This Fellowship offers a grant to undertake a 2 to 3-month research internship at the Institut Pasteur, Paris, France.

**SUMMER RESEARCH INTERNSHIP AT THE INSTITUT PASTEUR**

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This booklet outlines Institut Pasteur laboratories that have accepted to take part in the HKU-Pasteur Research Pole Fellowship as hosting laboratories.

Please note that internship space for each of these laboratories might differ from year to year. The applicant can contact hkuip@hku.hk to check the availability of the chosen laboratory.

In this document, hosting laboratories are displayed under the name of the Department to which they are affiliated. Then, they are listed in alphabetical order by the Head of the laboratory's last name.
HKU-PASTEUR RESEARCH POLE FELLOWSHIP

LKS Faculty of Medicine
HKU-Pasteur Research Pole
香港大學-巴斯德研究中心

CELL BIOLOGY & INFECTION
The aim of our research group is to decipher the rich and promising interface between membrane trafficking, lipid domain remodelling, cytoskeleton polarization and cell division in eukaryotic cells.

Cell division and thus cell proliferation ultimately relies on cytokinesis, which leads to the physical separation of the two daughter cells at the end of mitosis. Defects in properly orienting the mitotic spindle and the cytokinesis plane, as well as failure in completing cytokinesis have been shown to promote tumorigenesis in vivo. In the past, we and others demonstrated through RNAi-based screens that membrane traffic is essential for the late steps of cytokinesis. This was at the time a surprise, since these two fields were considered as independent areas of cell biology.

Using live-cell imaging and advanced fluorescent microscopy, microfabrication techniques, genome-editing, high-content RNAi-based screens, analysis in human cells from patients and in mice in vivo, our lab is interested in the role of membrane trafficking in lipid and cytoskeleton remodeling at each step of animal cell division.

Our current work thus addresses how membrane traffic polarizes cell lipids and associated cytoskeletons to control cytokinesis and successful cell division in normal and pathological situations. We predict that our results are likely to be relevant beyond the fields of cell division and cancer, such as in cell migration or phagocytosis of pathogens.

LATEST PUBLICATIONS

Systemic infections result from the invasion of hosts by microbial pathogens. A critical pathogenic determinant of microbes is their capacity to translocate from the external environment into the host across mucosal barriers, disseminate systemically and reach protected tissues such as the central nervous system and the fetus.

Our research is focused on understanding the molecular mechanisms underlying the ability of microbes to target specifically host cells, cross mucosal, blood-brain and placental barriers, disseminate systemically and within tissues.
Giulia Manina heads the Junior Group of Microbial Individuality and Infection at the Institut Pasteur in Paris, and is part of the Laboratory of Excellence Integrative Biology of Emerging Infectious Diseases Program. During her doctoral studies at the University of Pavia, Italy, as a member of the EU FP6 New Medicines for Tuberculosis Consortium (NM4TB), she discovered the mechanism of action and the mechanism of resistance of a new anti-tubercular drug, now in phase-II clinical trials. For this work she was awarded the Novartis Prize in 2009. During her postdoctoral studies at EPFL, Switzerland, Giulia focused on mycobacterial phenotypic heterogeneity, working in the laboratory that pioneered the single-cell studies of mycobacteria.

Thanks to her achievements, she received the Swiss TB Award in 2015. Later in 2015, Giulia started her own research group, where she builds up a cutting-edge program on tuberculosis persistence at the single-cell level, using microsystems engineering approaches, live-cell imaging and omics. Her group is also involved in unconventional single-cell screenings and subpopulation biomarkers. Thanks to her expertise, Giulia recently joined the large European Consortium ERA4TB, which is an accelerator for the discovery of new and fast-acting antitubercular regimens. Giulia’s aspiration is to bring scientific innovation, aiming to enhance the impact on global health. She hopes that her research approaches will not only have significant implications for tuberculosis diagnostics and therapeutics, but can also prove useful against other communicable and non-communicable diseases.

LATEST PUBLICATIONS

Chromatin modifications, at the level of histones, are fundamental regulators of gene expression in eukaryotes as they control the access of the transcriptional machinery to the targeted promoter regions. Recent studies have found that chromatin modifications induced by bacterial pathogens interfere with the host transcriptional program. However, the mechanisms at play are poorly characterized and the role of these modifications for the host or for the bacterium remain unknown.

Research in our team is centered on this new facet of host-pathogen interactions using 2 bacterial models, Listeria monocytogenes and Streptococcus pneumoniae, a pathogen and a natural colonizer respectively. The main goal of our research is to characterize the role of chromatin modifications induced upon bacteria-host interactions and their long term consequences.

Our work is at the interface between microbiology, chromatin biology/epigenetics and innate immunity. This multidisciplinary approach will allow the discovery of strategies used by bacteria to reprogram host transcription either during colonization or acute infection, and also provide new insight into fundamental cellular processes such as tolerance to prolonged stimulation and epigenetic memory. In addition, understanding bacteria-induced epigenomic regulation of immune responses could transform our view of immunological memory in vertebrates thereby leading to the development of new antimicrobial agents.

**LATEST PUBLICATIONS**

**WEBSITE:** https://research.pasteur.fr/en/team/chromatin-and-infection/
One of the projects of BIA unit is to study the mechanobiology of migrating cells. As model, our group study Entamoeba histolytica a pathogenic amoeba, which is the etiological agent of amoebiasis. E. histolytica is a highly motile protozoan which motility is crucial to its survival in the human colon and to invade and destroy the tissue. Only 20% of the infected persons develop intestinal amoebiasis and thus under conditions not fully understood. Very few studies look at the biomechanisms of invasion of microbes at tissue level.

Our aim is to study the mechanobiology of the invasive process of E. histolytica by analyzing the role of amoebic and environmental factors (biological and mechanical) on its migration through the mucus and colonic tissue.

To decipher the impact of mechanical forces (such as the colonic peristaltic movement) and commensal bacteria on the epithelium responses and on E. histolytica pathogenicity, we are using as colon model organ-on-chip microfluidics device under stretch. We combine classical cell biology and molecular analysis to live imaging and quantitative image analysis using automated software, (developed in the BIA unit) based on automated image analysis to understand the contribution of tissue forces to homeostasis and diseases.

**SELECTED PUBLICATIONS**

- 2020 Ximu Deng; Rituparna Sarkar; Elisabeth Labruyere; Jean-Christophe Olivo-Marin; Anuj Srivastava, Modeling Shape Dynamics During Cell Motility in Microscopy Videos, 2020 IEEE International Conference on Image Processing (ICIP), Abu Dhabi, United Arab Emirates, 2020.

**WEBPAGE:** [https://research.pasteur.fr/en/team/bioimage-analysis/](https://research.pasteur.fr/en/team/bioimage-analysis/)
Jean-Christophe Olivo-Marin received the Ph.D. and H.D.R. degrees in optics and signal processing from Institut d’Optique Théorique et Appliquée, University of Paris-Orsay, France. He is the Head of the BioImage Analysis Unit at Institut Pasteur and the director of the institute Carnot Pasteur Microbes & Santé. He chaired the Cell Biology and Infection Department (2010-2014) and was CTO and Director of the Center for Innovation and Technological Research (2015-2017) at Institut Pasteur. He was a staff scientist at the European Molecular Biology Laboratory, Heidelberg, from 1990 to 1998. He is a Fellow of IEEE and of SPIE, an IEEE Signal Processing Society Distinguished Lecturer, and was Chair of the IEEE SPS Bio Imaging and Signal Processing Technical Committee (BISP-TC) (2009-2011), Chair of the IEEE International Symposium on Biomedical Imaging Steering Committee (2014-2016), General Chair of the IEEE International Symposium on Biomedical Imaging in 2008, and a senior area editor of the IEEE Signal Processing Letters (2013-2015). His research interests are in image analysis of multidimensional microscopy images, computer vision and motion analysis for cellular dynamics, and in mathematical approaches for biological imaging.

