, ahead COVID-19, HIV/AIDS and malaria. According to the most recent WHO report, 10 million new TB cases occurred and the disease killed 1.6 million individuals in 2022. Despite considerable efforts, TB remains a major public health problem. An effective vaccine against TB is still not available and multidrug resistant (MDR) strains of MTB are continually emerging. The fight against TB requires new strategies and a better understanding of host-pathogen interactions.

Within the laboratory, we are developing several projects aimed at 1) studying the role of NK cells in TB, 2) finding new molecules that enhance the resistance or bactericidal functions of innate immune cells, 3) understanding the impact of antibiotic treatment on the host immune system, and 4) improving TB treatment.

Depending on the length of the internship, the candidates will work on one of these projects. They will be expected to use a combination of cell biology, microbiology and immunology techniques. In particular, they will learn how to isolate human cells from blood, differentiate these cells into macrophages (the main targets of the bacterium) and infect them with fluorescent strains of MTB or with attenuated bacteria. The interactions between MTB and its host are then studied using advanced imaging techniques. Other approaches commonly used in the laboratory include genomics (RNA sequencing), flow cytometry, RT-qPCR, *in vivo* studies (mouse model of TB).

Tutor/supervisor

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

1 Maure, A. et al. An oxadiazole-based compound potentiates anti-tuberculosis treatment by increasing host resistance via zinc poisoning. bioRxiv (2023).

2 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).

3 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).

4 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).

5 Groschel, M. I. et al. Recombinant BCG Expressing ESX-1 of Mycobacterium marinum Combines Low Virulence with Cytosolic Immune Signaling and Improved TB Protection. Cell Rep 18, 2752-2765, doi:10.1016/j.celrep.2017.02.057 (2017).

Scientific or technical background required for work program

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

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 24

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 show 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

- Oliveira Mendes et al. SARS-CoV-2 E and 3a proteins are inducers of pannexin currents. *Cells*, 2023, 12(11), pp. 1474.
- 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.
- 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.
- Lafaye, Escriou *et al.*, Patent: Neutralizing antibodies directed to SARS-CoV-2 spike protein. PCT/EP2022/073498 filed on August 23, 2022.
- Escriou *et al.*, Patent: Measles-vectored COVID-19 immunogenic compositions and vaccines. PCT/EP2021/053540 filed on February 12, 2021.
- 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.
- Anna et al. High seroprevalence but short-lived immune response to SARS-CoV-2 infection in Paris. *Eur J Immunol*, 2021, 51(1):180-190.
- Grzelak et al. A comparison of four serological assays for detecting anti–SARS-CoV-2 antibodies in human serum samples from different populations. *Sci Transl Med*, 2020, 12(559): eabc3103.

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 ≥ 6 months.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 25

Deciphering hepatitis C virus genotype-specific interference with hepatocytes

Description of the work program

Hepatitis C virus (HCV) chronic infection ultimately leads to liver cirrhosis and hepatocellular carcinoma via both virus-driven and indirect mechanisms. Some HCV genotypes are more frequently associated with specific pathogenic outcomes, e.g. genotype 3 strains with high prevalence of steatosis, an abnormal accumulation of lipid droplets in liver cells, and metabolic disorders. The virus-induced mechanisms are thought to be mainly mediated by two viral proteins, the capsid protein (or Core) and the nonstructural protein 5A (NS5A), which have been involved in the deregulation of several hepatocyte pathways. We have performed a high-throughput proteomic analysis of hepatoma cells infected with a panel of intergenotypic recombinant viruses encoding NS5A from various genotypic strains associated with diverse steatosis grades in some cases. This work led to the identification of common and differential cellular proteins interacting with NS5A that may account for the hijacking of essential cellular processes for HCV life cycle and/or metabolic disorders.

The project of the Erasmus+ student will be to contribute to the study of the role of selected HCV NS5A cellular interacting partners during the infectious life cycle. This work will involve a variety of methodological approaches including but not limited to protein expression and analysis (transient expression in cells, expression from infected cells, co-immunoprecipitation, protein complementation assay, western blotting), cellular gene silencing, RT-qPCR.

