amU Institut Marseille maladies rares Aix Marseille Université

RESEARCH BOOKLET

2nd edition - 2025

Editorial

The objective of the Marseille Rare Diseases Institute (MarMaRa) is to bring together researchers working in the field of rare diseases. By fostering the integration of diverse research themes, MarMaRa actively supports and promotes interdisciplinary collaboration. This second edition of our booklet provides a comprehensive overview of the research laboratories and teams affiliated with MarMaRa, along with the themes they are exploring. Through this presentation, we aim to encourage dialogue, facilitate exchanges, and cultivate meaningful collaborations across various aspects of health research, ultimately benefiting patients living with rare diseases.

Frédérique Magdinier, RST

MarMaRa' Institute

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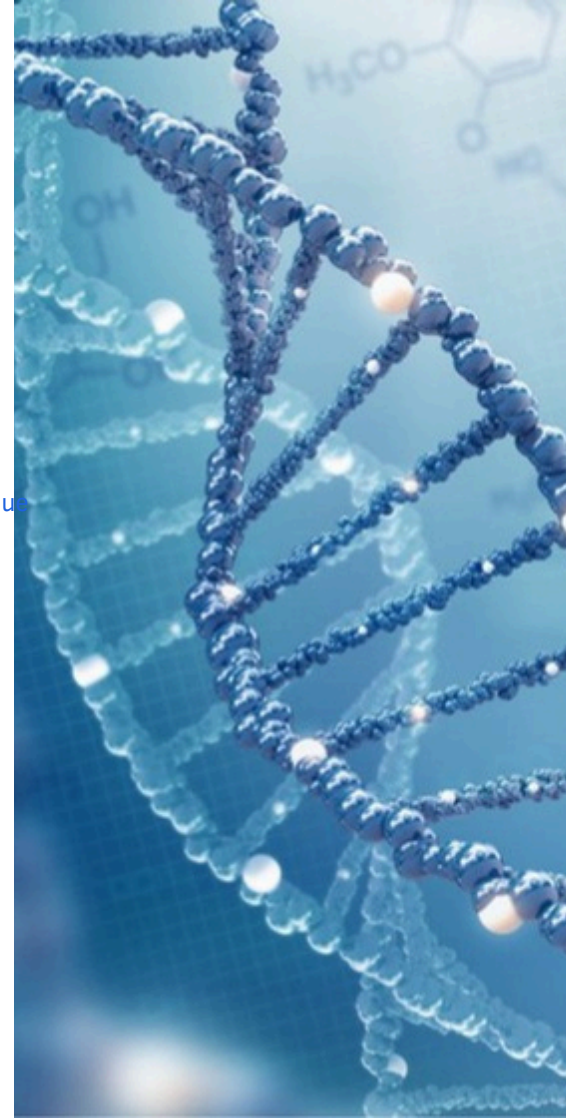
Responsable administratif & financier



Involved structures

5 Doctoral Schools

Engineering sciences (DS 353)

Mathematics & Informatics (DS 184)

2 Faculties

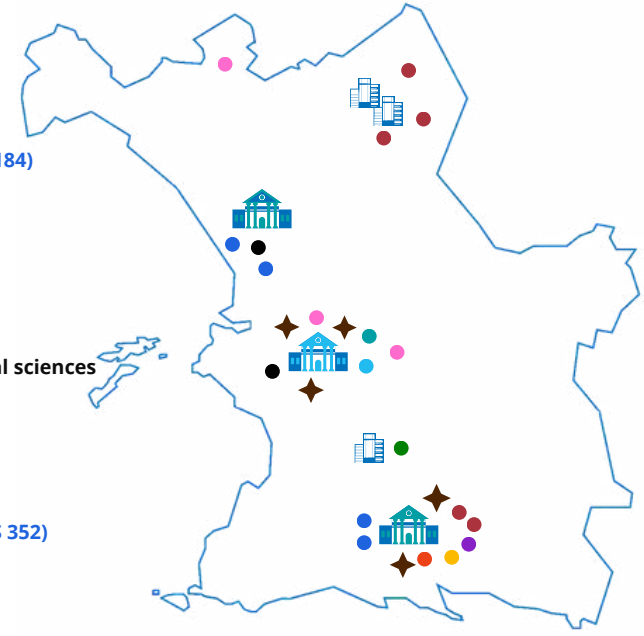
Faculty of sciences

Faculty of medical & paramedical sciences

Biomedical research (DS 659)

Life sciences (DS 658)

Physics and matter sciences (DS 352)