The Biological Image Analysis Unit (BIA) develops and improves on original and rigorous methodologies for the quantification of 3D multichannel image sequences in biological imaging, at the cellular and molecular level, but also at the level of organizations. This includes the spatial analysis of biomolecules, the dynamics of sub-cellular organelles, the biophysics of cell motility, the spatio-temporal orchestration of cellular trafficking, the spreading of pathogens or the analysis of social behaviour in mice. Our work focuses on mathematical imaging, biophysically augmented optical flow, active contours models, spatial statistics and deep learning. We also work on digital pathology and colour image analysis. Our mathematical tools are first developed in collaboration with biologists who provide images and biological questions. Then, our state of the art programs as well as those of other laboratories worldwide are made available to the scientific community through the free and open source software platform Icy developed in our unit.

LATEST PUBLICATIONS

WEBPAGE: https://research.pasteur.fr/en/team/bioimage-analysis/
Eukaryotic cells contain extensive internal membranes defining many compartments having each specific functions. However these organelles are constantly moving and reshaping, still retaining their identity. The maintenance of cell compartmentalization in eukaryotes is thus very complex and tightly controlled. Our team studies the intracellular trafficking of eukaryotic cells and its impact on the organization of the cell and tissues. We study in particular the pathways of entry into the cell (endocytosis) and exit pathways (secretion) and their links to plasma membrane composition, cell compartmentalization but also with intercellular communication (immunity) and host-pathogen interactions.

The target organ of our studies is the human intestine composed of multiple cells organized in 3D, acting as a tight barrier between the outside and the inside of an individual. This tissue is permanently exposed to microorganisms some being beneficial (microbiota) but others are detrimental like pathogens. The gut is also constantly subjected to physical forces such as variable oxygen pressure, fluid flow and peristalsis (stretching force). These parameters seem necessary for the organization of this tissue, so part of our work focuses on the role of the mechanical forces of the intestine on the integrity of this barrier. Our recent work using gut-on-chip technology, shows that the mechanical forces of the gut (particularly peristalsis) increases the effectiveness of intestinal infection by the bacterium Shigella (agent of bacillary dysentery).

Our team uses a set of techniques ranging from high resolution microscopy, single molecule tracking, robust image analysis, statistical classification, CrispR-CAS9 genetic editing 'organ on-chip.'

**LATEST PUBLICATIONS**


**WEBPAGE:** https://research.pasteur.fr/en/team/group-nathalie-sauvonnet/
The research focus of the lab is to understand the complex interplay of mitochondrial dynamics and metabolism in health and disease. Mitochondria are essential organelles whose morphology varies tremendously across cell types and tissues. Balanced fusion and fission events shape mitochondria to meet metabolic demands and to ensure removal of damaged organelles. The dynamism of mitochondria is highlighted by the dramatic changes in morphology they undergo in response to metabolic inputs. Mitochondrial fragmentation occurs in response to nutrient excess and cellular dysfunction and has been observed in cardiovascular and neuromuscular disorders, cancer, and obesity. The morphology of mitochondria is inextricably linked to its many essential functions in the cell and we are interested in understanding the relationship between mitochondrial shape changes and metabolism in the context of acquired and inborn human diseases.

Objectives. Mitochondria are essential organelles whose morphology varies tremendously across cell types. The physiological relevance of mitochondrial morphology and the mechanisms that regulate mitochondrial dynamics in vivo are poorly understood.

We seek to:
- Identify the metabolic signals that balance mitochondrial fusion and fission
- Define the molecular mechanisms of stress-induced fission
- Design strategies aimed at re-balancing mitochondrial dynamics in vivo
- Translate our experimental findings to acquired and inborn human diseases

Strategy.

Our research strategy builds upon frontier science in the areas of cell biology and biochemistry of mitochondria. We apply this knowledge to preclinical animal models and cellular models derived from patient biopsies to address fundamental translational knowledge gaps in rare genetic diseases of metabolism as well as common acquired age-associated diseases which include cardiovascular disease, cancer, and obesity.
We are investigating autophagy, which is the most versatile recycling machinery in human cells. Autophagy sequesters cytoplasmic material in a newly formed membrane vesicle, called autophagosome, and transports it to lysosomes. A major function of autophagy is to maintain cellular homeostasis by degrading protein aggregates or non-functional organelles which are potentially cytotoxic. However, starvation and toxic insults elicit another mode of action. Under these conditions, autophagy does not select cytoplasmic material for degradation but sequesters bulk cytoplasm. What sounds like wasting resources is indeed essential for cells to survive those conditions. Although the cell sacrifices functional proteins, organelles and ribosomes, it replenishes building blocks that are needed to maintain the most essential vital functions of human cells.

What happens if autophagy fails a major research focus of our team.

We are using a combination of cell biology, biochemistry, high resolution microscopy, electron tomography and genome editing tools.

**LATEST PUBLICATIONS**


**WEBPAGE:** https://research.pasteur.fr/en/team/membrane-biochemistry-and-transport/
Elucidating the molecular basis of cell polarity and mechanisms of intracellular trafficking are fundamental goals in cell biology, not only for the understanding of basic cell function but also because alteration of these processes underlies many diseases. The work in our lab is focused on the study of the molecular mechanisms regulating protein sorting and intracellular trafficking in polarized epithelial cells and neuronal cells, and on the mechanisms of protein(s) and organelle(s) exchanges between cells, with the aim of understanding how these pathways contribute to/are altered in diseases like cancer and neurodegenerative disorders.

To unravel these questions we have applied different approaches including molecular biology, protein/lipid biochemistry, biophysics, mathematical modeling, quantitative high resolution and live imaging in four projects listed below:

- **Project 1:** Mechanisms of GPI-anchored protein apical sorting and plasma membrane organization in polarized epithelial cells.
- **Project 2:** Prion-like proteins spreading in neurodegenerative diseases (NDs): role of Tunneling Nanotubes (TNTs).
- **Project 3:** Role of TNTs in tumor networking, heterogeneity, and resistance to therapy.
- **Project 4:** Unraveling the structure/function of TNTs in vitro and in vivo.

**LATEST PUBLICATIONS**

HKU-Pasteur Research Pole Fellowship

Computational Biology
We are a new computational team that researches algorithms for big biological data, such as next-generation sequencing data. Our background is in computer science and programming, yet the primary goal of the group is to perform computational research that is directly applicable to bioinformatics and biology. Our applications cover genomics, metagenomics, pan-genomics, transcriptomics and proteomics. Concretely, the group creates and implements algorithms and data structures into software tools, and also collaborates with biology groups. Some examples of recent projects are the development of data structures to index large collections of sequencing datasets, methods for improving bacterial genome assemblies with long reads, and genome assemblies (giraffe, gorilla Y, mountain goat). Our ongoing projects include the analysis of variants in Alzheimer’s disease whole-genome sequencing data, the development of algorithms on linked-reads sequencing data, and a search engine for all previously sequenced human RNA-seq experiments.

We can welcome early-stage researchers in bioinformatics who have experience with next-generation sequencing data analysis and wish to get involved in projects that involve tool development, ranging from fundamental algorithms design to cutting-edge sequencing data analysis.

LATEST PUBLICATIONS

C. Zimmer is a computational biophysicist. He holds a PhD in astrophysics from University Paris 11 and did a postdoc in space physics at UCLA (USA). He then moved to Institut Pasteur (Paris) for a second postdoc on image processing for biology. Since 2008, he heads the Imaging and Modeling Unit, which develops imaging and modeling approaches for biomedical research. Since mid-2020, he is also head of the Computational Biology Department of Institut Pasteur.

We are an interdisciplinary team with expertise in physics, optics, computer science, cell biology and microbiology.

Our lab develops advanced experimental imaging approaches and computational models and focuses on three research axes:

- understanding the dynamic 3D architecture of chromosomes and its implications for cellular function;
- developing single molecule super-resolution imaging methods;
- developing deep learning methods for biomedical applications.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/imaging-and-modeling/
DEVELOPMENTAL & CELL BIOLOGY
Laure Bally-Cuif is leading a Research Unit at the Institut Pasteur in Paris since 2016. Before this, she was a group leader at the Helmholtz Research center in Munich, Germany (1997-2010) and a CNRS Research Director at the NeuroPSI Institute in Gif-sur-Yvette, France (2010-2016).