Tutor/supervisor

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

- 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.
- Lafaye *et al.*, Patent: Neutralizing antibodies directed to SARS-CoV-2 spike protein, US provisional applications No 63/303,227 & No 63/303,252, filed on Jan. 26, 2022.
- Lesage et al. Discovery Of Genes That Modulate Flavivirus Replication In An Interferon-Dependent Manner. *J. Mol. Biol., 2022 Mar 30;434(6):167277.*
- Escriou *et al.*, Patent: Measles-vectored COVID-19 immunogenic compositions and vaccines. PCT/EP2021/053540 filed on February 12, 2021.
- 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.
- 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.
- Aicher et al. Differential Regulation Of The Wnt/B-Catenin Pathway By Hepatitis C Virus Recombinants Expressing Core From Various Genotypes. *Sci. Rep., 2018,* Jul 25;8(1):11185.

Scientific or technical background required for work program

Hands-on experience with virology techniques, protein western blotting, immunoprecipitation and/or gene silencing would be an asset. Training to work in BSL3 laboratory will be provided for students able to stay ≥ 6 months.

Erasmus+

Institut Pasteur, 2023-2024

Title of the work program 26

Parental effect in the mosquito *Anopheles* contributing to differential susceptibility of progeny to *Plasmodium* malaria parasites, a functional analysis.

Description of the work program

Malaria, a vector-borne disease, is still affecting heavily human populations in many developing countries, notably in Africa. The situation worsened in the last years as a possible consequence of the COVID-19 situation in those countries. *Plasmodium falciparum* is responsible for most cases world-wide and the majority of deaths due to malaria occurs essentially in Africa, where its major vector is *Anopheles gambiae*.

We previously discovered that a parental effect drives *An. gambiae* susceptibility to *P. falciparum* malaria parasite with progeny from older females being more susceptible to *P. falciparum* than progeny from young females and live longer. Thus, older females, that are the most epidemiologically important are also producing offspring with enhanced vectorial capacity due to higher susceptibility and higher longevity.

Maternal effect and more generally parental effects, at least in invertebrates, are associated with variation in the quality and quantity of nutrients that mothers provide to their eggs. There is however limited studies addressing the molecular mechanisms responsible for the phenotypes arising in progeny where the maternal/parental effected have been evidenced.

Our current fully funded project aims at analysing the molecular basis that render progeny from old females more susceptible to *P. falciparum* than progeny from young females. To this aim we are combining RNAs-Seq and state to the art proteomic analyses to characterize the gene regulatory network from adult progeny exposed or not to *P. falciparum*. Our working hypothesis is that adult progenies differ in their basal innate immunity and metabolic processes that would favor or hinder *Plasmodium* development.

Through a carefully design of the progeny to analyse, our approach will permit to disentangle the contribution of parental traits leading to differential susceptibility of progeny to *P. falciparum*. Those parental traits are : age of the mosquito mothers, the number of blood meals they received to produce progeny as well as the age of the sperm stored in their spermatheca. Indeed, females mate only once, so old females harbour old sperm while young females harbour young sperm.

As the genotypes of mothers and progeny are similar, results from this project should open the way for understanding/identifying epigenetic signatures controlling the studied phenotypes.

It will provide novel fundamental knowledge on the contribution of parental traits to differential susceptibility of progeny to *P. falciparum* and impact on their longevity, a previously unknown phenomenon.

In the context of a 6 to 9 month ERASMUS+ internship the selected candidate will be involved in functional analysis of candidate genes selected from both the RNAseq and proteomic analyses. The functional analyses will be based on RT (Reverse transcription)-qPCR analysis and RNAi knowdown experiments followed by relevant phenotypic analyses : susceptibility to *Plasmodium* and survival assay. In addition, depending upon time, a targeted small proteomic project could be proposed to investigate the proteome of spermatheca isolated from virgin and mated females, mated as young or old females. This analysis should help identifying the molecular contribution of young and aged sperm in the overall analysis of the parental effect leading to differential susceptibility of mosquito progeny to *P. falciparum* and their differential survival

Tutor/supervisor

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

1. Lavazec, C. And **Bourgouin, C**. Mosquito-based transmission blocking vaccines for interrupting *Plasmodium* development ; review, Microbes and Infection, Epub, May 22, 2008

2. *.Mitri, C*. Jacques, J.-C., Thiery, I. Riehle M.M., Xu J., Bischoff E., Morlais I., Nsango S.E., Vernick K.D., And **Bourgouin C**. 'Fine pathogen discrimination within the APL1 gene family protects Anopheles gambiae against human and rodent malaria species, 2009, PLoS Pathog *5*, e1000576. PMID: 19750215

3. Alison T. Isaacs , Nijole Jasinskiene , Mikhail Tretiakov , Isabelle Thiery , Agnes Zettor , **Catherine Bourgouin** , Anthony A. James, Transgenic Anopheles stephensi Co-expressing Single-Chain Antibodies Resist Plasmodium falciparum Development, PNAS, 2012, Jul 10;109(28):E1922-30. Epub 2012 Jun 11.