DS: Doctoral School
RU: Research Unit
MRU: Mixed Research Unit

13 Research Units / 36 Teams

ADES (MRU 7268)
Bio-cultural anthropology, law, ethics & health

IRPHE (MRU 7342)
Institute for Research on Out-of-Balance Phenomena

LMA (MRU 7031)
Mechanics & Acoustics Laboratory

FRESNEL institute (MRU 7249)

CEReSS (3279 RU)
Center for Studies & Research on Health Services & Quality of Life

MMG (MRU 1251)
Marseille Medical Genetics

C2VN (MRU 1263)
CardioVascular & Nutrition Research Center

CRCM (MRU 7258)
Marseille Cancer Research Center

I2M (MRU 5295)
Institute of Mathematics of Marseille

LP3 (MRU 7341)
Lasers, Plasmas & Photonic Processes

IBDM (MRU 7288)
The Developmental Biology Institute of Marseille

INMED (MRU 1249)
Mediterranean Neurobiology Institute)

TAGC (MRU 1090)
Theories & approaches of genomic complexity

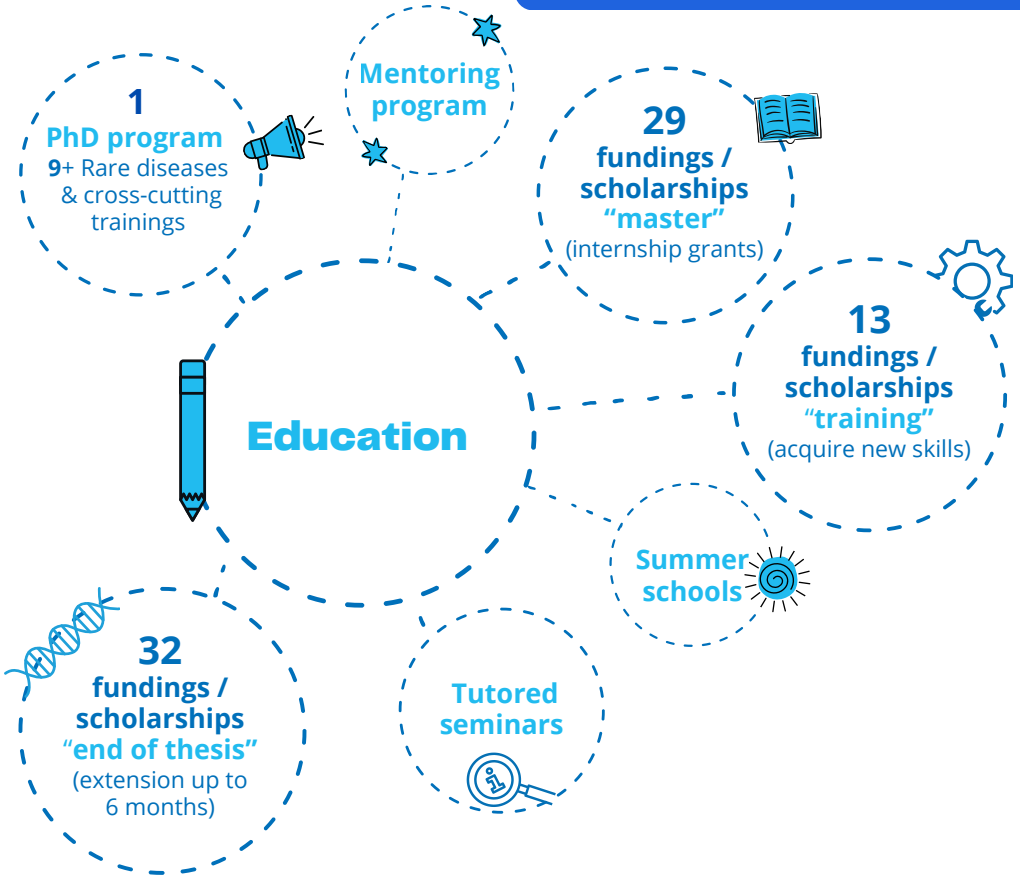
Tech core facilities

Marseille Stem Cells (MaSc) ✦
Genomic/Transcriptomicsfacilities (TGML; GBiM) ✦✦
Microscopy facilities (PICsl; MMG) ✦✦

Our actions

2019 - 2024

Our actions



2019 - 2024

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SUMMARY

Dysimmunity and inflammation during cardiovascular damage

Our team is studying the role of inflammation and the immune system in heart failure associated with dysimmune cardiopathies. These cardiac diseases are caused by disorders of the immune system, with complex pathophysiological pathways, for which the precise mechanism of action or trigger is not known