The research interests of her lab focus on the mechanisms controlling the formation and activity of neural progenitor cells (NPs) / neural stem cells (NSCs) in the vertebrate central nervous system, using as main model the adult zebrafish brain. Her group notably contributed to promoting the zebrafish adult as a powerful model for the study of adult NSC properties. She is using this model to probe the molecular and cellular mechanisms controlling NSC pools formation, maintenance and recruitment, and driving the NSC quiescence/activation cycle, with specific emphasis on how population properties impact individual NSC cell behavior. Among recent findings, her lab identified key pathways controlling homeostasis of the NSC pool of the dorsal telencephalon (pallium), and traced the developmental source of adult pallial and midbrain NSCs, highlighting different NSC properties based on NSC origin. Her lab also developed an intravital imaging approach permitting to record over weeks the behaviour of adult pallial NSCs in their endogenous niche, opening unprecedented possibilities to analyse NSC behaviour in vivo. She used this approached combined with genetic clonal tracing to provide a comprehensive model of NSC dynamics in the adult vertebrate brain, and to address the spatial organization of NSC pools, its control and propagation through time.

**LASTEST PUBLICATIONS**

- Dray N, Than-Trong E, Bally-Cuif L, Neural stem cell pools in the vertebrate adult brain: Homeostasis from cell-autonomous decisions or community rules?, Bioessays 2020 Dec; (): e2000228. 2020

**WEBPAGE:** [https://research.pasteur.fr/en/team/zebrafish-neurogenetics/](https://research.pasteur.fr/en/team/zebrafish-neurogenetics/)
The general objective of our laboratory is to understand in molecular details the epigenetic functions of nuclear Argonaute proteins and their associated short RNAs in animals. We are using the nematode Caenorhabditis elegans as a model system to test the hypothesis that nuclear Argonaute proteins and their associated short RNAs constitute an RNA-based epigenetic system for propagating the memory of the transcriptional status of the genome during cell division or across generations.

Specifically, we are investigating:

- The molecular mechanism by which short RNAs regulate transcription and chromatin organization.
- The role of short RNAs in epigenetic inheritance during animal development.
- The function of short RNAs as an adaptive epigenetic system for propagating the memory of stress responses.

*C. elegans is an excellent model system to systematically address these questions.*

**LATEST PUBLICATIONS**


**WEBSITE:** https://www.cecerelab.com/
I did my bachelor studies in the Ecole Normale Supérieure in Paris. After a long hesitation between evolution, ecology and developmental and cell biology, a long internship working on C. elegans early development (in Pr. Seydoux lab, John Hopkins University) definitely pushed me toward cell and developmental biology side. My interest for quantitative approaches brought me to an interdisciplinary master (AIV, Paris) where I start being interested by morphogenesis. I then joined the laboratory of Thomas Lecuit (IBDM, Marseille, France) to start my PhD working on epithelial morphogenesis in early Drosophila embryo and the role of the modulation of cell-cell adhesion. I then moved to Switzerland in the group of Eduardo Moreno for my postdoc (IZB, University of Bern) working on cell competition.

The plasticity of living tissue is illustrated by their capacity to cope with massive perturbations and yet maintain their function and architecture. This plasticity is mostly based on their self-organizing property where every cell can adjust its behaviour/fate to local and tissue wide inputs. This includes the regulation of cell death and apoptosis. While the upstream regulators of apoptosis are well characterized, the processes that fine tune locally the rate of cell elimination and adjust the spatiotemporal distribution of cell death are not known. Similarly, the decision steps leading to the irreversible engagement in apoptosis have never been characterized. Finally the plasticity of cell death can also be co-opted by pre tumoural cells to eliminate ectopically wild type cells and expand in the tissue through “cell competition”. The long term goal of our group is to build a predictive framework that will help to define when and where an epithelial cell will die, both in physiological conditions or during competitive interactions. Combining quantitative live imaging, optogenetics, modeling and mechanical perturbations in Drosophila, we are focusing on 3 majors aims:
1. Characterizing the impact of mechanical stress on cell death during morphogenesis and cell competition
2. Characterizing systematically the distribution of cell death and study its buffering functions during development
3. Studying the regulation of the engagement in apoptosis and cell extrusion by caspases

LATEST PUBLICATIONS
The major objective of our group is to understand the cause and consequence of cellular plasticity in cancer and ageing. Although it has been increasingly recognized that adult somatic cells can acquire plasticity under both physiological and pathological conditions, the mechanisms underlying cell fate conversions are mostly unknown.

Cellular senescence is a form of stress response to various stimuli that leads to a stable cell-cycle arrest, which plays a crucial role in tumor suppression and negatively impacts healthy aging. Recent works have expanded its role in embryonic development and tissue regeneration.

Recently, we identified that cellular senescence could promote cellular plasticity and facilitate in vivo reprogramming in the skeletal muscle. Currently, we focus on understanding the interplay between senescence on cellular plasticity in the context of in vivo reprogramming, muscle regeneration, and breast cancer.

**SELECTED PUBLICATIONS**


**WEBPAGE:** [https://research.pasteur.fr/fr/team/cellular-plasticity-and-disease-modelling/](https://research.pasteur.fr/fr/team/cellular-plasticity-and-disease-modelling/)
Sigolène MEILHAC is a developmental biologist, leading the team of Heart Morphogenesis jointly affiliated to the Institut Pasteur and Institut Imagine, Paris, France.

Our aim is to understand how the heart acquires its shape to sustain its function. We are interested in the left/right asymmetry of the heart, essential for the establishment of the double blood circulation, and in the mechanisms of heart growth, underlying the efficiency of heart contraction. We address the coordination of cell behaviour in the context of mouse embryonic development, using genetic tools and state-of-the-art quantitative analyses of spatiotemporal gene patterning, cell behaviour and tissue shape changes. Our work on fundamental mechanisms of morphogenesis is relevant to congenital heart diseases, as explored in collaboration with clinicians.

**LATEST PUBLICATIONS**

- Desgrange A, Le Garrec JF, Meilhac SM, Left-right asymmetry in heart development and disease: forming the right loop, Development 2018 Nov;145(22).

**WEBPAGE**: [https://research.pasteur.fr/en/team/heart-morphogenesis/](https://research.pasteur.fr/en/team/heart-morphogenesis/)
Our lab is addressing curiosity-driven questions in the field of developmental biology: how do cell acquire different fates during development and produce stereotyped patterns of cell fates? In this context, how does self-organization, e.g. Turing-like process, combine with positional cues instructing cells about their position in the tissue? To decipher the inner logic of fate decisions in time and space, our laboratory is using fruit flies as it provides outstanding tools to examine in a rapid and with unsurpassed temporal and spatial resolutions the effects of controlled perturbations.

We are currently investigating how patterns of cell fates emerge during the development of sensory organs. We have recently shown that a self-organized process mediated by Delta-Notch signaling operates at the tissue scale to produce a stereotyped pattern of bristle in the adult fly (Corson et al., 2017). A similar self-organized process can produce a regular pattern of founder photoreceptor cells, R8, in the eye. Using live imaging, we have discovered that a key and conserved transcription factor involved in generating this pattern is expressed in a pulsatile manner. We hypothesize that these pulses may contribute to the precision of the R8 pattern.

In this project, you will measure through live imaging the precision of the R8 pattern and test the role of transcription factor pulses in achieving precision. Through this project, you will learn about fly genetics, live imaging, transcription factor dynamics, cell-cell interaction via the Notch receptor and you will discover how multicellular organisms are built through highly precise patterning mechanism.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/4d/
Shahragim Tajbakhsh obtained a Doctor of Philosophy degree in Biology from Carleton University, Canada (1988) working on the molecular biology of viruses. Following postdoctoral research at the Pasteur Institute he established an independent group in 2001 called "Stem Cells & Development" to study how stem cells establish and regenerate organs and tissues, with a focus on skeletal muscle. Our aim is to investigate stem cell properties during development and postnatally to understand how skeletal muscle is established, and how it regenerates during disease, and after injury. Areas of focus include quiescence, niche, self-renewal, symmetric and asymmetric cell divisions, ageing.