4. *Pondeville E*, Puchot N, Meredith JM, Lynd A, Vernick KD, Lycett GJ, Eggleston P, **Bourgouin C**. Efficient ΦC31 integrase-mediated site-specific germline transformation of Anopheles gambiae. Nat Protoc. 2014 Jul;9(7):1698-712. doi: 10.1038/nprot.2014.117. Epub 2014 Jun 19. PMID:24945385

5. *Pondeville E*, Puchot N, Lang M, Cherrier F, Schaffner F, Dauphin-Villemant C, Bischoff E, **Bourgouin C**. Evolution of sexually-transferred steroids and mating-induced phenotypes in Anopheles mosquitoes. Sci Rep. 2019 Mar 15;9(1):4669. doi: 10.1038/s41598-019-41094-4.PMID: 30874601

6. Goupeyou-Youmsi, J., Rakotondranaivo, T., *Puchot, N*., Peterson I., Girod R., Vigan-Womas I., Ndiath, M.O., **Bourgouin C.** (2019). "Differential contribution of *Anopheles coustani* and *Anopheles arabiensis* to the transmission of *Plasmodium falciparum* and *Plasmodium vivax* in two neighboring villages of Madagascar." Parasites & Vectors 2020 Aug 26;13(1):430. https://doi.org/10.1186/s13071-020-04282-0

7. Emilie Pondeville, Nicolas Puchot, JeanPhilippe Parvy, Guillaume Carrissimo, Mickael Poidevin, Robert M. Waterhouse, Eric Marois, **Catherine Bourgouin (**2020) Hemocyte-targeted gene expression in the female malaria mosquito using the *hemolectin* promoter from *Drosophila* Insect Biochem Mol Biol. 2020 May;120:103339.

8. Christian Mitri, Isabelle Thiery, Marie-Thérèse Lecoq, Catherine Thouvenot, Solange Touron, Annie Landier, Emmanuel Bischoff, **Catherine Bourgouin.** (2020). *Anopheles gambiae* maternal age and parous state control offspring susceptibility to *Plasmodium falciparum*. BioRxiv, doi: https://doi.org/10.1101/2020.01.27.922070

9. Tsapi, M. T., E. Kornobis, N. Puchot, S. English, C. Proux, J. *Goupeyou-Youmsi*, A. Sakuntabhai, Marie-Agnes-Dillies, R. Milijaona, R. Girod, M. O. Ndiath and **C. Bourgouin** (2021). "Differential transcriptomic response of *Anopheles arabiensis* to *Plasmodium vivax* and *Plasmodium falciparum* infection." bioRxiv: 2021.2005.2028.446219. doi: https://doi.org/10.1101/2021.05.28.446219

10. **Bourgouin, C.,** & Paul, R. (2021). [Flying high: How anopheles mosquitoes recolonize the arid Sahel and impact on malaria transmission]. *Med Sci (Paris), 37*(1), 11-14. https://doi.org/10.1051/medsci/2020249

11. Puchot, N., Lecoq, M.-T., Carinci, R., Duchemin, J. B., Gendrin, M., & **Bourgouin, C**. (2022). Establishment of a colony of Anopheles darlingi from French Guiana for vector competence studies on malaria transmission. *Frontiers in Tropical Diseases, 3*. https://doi.org/10.3389/fitd.2022.949300

Scientific or technical background required for work program

The candidate should have a general background in biology and molecular biology as well as interest in infectious diseases.
Knowledge in epigenetics mechanisms would be a plus.

No specific technical skills are required for this project except motivation and commitment to work on mosquitoes and acceptance of delicate experiments. Training will include mosquito production, dissection, DNA purification, dsRNA production and depending on the skill and time some bio informatic analyses.
The student will be hosted in C. Bourgouin group, member of the Biology of Host-parasite Interactions Unit directed by Artur Scherf. The Unit belongs to the Parasitology and Insect Vector department that will offer broad interaction with many PhD students and postdocs, as well as with junior and senior scientists of the department.