FIELDS OF STUDY

Our group aims to identify markers of poor clinical prognosis and to decipher the pathophysiological mechanisms leading to the most severe forms of dysimmune cardiopathies

FOCUS

We are focusing on severe forms of dysimmune cardiopathies and cardiotoxicity:

- Immune-related myocarditis, the most serious cardiac adverse event of cancer immunotherapies
- Cardiac damage in autoimmune diseases such as lupus
- Septic shock in septic cardiopathy

STRENGTHS

- Our project is based on translational approaches integrating basic, biological and clinical data, ranging from in vivo and cellular cardiac electrophysiology to functional genomics. We use different models:
- Cohorts of patients from the Medi-CO centre (https://www.gmedico.fr/), and from the Intensive Care Unit of the North Hospital
- Induced pluripotent stem cells (hiPSCs) generated from patients followed in our care centres
- Preclinical murine model

FUTURE PRIORITIES

- To unravel the signalling pathways associated with immune-related cardiopathies and septic shock ·
- To better understand the pathophysiological mechanisms of myocarditis induced by immune check-point inhibitors (ICIs) and of cardiac dysfunction during septic shock
- To identify predictive and/or prognostic markers of very severe forms of these dysimmune cardiopathies

NOTABLE COLLABORATIONS

- We are working in close collaboration with F. Magdinier's team at MMG to set up cellular models for the study of dysimmune cardiopathies, supported by the expertise of the MaSC platform for generating hiPSCs
- We work with the groups of D. Puthier and L. Pradel at TAGC to unravel the genomic and epigenomic mechanisms of cardiomyopathies, supported by the expertise of the TGML platform.
- In close collaboration with L. Miquerol's group (IBDM) and M. Bernard and F. Kober's team (CRMBM), we are characterising cardiac dysfunction in adult murine models of genetic, septic and immune-related cardiomyopathy

SOURCES

- https://publons.com/researcher/2224946/nathalie-lalevee/
- https://doi.org/10.3390/jcdd10050194
- https://doi.org/10.1148/radiol.211765
- https://doi.org/10.1186/s40635-019-0263-0

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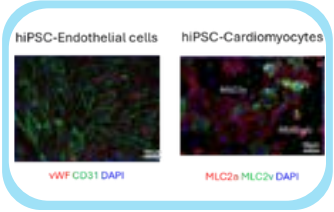

FIELDS OF STUDY

Combined expertise in haemostasis, thrombosis and platelet dysfunction, with a particular focus on high-throughput genetic screening strategies and functional studies to identify new biomarkers and pharmacological approaches regarding thrombosis, bleeding and vascular risk disorders (e.g. thrombocytopenia, lipodystrophies, laminopathies, ectopic fat depot, ..)

STRENGTHS

The team use a combination of biochemical, genetic, cellular and murine models to maintain solid basic research in the fields of haemostasis/thrombosis and vascular risk factors and conduct original translational research.

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FOCUS

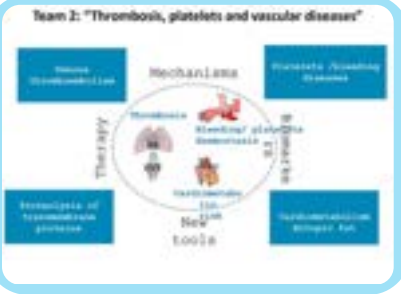
- The VTE (Venous thromboembolism) program we launched in 2010 builds upon the application of complementary omic research strategies on various bio-collections of several thousand of unrelated individuals and families as part of national (F-CRIN supported INNOVTE network) and international (INVENT consortium) collaborations, led to the identification of associated loci in VTE: ABO system, CFHR5 (complement), SLC44A2 and thrombomodulin (TM) 1,2.
- We developed specific functional programs to identify the mechanisms responsible for the association between these loci and coagulation disorders 3,4.
- We have a strong expertise in the genetics of common multifactorial diseases, combined with extensive epidemiological and omics databases from several thousand patients with clinically and biologically characterized cardiovascular phenotypes, as well as a certified biobank containing plasma and DNA, that are invaluable resources.