Prof. Tajbakhsh is an EMBO member, former Head of the Dept. of Developmental & Stem Cell Biology and co-Director of the "Laboratory of Excellence" Consortium, REVIVE, regrouping leading labs working on stem cells (2011-2024). He is member of 2 scientific councils for associations, several SABs and presides on editorial boards of 4 scientific journals. He has participated in a number of EU consortia (FP6, EuroStemCell; FP7, EuroSyStem, Optistem, NotchIT) and received several awards including the Chair of Excellence Louis Pasteur (Institut Pasteur, 2017) and the French Academy of Sciences/Fondation Generale de Santé, for achievements in stem cell research.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/stem-cells-and-development/
GLOBAL HEALTH
LABORATORY - Previously controlled bacterial infections can re-emerge due to antibiotic resistance or vaccine escape. Species of pathogenic bacteria comprise a huge amount of genotypic and phenotypic diversity. Our lab is interested in the diversity, evolution and epidemiology of bacterial pathogens and in the links between the genotypic and phenotypic (ecology, colonization, transmission, virulence, antibiotic resistance, immune response) diversity of the strains within particular species. We focus on three pathogens of high public health importance: Klebsiella pneumoniae, which causes various types of infections including urinary tract, respiratory and blood infections; Bordetella pertussis, the agent of whooping cough; and Corynebacterium diphtheriae, the agent of diphtheria. We use genomics, proteomics, bioinformatics and immunological approaches as well as in-vivo and in-vitro models of infection. We also develop databases of bacterial genotypes and strain nomenclatures that facilitate global collaborative surveillance of bacterial pathogens.

CBRIP - The Centre de Ressources Biologiques de l’Institut Pasteur, CRBIP, was created in 2002 as a transversal functional structure that encompasses the five biobanks of the Institut Pasteur, Paris, for a common strategy aligned with the strategic plan of the Institute.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/member/sylvain-brisse/
I am a medical epidemiologist (MD in 1988 at Paris V, specialisation in rheumatology in 1990, Paris V, and DrPH from Harvard School of Public Health in 1993) specialized in infectious diseases epidemiology. After working at WHO at the clinical research unit of the Global Program on AIDS (1993-1994), I spent five years in Ethiopia and two years in the Netherlands working as the Program Manager of the Ethio-Netherlands AIDS Research Project (1994-2001). In 2002, I joined Institut Pasteur to launch the Emerging Diseases Epidemiology unit. There, my focus has been on viral hepatitis C and emerging infections such as the SARS and the MERS-CoV.

The Emerging Diseases Epidemiology Unit was founded on July 1st, 2001. Its mandate was to develop its own research agenda in the field of infectious diseases epidemiology, and to provide expertise in epidemiology and biostatistics to other laboratories. Based on the potential for collaborations with the international network of Institut Pasteur, and on our past experience in international health, we decided to focus on the epidemiology of infectious and tropical diseases in resource-limited countries.

Main projects include hepatitis C in Egypt, children diarrhea in Central African Republic, Buruli ulcer in Cameroun, acute encephalitis in Vietnam, bacterial meningitis in Niger, and emerging viruses (MERS-CoV). Emphasis has been put in clinical research, i.e., cohort studies and clinical trials. In addition, four staff members, Yoann Madec, Loïc Chartier, Lénaïg Lefouler and Laura Tondeur provide transversal support to all projects of the unit in biostatistics and data management.

LATEST PUBLICATIONS
Tamara Giles-Vernick currently conducts research at the interstices of medical anthropology and ethnohistory (historical research using anthropological tools), investigating infectious disease transmission and global health interventions. She currently coordinates SoNAR-Global, a European Commission-funded (Horizon 2020) global social sciences research network for preparedness and response to infectious threats. A specialist in the medical anthropology and history of central and west Africa, her current research focuses on emerging zoonotic diseases and epidemics, including the COVID-19 pandemic. She is conducting a national study for Ebola preparedness and response for UNICEF in the Central African Republic. She also directs the MICROTONE study, which offers a pre-history of zoonotic disease emergence; the study brings together anthropological-historical analyses with comparisons of microbial and viral profiles among people, domesticated animals and wild animals along an ecological gradient in the Democratic Republic of Congo. She has also led a three-country study on the anthropology, history and geography of human-nonhuman primate contact and emerging zoonotic diseases in central Africa. In addition, she has published on viral hepatitis (diagnostics, linkage to care, vaccination), Ebola, Buruli ulcer, the historical emergence of HIV in Africa, global health in Africa, the history of influenza pandemics, and environmental history.

The Anthropology & Ecology of Disease Emergence Unit is a team of social sciences researchers focusing on multiple global health problems. We are anthropologists, historians, sociologists and ecologists working primarily in sub-Saharan Africa. Some of our projects address human-animal and human-environment interactions and emerging diseases. We are particularly concerned with mobilizing our research to contribute to preparedness and response to epidemic outbreaks, including COVID-19. Others projects focus on infant health and vaccination, as well as the problems of diagnosis, monitoring and treatment of viral hepatitis, particularly hepatitis B in sub-Saharan Africa. We also work in close collaboration with other teams at Institut Pasteur and in the Pasteur network.

LATEST PUBLICATIONS

- Brett Finlay...Tamara Giles-Vernick*, "The hygiene hypothesis, the COVID-19 pandemic, and consequences for the human microbiome", Proceedings of the National Academy of Sciences (forthcoming).

We are a multi-disciplinary team working on the interface between physical sciences, engineering, mathematical modeling, and applications of these fields to biological sciences.

Microfluidics: In recent years we have developed a large set of microfluidic tools to culture and observe cells (bacteria, mammalian cells, protists, …) under well-controlled conditions of a confined microchannel. These tools are based on easy to use droplet manipulations, coupled with some robust chemical and biological protocols. The engineering of these tools has been coupled with a strong physical modelling aspect that allows us to understand the limits and capacities of the droplet manipulation, while also pointing us to new innovations.

Biological focus: Our current work is more focused on using these tools to gain new understanding of biological processes, by addressing biological questions through quantitative measurements and mathematical modelling, in a quantitative biology approach. This combination now allows us to obtain new types of information on the cells under normal or stressed conditions.

Example projects: We are applying this approach to bacterial cells, namely to understand the emergence of antibiotic resistance in small populations of cells. We are also studying three-dimensional cultures of mammalian cells, which are thought to represent in vivo conditions much better than traditional 2D cell culture. Here, we are questioning the link between distribution of mechanical forces within a 3D culture and the biological function of the individual cells.

Technology transfer: In addition to the fundamental scientific research that we perform, we are also interested in transferring our technologies to companies. This transfer allows the innovations that emerge from our lab to become useful to a large number of other researchers, in a way that cannot be achieved by academic groups. The technology transfer can take place either by the spinning-off of startup companies or by licensing agreements.

Group: Our group is made up of several bright scientists wishing to work across scientific boundaries. As part of our recent installation on the Pasteur campus, we are looking to recruit several brilliant post-docs wishing to work along areas combining physics and engineering with biology.

LATEST PUBLICATIONS

- Tomasi RF, Sart S, Champetier T, Baroud CN, , Individual Control and Quantification of 3D Spheroids in a High-Density Microfluidic Droplet Array., Cell Rep 2020 May; 31(8): 107670.2020
Ana Cumanos research focuses on analyzing the molecular pathways that determine the differentiation of the first wave of thymic seeding progenitors that are required for the maturation of the medullary epithelial cells that eliminate autoreactive T cells throughout life.

The Lymphocytes and Immunity Unit, attached to the Immunology Department of the Institut Pasteur, was created on March 1st, 2020 and is the follow up of: the Lymphopoiesis unit created in January 2011 the Unit for Lymphocyte Development created in 1998.

It joins the Inserm unit U1223 (previously U668) “Physiopathologie du Système Immunitaire” directed by James Di Santo. Since 2014, the Lymphocytes and Immunity unit is under contract with Université Paris Diderot.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/lymphopoiesis/
Caroline Demangel trained in the National Institute of Agronomy Paris-Grignon (AgroParisTech). After a PhD in Biotechnology in the Bertin company (Plaisir, France), she opted for a career in academic research. She did a post-doc in the Centenary Institute (Sydney, Australia), designing and testing anti-tuberculous vaccines that target dendritic cells in Warwick Britton’s Lab. Back in Paris in 2002, she joined the team of Stewart Cole at the Institut Pasteur to develop novel approaches to mycobacterial disease diagnosis and treatment, with a particular focus on Leprosy and Buruli ulcer disease. Since 2011, she’s been directing the “Immunobiology and Infection Unit in the Immunology Department of the Pasteur Institute.

Pathogenic mycobacteria constitute a major cause of mortality and morbidity worldwide. Those causing Tuberculosis, Leprosy and Buruli ulcer, the most common mycobacterial diseases, have in common the ability to escape protective immunity. The Demangel Lab studies the mechanisms by which pathogenic mycobacteria establish chronic infections in humans, in particular the bacterial virulence factors interfering with cellular immunity and metabolism. The aim of these studies is to find innovative approaches to better treat mycobacterial infections, and identify novel natural compounds with therapeutic potential.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/immunobiology-of-infection/
Darragh Duffy leads the Translational Immunology lab at the Institut Pasteur, Paris and is co-coordinator of the LabEx Milieu Interieur project. The overall goal of his research is to better understand the fundamental mechanisms behind inter-individual differences in immune responses, and apply these discoveries to relevant clinical questions. To do this they use cellular mechanistic models, population immunology cohorts, and experimental clinical studies in infection and autoimmunity. They work closely with clinical collaborators with the goal that the research findings will help to develop new patient management strategies. For fundamental questions related to understanding immune variability they apply systems immunology approaches to diverse phenotypes and integrate with genetic and environmental factors.

Selected projects:
- Understanding Immune Variability. Applying systems immunology to a cohort of well-defined healthy donors (Milieu Intérieur) to dissect the determinants of healthy immune responses.
- Predictive biomarkers of treatment response/disease. Experimental medicine studies to identify predictors of non-response to treatment in TB patients, predictors of retinopathy development in T1D patients, or clinical outcome in COVID-19.

LATEST PUBLICATIONS

WEBPAGE:https://research.pasteur.fr/en/team/translational-immunology/
Microbiota, lymphoid cells and “stromal” cells develop a crosstalk that allows maintaining homeostasis, organize defense, and resolve inflammation to restore tissue integrity. Deregulation of this crosstalk prolongs inflammation or prevents the healing process, resulting in chronic inflammatory pathologies. Our previous work has led us to define central actors among pro-inflammatory lymphoid and stromal cells (in collaboration with the team of Lucie Peduto, https://research.pasteur.fr/en/team/group-lucie-peduto/), and to identify components of the symbiotic microbiota that efficiently modulate immunity.

Immunity comes into mainly 3 types of effector responses directed against intracellular microbes and tumors, large parasites or extracellular microbes. These responses are orchestrated by dendritic cells (DCs) and regulated by T (helper) Th1, Th2 and Th17 cells. Three types of ILCs have recently been described that mimic the activity of Th cells and that are termed ILC1, ILC2 and ILC3. As ILCs act promptly upon infection and injury, and express large amounts of effector cytokines, it is expected that they play an important role early in the regulation of immune responses. To directly explore this hypothesis, we have generated a panel of transgenic mice that allow for the timed ablation of each individual subset of ILCs, without damage to other immune cells. As ILCs are also involved in inflammatory pathology in response to chronic injury and metabolic stress, we explore how ILCs can be manipulated to restore normal immune functions, and extend our findings to human disease.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/microenvironment-and-immunity/
MICROBIOLOGY
DEPARTMENT - Besides their major role in many infectious diseases, bacteria also serve as models to understand fundamental biological mechanisms. The research performed in the Department of Microbiology mainly focuses on the molecular characterization of functions that enable bacteria to interact with their environment and, in some cases, to cause diseases. The scientists of the Department of Microbiology study various bacteria and Archaea (and their viruses) as model systems to analyze fundamental biological processes at the population, cellular and molecular levels. They also focus on mechanisms rendering some of these microorganisms virulent and enabling them to evade the host immune system, or to develop resistance to antibiotics. For these studies, the scientists of the Department of Microbiology possess a wide range of expertise and use diverse integrative approaches to improve our understanding of the biology of these microorganisms. These studies also constitute a prerequisite for the development of new therapies or new diagnostic tools that can be used to treat or prevent bacterial infections.

GROUP - Bacteria are remarkable models for biology and have phenotypic characteristics of great cognitive, health or biotechnological values. Most bacteria are constantly exposed to fluctuating environments, thus are ideally set to detect, react and adapt to various stress conditions. The Pasteur unit “Adaptation to stress and metabolism of enterobacteria” aims to understand the stress response at the populational, cellular and molecular level. Our unit comprises 12 scientists, including Pasteur and CNRS researchers, engineers and technicians, post-docs and students. We study how a wide range of basic functional processes are modified, and possibly coordinated, to control cellular homeostasis. Our research mainly uses E. coli as a model, but concepts will be as well tested on pathogens such as Salmonella or Shigella. Focusing on two global cellular processes, Fe-S cluster biogenesis and lipid homeostasis, allows us to study the impact of stress on aerobic and anaerobic metabolism, cell envelope and membrane homeostasis, redox changes, limitation of nutrients, metabolic and antibiotics stresses. Molecular, biochemical and genetic approaches, as well as cutting-edge technologies (-omics, imaging, single-cell analysis), aim to achieve an integrated and mechanistic vision of the bacterial cell. To multiply and diversify the ways to approach a process is very rewarding, and we collaborate with biochemists, structuralists, chemists, biophysicists, bioinformaticians and phylogeneticists.

LATEST PUBLICATIONS

- Bartoli J, Citerne S, Mouille G, Bouveret E, Field B, , Quantification of guanosine triphosphate and tetraphosphate in plants and algae using stable isotope-labelled internal standards., Talanta 2020 Nov; 219(): 121261. 2020

WEBPAGE: https://research.pasteur.fr/en/member/frederic-barras/
The Synthetic Biology Group is interested in applying genetic engineering technologies to better understand pathogenic bacteria and fight them. The rise of emerging pathogens and antibiotic resistances is becoming a major public health issue. Using engineering principles we are creating new strategies to quickly decipher the mechanisms of bacterial virulence and provide tools to specifically kill antibiotic resistant and virulent bacteria. In particular we are studying the bacterial immune system known as CRISPR, and developing novel CRISPR tools to edit bacterial genomes, control their gene expression and specifically eliminate dangerous bacteria.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/synthetic-biology/
She was born in Belgium and obtained her Master degree from the University Pierre et Marie Curie, Paris (France). She completed her PhD studies at the Institut Pasteur, Paris (France) on the regulation of the expression of the central genes of the Escherichia coli PEP-dependent phosphotransferase system under the supervision of Professor Antoine Danchin (former HKU-Pasteur Research Centre director). During her postdoctoral fellowship, she moved from fundamental to medical microbiology and studied the control of the expression of the pili of the bacterial pathogen Neisseria gonorrhoeae. She is currently a Research Director at the Institut Pasteur and head of the Helicobacter Pathogenesis group since 2008, a team of 8 people in total. Between 2014 and 2019, she was head of the Microbiology department of the Institut Pasteur. The research in her group focuses on the pathogenesis of the gastric bacterial pathogen Helicobacter pylori by studying both the bacterial virulence factors and the host response. H. pylori colonizes the stomach of about half of the human population worldwide. H. pylori is an extraordinarily successful pathogen adapted to colonization of a unique niche, the acidic stomach. Infection by H. pylori is chronic and can evolve from gastritis to severe pathologies such as peptic ulcers and gastric cancer accounting for about 800,000 deaths per year worldwide. Gastric cancer develops in 1-3% of the infected individuals and constitutes the third cause of cancer related death in the world. H. pylori is till now the only bacterium to be recognized by IARC as a type 1 carcinogenic agent.