NOTABLE COLLABORATIONS

- Partner of the Thrombo-inflammation in cardiovascular disease (TICARDIO) project
- An international, interdisciplinary joint doctoral degree program, as part of the Marie Skłodowska-Curie Innovative Training Networks within Horizon 2020
- Partner of the “MORPHEUS” project prognosis iMprOvement of unpRovoked venous tHromboEmbolism Using perSonalized anticoagulant therapy HORIZON-HLTH-2022-TOOL-11-01
- Member of the international Charge Consortium
- Member of the international INVENT consortium
- Participation in the French nationwide registry of laminopathies (OPALE, ClinicalTrials.gov No. NCT03058185) OPALE group
- Coordinator of the French reference centre for rare platelet disorders

FUTURE PRIORITIES

- Identifying genetic loci associated with the risk of venous thrombosis recurrence.
- Investigating how these loci functionally contribute to the development of thrombotic disease.
- Developing a genetic risk score to predict thrombosis risk in women of childbearing age, addressing a significant women’s health issue.



SOURCES

- Goumidi, L. et al., Association between ABO haplotypes and the risk of venous thrombosis: impact on disease risk estimation. Blood 137, 2394–2402 (2021).
- Iglesias, M. J. et al., Elevated plasma complement factor H related 5 protein is associated with venous thromboembolism. Nat Commun 14, 3280 (2023).
- Bernard, C. et al., Thrombomodulin (p.Cys537Stop) is released from cells by an unusual membrane insertion/leakage mechanism. Blood Advances 8, 5467–5478 (2024).
- Zirka, G. et al., Impaired adhesion of neutrophils expressing Slc44a2/HNA-3b to VWF protects against NETosis under venous shear rates. Blood 137, 2256–2266 (2021).

Telomeres and Chromatin

Telomeres are nucleoprotein structures at the end of chromosomes that preserve the stability and function of the genome. Telomere biology is closely linked to cell senescence, aging disease, stem cell biology and cancer development. Our aim is to identify news genes responsible for telomere biology disorders that are rare genetic diseases caused by premature telomere shortening.
We are seeking to understand how these genes are involved in telomere maintenance and genome stability.
The team belongs to the Genome Integrity department at CRCM (Institut Paoli-Calmettes site)

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FIELDS OF STUDY

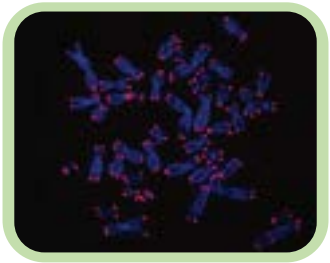
- Telomere
- Telomere biology disorders
- Aging
- Genome stability
- Replication stress

FOCUS

- Identification of new genes that cause rare genetic disease named **telomere biology disorders**
- Understanding how telomeres are maintained
- Identification of telomeric biomarkers to target cancer cells

STRENGHTS

- Strong expertise in telomere maintenance mechanisms
- Identification of new genes that are genetic drivers of telomere biology disorders
- National and international networks
- Communication at international meetings
- Publication



NOTABLE COLLABORATIONS

- Collaboration with Christophe Lachaud' team, CRCM (MarMaRa)
- Collaboration with the team of Patrick Revy, Institut Imagine and Caroline Kannengiessser, Hopital Bichat

FUTURE PRIORITIES

- Identification of new genes that cause rare genetic disease named telomere biology disorders
- Development of telomere sequencing method for diagnostic
- Development of national and international network

SOURCES

- Kochman R, Coulon S, et al., Heterozygous RPA2 variant as a novel genetic cause of telomere biology disorders. http://www.genesdev.org/cgi/doi/10.1101/gad.352032.124
- Coulon S. Telomeres: Chromosome sentinels. In: Saintomé C, ed. Dealing with replication stress at telomeres. Londres: ISTE Editions; 2024:157-190. ISBN eBook: 9781789490978
- Sharma R, Sahoo SS, et al., Gain-of-function mutations in RPA1 cause a syndrome with short telomeres and somatic genetic rescue. Blood. 2022 Feb 17;139(7):1039-1051.
- Escandell JM, Carvalho ES, et al., Ssu72 phosphatase is a conserved telomere replication terminator. EMBO J. 2019 Apr 1;38(7):e100476. doi: 10.15252/embj.2018100476.

DNA interstrand crosslink lesions and blood disorder

Many rare diseases *are caused by mutations in genes involved in the* ***DNA damage response (DDR)****, causing* ***genome instability****, a hallmark of* ***cancer.*** *DDR genes are crucial for maintaining genome stability and their inactivation is associated with cancer predisposition or neurodegenerative disorders. Hence,* ***understanding the biology of rare DNA repair diseases*** *can help improving the diagnosis of patients at risk for cancer.* ***In our laboratory,*** *we mainly focus on* ***DDR genes that prevent genome instability in blood*** *and that are* ***mutated in rare genetic diseases****.*

FIELDS OF STUDY

Genome stability, rare genetic diseases with defect in DNA repair:

- Fanconi Anemia
- Neurodevelopmental disorders involving the UFM1 pathway
- Prediction of patients response to chemotherapy

STRENGTHS

We developed and patented state of the art technology to measure DNA repair in cells. We combine clinical genetics and animal models. We combine basic and translational research and collaborate with clinicians and pharmaceutics industry.