Current projects of the laboratory aim at
1) Identifying and characterizing the H. pylori factors and mechanisms that make this bacterium a successful and persistent pathogen colonizing the stomach, a hostile acidic niche. One of these factors is the metal nickel, essential for the activity of urease, the enzyme that allow H. pylori resist acidity. The lab has discovered and characterized several factors essential for nickel acquisition and distribution within H. pylori, these factors were shown to be essential for colonization.
2) The metal bismuth is associated to antibiotics in a new medicatino particularly active against H. pylori infection including against antibiotic resistant strains. The lab explores the mode of action of bismuth in H. pylori and has recently initiated a collaboration on this topic with Prof Hongzhe SUN, chair professor at the university of Hong Kong, department of Chemistry.
3) Investigating the mechanisms involved in the induction of genotoxic events by H. pylori infection and their role in the development of malignant lesions.

SELECTED PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/helicobacter-pathogenesis/
Ivo Boneca worked for his Thesis under the supervision of Prof. Alexander Tomasz, at The Rockefeller University, New York, USA, and finished his Ph.D in Biology in 2000. He obtained his Ph.D from the Institut of Technical Chemistry and Biology (ITQB) from the New University of Lisbon (UNL), Portugal. From 2000 to 2004, he was a post-doctoral fellow at the Institut Pasteur where he did research on Helicobacter pylori and host-microbe interactions. In 2004, he joined the INSERM as an INSERM Investigator at the Institut Pasteur. From 2004 to 2006, he coordinated a transversal program (PTR 153) on the mechanism of bacterial escape to Nod-like receptors sensing. In 2008, Ivo was awarded a junior group at the Department of Microbiology, Institut Pasteur, Paris, France. In 2010, Ivo defended his HDR at the Université Paris Descartes. In 2013, Ivo was awarded a unit in the Department of Microbiology and was deputy Director of Department in 2017-2019. In 2015, he became INSERM Research Director.

For his research on the cell wall metabolism of Helicobacter pylori, he received in 2002, the Jacques Monod award from the Fondation de France, as one of the 2 best Young scientists in the field of Molecular Biology, and in 2003, the Roux fellowship. In 2007, for his research on cell wall metabolism and host-microbe interactions, he received the INSERM Avenir 2007 award and an European Research Council starting grant. In 2011, he received the Pasteur Valley-Radot award from the French Academy of Science and the Bibliothèque Nationale de France for his work cell wall metabolism and host-microbe interactions. His on-going work and projects are aimed at deciphering new knowledge on one of the major “Achilles heals” of bacteria, their cell wall and to improve our future options in dealing with old and “emerging” infectious diseases. Our research can be separated in two complementary subjects: 1) the study of peptidoglycan (PG) metabolism and its role in cell physiology and antibiotic resistance, and 2) the role that cell wall, and in particular, PG metabolism has on host-microbe interactions. In particular on this last aspect, he is interested in studying the effects of PG as a signaling molecule on host physiology. The PG is constantly released by the gut commensal flora and transported systemically in the host. Some of the effects are local on the gut homeostasis but others occur at distant tissues and organs. The brain is such an organ where the PG can have effects on sleep patterns and behavior, effects that we are currently investigating.

**LATEST PUBLICATIONS**
Javier Pizarro-Cerdá obtained B.Sc. and M.Sc. degrees from the University of Costa Rica while working in the laboratory of Edgardo Moreno, studying the adaptations of the outer membrane of the Gram-negative pathogen Brucella abortus to cationic peptides. In 2001 Javier Pizarro-Cerda joins the Pasteur Institute as a permanent researcher and obtains his first grant from the French Ministry of Research. Since, he has been involved in local (Pasteur Institute Transversal Programs), national (French National Agency for Research, Defense Innovation Agency) and international (ERANET, Systems X, National Institutes of Health) research initiatives, investigating the adaptations of bacterial pathogens to intracellular and extracellular life.

The activities of the Yersinia Research Unit are primarily devoted to the analysis of:
- Mechanisms of horizontal gene transfer in Yersinia;
- Comparative genomics and transcriptomics between Y. pestis and Y. pseudotuberculosis;
- Molecular bases for the exceptional pathogenicity of Y. pestis. – Pathophysiology of Yersinia infections;
- Host’s mechanisms of innate and adaptive immunity;
- Genetic bases of host susceptibility to plague;
- Resistance of pathogenic Yersinia to antibiotics;
- Evolution of pathogenic Yersinia.

The Unit is also developing:
- A vaccine against plague and pseudotuberculosis;
- Typing tools for molecular epidemiology;
- Real time in vivo imaging technology to follow the kinetics of Y. pestis development in its host;
- Tools for stable gene complementation and gene expression in vitro and in vivo;
- Techniques for molecular characterization of the various Yersinia species.
- The Unit participates actively to the surveillance and control of enteropathogenic Yersinia through its activities at the National level (Reference Laboratory and French Surveillance Network), and to the fight against plague at the international level (World Health Organization Collaborating Center for Yersinia).

**LATEST PUBLICATIONS**
HKU-PASTEUR RESEARCH POLE FELLOWSHIP

MYCOLOGY
Christophe d’Enfert gained his PhD at Institut Pasteur working on protein secretion in Gram-negative bacteria. During his post-doctoral training at the University of California at Berkeley, he studied protein secretion in yeast. Since 1992, he joined Institut Pasteur to study human pathogenic fungi and has developed both fundamental and applied research on two major fungal pathogens, Candida albicans and Aspergillus fumigatus.

Current research in Dr. d’Enfert's laboratory investigates various aspects of C. albicans biology, namely genome plasticity, morphogenesis, biofilm formation and colonization of the gastrointestinal tract, including C. albicans-microbiota interactions. Dr. d’Enfert’s research relies on unique resources that have been established in his lab: a C. albicans ORFeome and a genome-wide collection of C. albicans overexpression strains that allow overexpression screens to be carried in C. albicans; a resource of >300 genome-sequenced C. albicans isolates that can be used to perform genotype-phenotype association studies in C. albicans, complementing reverse genetics approaches.

LATEST PUBLICATIONS

- Znaidi S, mSphere of Influence: Decoding Transcriptional Regulatory Networks To Illuminate the Mechanisms of Microbial Pathogenicity, mSphere 2020 Jan;5(1).

After a PhD in Neuroscience from the University of Lyon-I in 1995, he joined the Institut Pasteur where resorting to dozen identified deafness genes, several of which are involved in Usher syndrome, as entry points has enabled him to enlighten both fundamental and medical aspects of hearing & vision functioning and related disorders. Multidisciplinary approaches owing to the biochemical properties of the encoded proteins, identification of their molecular networks, animal modelling of the disease have provided major insights into how the inner ear & eye sensory organs develop an function (Jean-Valade Prize 2005, Fond Mazet-Danet Fondation de France, 2006; Chaire of Excellence Charles Nicolle, Institut Pasteur (2017-2019).

In his team “Progressive Sensory Disorders”, the member's current efforts are focused on late-onset and/or progressive hearing and vision impairments, aiming to i) elucidate the precise underlying pathogenic pathways, and ii) identify therapeutic targets and solutions to delay, prevent and/or cure progressive sense deterioration in animal preclinical models, and accelerate their transfer into clinics.

Lab research program : Senses4All: from hearing and/or balance disease mechanisms to adapted gene therapies: Despite their high prevalence, inherited or acquired progressive hearing disorders have not been well studied or understood; resulting in many important unanswered questions: how do our inner ear sensory organs ensure long-term normal function? what are the causal genes & related pathways involved in hearing and balance maintenance? how do external factors and age impact senses' maintenance and/or decline? & what are the treatment solutions?

Our projects call upon cutting-edge techniques in "Omics", biochemical and computational analyses, imaging, cell biology, physiology (some benefiting from external collaborations), and gene therapy tools (gene supplementation & CRISPR/Cas9 gene editing) to enable a thorough and accurate phenotyping and treatment of available defective mutant mice. The projects are designed to:
1- identify molecular properties of deafness defective proteins and elucidate their related protein-protein interactions networks.
2- determine where, when and how inner ear abnormalities manifest in the available defective mice to elucidate the precise molecular and cellular mechanisms underlying their hearing and balance sensory deficits (disease signature).
3- Decipher if (& how) external factors, notably exposure to intense sound, impacts the onset, progression and/or severity of the disease.
4- Evaluate gene therapy (gene replacement & gene editing via CRISPR/Cas9) efficacy to restore normal sensory modalities in available defective mice.

LATEST PUBLICATIONS

- Céléc GGS, El-Amraoui A., Disease mechanisms and gene therapy for Usher syndrome., Hear. Res. 2020 Sep; 394(): 107932.

I hold a PhD in Neuroscience from Bordeaux University and I am at the head of the Laboratory "Perception and Memory" at the Institut Pasteur since 2001. Besides other Director positions, I am a member of both the Scientific Council for the London Interdisciplinary Doctoral programme and the National Ethical Committee for advertisement since 2018.

With interests ranging from neural circuit functions to adult brain plasticity (and its related disorders), our laboratory is best known for our interest on the interplay between sensory perception and memory, and for our studies on the malleability of the nervous system triggered by experiences. More recently, we have added an emotional component in our investigations to decipher how perception generates emotions and, in turn, how emotions alter our perception and memory. To tackle those questions, we believe that the idea that our brains are like giant supercomputers, orchestrating and determining everything we do is totally wrong. We have chosen to go beyond the dichotomy between the brain and the body by taking into account bodily influences on our psychology. In particular, we are investigating the role of neural invasion of gut microbiota and viral infection on brain functions. To achieve these goals, our expertise range from cellular biology to behavioural sciences requiring several tools from imaging (two-photon microscopy, light-sheet microscopy, Miniscope) combined with viral tools used to label circuits and manipulate them (optogenetic).

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/team/immunobiology-of-infection/
PARASITES AND INSECT VECTORS
Microtubules are essential components of the cell cytoskeleton composed of alpha and beta-tubulin heterodimers playing important roles in many cellular processes. Specialisation of tubulin functions is governed by the so-called “tubulin code”, where tubulin post-translational modifications provide distinct structural and functional properties to microtubules. Notably, glutamylation corresponding to the addition of one or more glutamates forming a side chain is one of the most abundant modifications, especially represented in cilia and flagella. Trypanosoma brucei is an ideal model to study the tubulin code since their cytoskeleton relies mostly on microtubules and the tubulin code is less complex, facilitating interpretation. Our group has identified several tubulin tyrosine ligase-like enzymes (TTLL) potentially involved in glutamylation and the first knockout studies, combined with proteomic analysis revealed unexpected contributions of one particular flagellar TTLL to this process. The aim of this project will be focussed on using tetracycline-inducible expression system for T. brucei to ascertain the role, and glutamylation signature, afforded by this TTLL enzyme. Using well established genetic manipulations of this cell, together with the use of expansion microscopy (ExM), a recently and very powerful developed technique enabling imaging with nanoscale precision by standard fluorescence microscopy, this project will provide key information about this TTLL enzyme function in T. brucei and importantly will help to decipher the distribution of the polyglutamylation tubulin modifications along individual microtubule doublets of the axoneme and their possible role during intraflagellar transport.

Scientific background: Good knowledge in cell and molecular biology
Technical background: Some expertise in cell culture and/or light microscopy would be desirable.
Dr Michael White is a mathematician and epidemiologist specializing in inter-disciplinary studies of infectious diseases. Dr White created the Infectious Disease Epidemiology & Analytics (IDEA) G5 Unit in 2021 which builds on the research agenda of the former Malaria: Parasites and Hosts Unit. The team at the IDEA unit combine epidemiological field studies, multiplex assays, and mathematical models to investigate the transmission dynamics of infectious diseases such as malaria, neglected tropical diseases, and coronaviruses.

Infection with SARS-CoV-2 induces a complex antibody response, with antibodies of several classes (IgG, IgA, IgM) targeting multiple antigens (Spike, Nucleoprotein, ...). We are seeking an enthusiastic and competent candidate to help us characterise the kinetics of the anti-SARS-CoV-2 antibody response in serum samples from individuals followed longitudinally after infection. The candidate will use multiplex assays to measure antibody responses and learn new statistical classification and machine learning techniques.

LATEST PUBLICATIONS


WEBPAGE: https://research.pasteur.fr/en/member/fr-michael-white/
HKU-PASTEUR RESEARCH POLE FELLOWSHIP

STRUCTURAL BIOLOGY & CHEMISTRY
Epigenetics defines when and where genes are expressed. Epigenetic marks are reversible and inheritable, integrate the impact of the environment and provide cellular plasticity. Aberrant epigenetic patterns are involved in tumor formation, maintenance and resistance. Notably, epigenetic modifications can be modified by chemical agents. In this context, we developed an original approach at the interface of Chemistry and Biology to identify new inhibitors of DNA methylation. We have successfully used several chemical strategies (rational drug design, pharmacomodulation, chemical library screening) and set up biological assays to characterize the cellular consequences induced by these inhibitors in cancer cells. Our findings encouraged us about the role of DNA methylation in tumor aggressiveness and the ability of epigenetic drugs to reprogram cancer cells.

We focus on 3 main research topics:
1/ Epigenetics chemical targeting to reprogram cancer cells and human infections
2/ Design and synthesis of novel chemical libraries for epigenetic targets
3/ Use of chemical probes to dissect the molecular Epigenetic mechanisms in diseases.

LATEST PUBLICATIONS

- 2020

WEBPAGE: https://research.pasteur.fr/en/member/paola-arimondo/
Exploring cellular self-organization and substrate dimensionality: The understanding of the processes of self-organization of cells into three-dimensional multicellular structures might provide clues for organ (mal)function therapies and new perspectives for tissue engineering.

Exploring host-pathogen interactions with nanometer resolution: By adapting correlative cryogenic high-end light and electron microscopies (cryo-CLEM) and combining it with in-situ cellular tomography (cryo-ET) and three-dimensional (3D) computational data analysis, we aim generally to study the invasion of host cells by viruses. Specifically, with SARS-CoV-2 emerging as a pathogen spreading worldwide and causing the COVID-19 pandemic, we focus on employing this new workflow to provide high-resolution in-situ structural 3D snapshots of the virus spike interactions with cell receptors and with the antibodies that abrogate their cell entry.

Dorit Hanein was educated at the Weizmann Institute, Israel. She completed training as a Fulbright postdoctoral fellow at Brandeis University with David DeRosier, the founding father of three-dimensional image reconstruction techniques via electron microscopy. Dr. Hanein is a PEW Innovation Fund Investigator. She is directing the Structural Studies of Macromolecular Machines in Cellula Unit (ESMMC) here at Institut Pasteur. With her team, Dr. Hanein specializes in developing ways to directly see inside our bodies the tiny, nanomachines that work tirelessly to allow us to fight intruders, to see and hear, to heal bruises, cuts and diseases, to run and practice yoga and to be happy. To visualize these nano machines, her talented unit members employ and operate a versatile and unique set of high-end electron microscopes instrumentations including Titan Krios, Glacios and Aquilos Dr. Hanein commissioned for Institut Pasteur in 2019. The capabilities of these microscopes allow to obtain a quantitative representation of life at the atomic scale. This holistic approach to research is at the interfaces between structural biology, cell biology, systems biology, and engineering science and at the forefront of exciting new developments bridging cryogenic electron microscopy, cell biology, and systems biology which carries high impact in both medicine and basic biological research.

Projects:
- Exploring cellular self-organization and substrate dimensionality: The understanding of the processes of self-organization of cells into three-dimensional multicellular structures might provide clues for organ (mal)function therapies and new perspectives for tissue engineering.
- Exploring host-pathogen interactions with nanometer resolution: By adapting correlative cryogenic high-end light and electron microscopies (cryo-CLEM) and combining it with in-situ cellular tomography (cryo-ET) and three-dimensional (3D) computational data analysis, we aim generally to study the invasion of host cells by viruses. Specifically, with SARS-CoV-2 emerging as a pathogen spreading worldwide and causing the COVID-19 pandemic, we focus on employing this new workflow to provide high-resolution in-situ structural 3D snapshots of the virus spike interactions with cell receptors and with the antibodies that abrogate their cell entry.

**SELECTED PUBLICATIONS**
Niels Volkmann heads the Structural Image Analysis Unit at Pasteur. He holds a PhD in Physics and Biophysics from the University of Hamburg. As a postdoc at the Max-Planck Institute he carried out experimental and computational aspects of ribosome crystallography under the guidance of Prof. Ada Yonath who won the 2009 Nobel Prize in chemistry. As a postdoctoral fellow at the Keck Center, Brandeis University in Boston, USA, he expanded his research to include cryo-EM, cryo-ET, and image analysis under the guidance of Prof. David DeRosier, one of the founding fathers of three-dimensional reconstruction and analysis techniques. Since then, his research focuses on the development and application of innovative new computational and data science tools to bridge information between the atomic and cellular scales, covering more than six orders of magnitude from Ångstroms to tens of microns. Central to this effort is the analysis and interpretation of reconstructions from electron cryo-microscopy (cryo-EM) and cellular electron cryo-tomography (cryo-ET) and their correlation with other techniques and imaging modalities. With the recent increase in data throughput provided by new hardware and improved sample preparation techniques, quantitative and rapid data and image analysis are quickly becoming the primary bottlenecks in cryo-EM and cryo-ET.

Projects:
- Locating the right molecules in a haystack: Solving three-dimensional structures of macromolecules in their cellular environment requires identification and averaging of images collected on an electron microscope under very low contrast conditions (cryoEM). This project focuses on the initial steps of molecule identification in an ongoing effort for automation of this process. The project involves evaluation and ranking of available computational approaches based on template matching and/or artificial intelligence approaches such as deep learning. We are looking for someone with a background in bioinformatics, structural biology, or computational biology and with experience in Linux based systems.
- Scale integration: In order to merge information from lower resolution techniques such as light microscopy with the high resolution information that can be obtained from electron microscopy, images of the different modalities need to be aligned. This project involves exploration of computer vision techniques such as those used in robotics or driverless cars can be useful in the context of three-dimensional image alignment. We are looking for someone with a background in computer vision with experience in Linux based systems.

LATEST PUBLICATIONS

WEBSITE: https://research.pasteur.fr/fr/team/structural-image-analysis/
HKU-PASTEUR RESEARCH POLE FELLOWSHIP

Virology
Professor Anna-Bella Failloux, PhD, is a medical entomologist and chief of the unit “Arboviruses and Insect Vectors” in the department of Virology at the Institut Pasteur in Paris. Her work mainly focuses on investigations of arbovirus–mosquito interactions in order to decipher the factors leading to the viral emergence.

Dr. Failloux earned her Ph.D. in Ecology/Entomology from Orsay University (Paris XI). She performed Postdoctoral Research training at the Institut Pasteur where she obtained a full position as assistant professor in 1996. She has authored over 190 scientific publications on vectors of alphaviruses, flaviviruses and phleboviruses. She participates actively in teaching medical entomology as co-director of the course "Insect Vectors and Pathogens Transmission" and the MOOC "Medical Entomology" of the Institut Pasteur.

The laboratory “Arboviruses and Insect Vectors” has been transformed into a Unit of Research and Expertise (URE) – Network on November 1st 2014 in the Department of Virology at the Institut Pasteur in Paris. Dr Anna-Bella Failloux is the leader of this unit.

In this context, our unit has set some of its objectives of research with the support of the International Network of Institut Pasteur (INIP). This global network of 32 institutes on 5 continents is uniquely positioned to play a major role both in furthering our understanding of vector borne diseases and the challenge of controlling them. Our unit relies on the field experience offered by our collaborators within the INIP to anchor our projects and multiple trips between the field and laboratory are necessary in order to test hypotheses and direct future research.

Arthropod-borne viruses (arboviruses) are transmitted among vertebrate hosts by hematophagous arthropod vectors such as mosquitoes. Vertebrates are “blood-sources” required by this kind of arthropods to complete their life cycle. Blood providing nutrients for ovogenesis, females must feed on host to be able to mature their eggs. In the course of this blood-meal, saliva is injected and transmission of the pathogen to the vertebrate can occur if infectious particles are present in saliva. Blood-feeding arthropods may feed several times during their life span and can ingest genetically distinct variants of a given virus species playing a key role in generating and maintaining genetic diversity and in selecting genotypes involved in epidemics.

LATEST PUBLICATIONS

Our lab investigates the ecology, evolution and genetics of insect-virus interactions to advance our basic understanding of arthropod-borne virus (arbovirus) transmission by mosquitoes.

Why is there variation in the ability of mosquitoes to transmit human pathogens and what causes this variation? Our research addresses these questions using the tools of genomics, quantitative genetics, and evolutionary ecology. Our primary model is the transmission of dengue viruses by the mosquito Aedes aegypti. A major emphasis of the lab is to develop experimental approaches that account for the complexity of natural systems, where genetically diverse populations of mosquitoes interact with a wide variety of viruses, in a variable environment.

**LATEST PUBLICATIONS**

- Hol FJ, Lambrechts L, Prakash M., BiteOscope, an open platform to study mosquito biting behavior., Elife 2020 Sep; 9():.
Pr Carla Saleh was born in Argentina, where she obtained her Master degree in Biology at the National University of Cordoba. She earned her PhD on Cellular and Molecular Physiopathology at the University of Paris 6, and then moved to UCSF, where she trained as a postdoctoral researcher. In 2008, she obtained a tenure-track position at the Institut Pasteur, where she was appointed head of the “Viruses and RNAi” research group, which was converted to a full unit in 2013 (equivalent to tenure in the USA). She is since 2020 Full Professor at Institut Pasteur. Pr Saleh has a strong experience in coordinating international and national projects funded by a diversity of agencies (ERC, DIM, LabEx, DARPA...). She has received several distinctions and awards such as Pasteur Vallery-Radot Award from the French Academy of Sciences (2013), Langevin Award from the French Academy of Sciences (2014), Lucien Tartois Award from the Medical Research Foundation (2020). Dr Saleh was the laureate for the MEP-Scientists Pairing Scheme (European Parliament for Scientific Policy) (2016), the Commencement Speaker for the Promotion Louis Pasteur, Ecole Nationale d’Administration, France (2019). In 2020 she was elected as an EMBO Member. Pr. Saleh has been recognized by regular invitations to speak at leading international meetings such as the Gordon Conference on Viruses and Cells, the Keystone Meeting on Positive Strand Viruses and the American Society of Virology Meeting. She has lectured on various Master’s degree courses in Paris, Strasbourg, Lyon, Brazil and Argentina.

In recent years, we have witnessed an alarming increase in deadly virus transmission from mosquitoes to humans. For example, it is predicted by the WHO that about half the population of the world is now at risk for diseases such as dengue fever. Insects have an immune system that allows them to remain asymptomatic when they are infected with a virus that is deadly when transmitted to humans. How is this possible and how does this immune system work? Can we remodel this insect immunity to protect humans from devastating insect-borne viral diseases? The mission of the Saleh Lab is to search for a new way of eliminating the transmission of viral infectious disease from insects to humans. Many scientists are trying to understand the way that diseases spread or how viruses can be altered to transform them into safe vaccines. We have chosen an alternate approach, to redefine immunity. Our goal is to understand the intricate relationship between the immune system of infected insects and the viruses in order to control it. The approach we use to tackle the problem is interdisciplinary and multidisciplinary: experimental viral infections are performed on Drosophila melanogaster, for which there is powerful genetics, and the mechanisms identified are then validated in mosquitoes; concepts and techniques are from classical and molecular virology, immunology, biochemistry and cell biology; next-generation sequencing and state-of-the-art bioinformatics tools are also applied. We believe, therefore, that our scientific strategy offers new perspectives on emerging viral disease transmission and will inspire a new way of thinking about immunity.

LATEST PUBLICATIONS


WEBPAGE: http://salehlab.eu/