FOCUS

We developed a **detectable drug inducing DNA interstrand crosslinks (ICL)** allowing us to propose an **alternative way to diagnose FA patients** based on their specific DNA repair defect. (see graphical abstract below and https://academic.oup.com/nar/article/51/15/7988/7217049)
This molecule presents several advantages for **both basic research and clinical applications**.

FUTURE PRIORITIES

Understand how the FA pathway prevents genome instability in blood. Understand how the UFM1 pathway prevents genome instability. Diagnosis of patient at risk for cancer due to a defect in DDR and prediction of the response to chemotherapy. Treat patients with blood disorders (genetic anemias or leukemia) using lipid nanoparticle (LNP) packaged mRNA.

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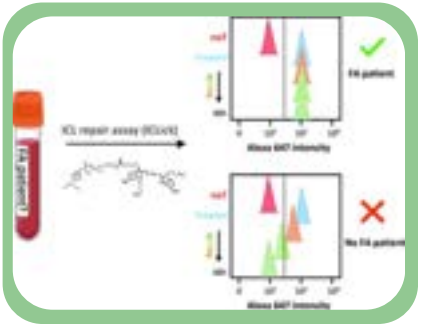
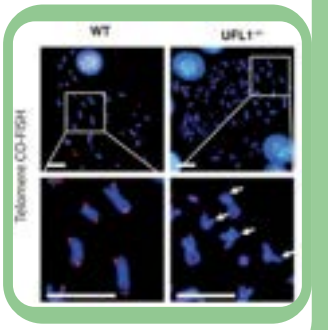
NOTABLE COLLABORATIONS

- Concerning our work on Fanconi Anemia, we collaborate with **Jean Soulier (France)** and **Ana Belen Perez Oliva (Spain)** to identify patients, new diagnosis protocols and potential new treatments.
- To determine how the UFM1 pathway prevents neurodevelopmental disorders, we collaborate with **Yogesh Kulathu (UK)** for the biochemistry part of the work, **Victor Mulero (Spain)** to generate Zebrafish model, **Estelle Colin (France)** to identify patients as well as **Frédérique Magdinier (MMG, MarMara)** to develop new cellular models.





Transcriptional regulatory networks in development and diseases

*Our laboratory is interested in the **mechanisms that control normal development and how their deregulation causes disease**. We have identified **a new chromosome 19q12 deletion syndrome (19q12DS)**. This syndrome is a rare genetic disease caused by the absence of one copy of the TSHZ3 gene. The most common symptoms in people with 19q12DS are congenital malformations of the renal tract (CAKUT) and autism spectrum disorder (ASD).*

FIELDS OF STUDY

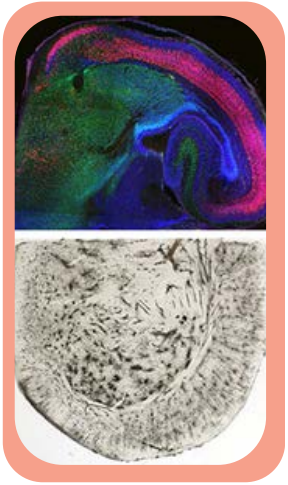
- When development goes away: exploring the origin of disease(s): ASD & CAKUT
- Choosing a fate: how do cells acquire their identity?

STRENGTHS

We use different Tshz3 mouse models to perform a multilevel study, from molecule to behavior, to unravel the function of TSHZ3 in relationship with 19q12DS syndrome.

FUTURE PRIORITIES

- **Identify TSHZ3 target genes in neurons that govern core autistic-like behaviors.**
- **Determine whether restoration of Tshz3 expression at postnatal stage can rescue autistic-like behaviors.**
- **Develop powerful behavioral analysis tools to perform longitudinal study of mouse models of neurodevelopmental disorders** (collaboration with the teams of F. Muscatelli (INMED), L. Villard (MMG) and S. Dubuisson (LIS)).



NOTABLE COLLABORATIONS

- Our collaboration with **the team of Lydia Kerkerian-Le Goff (IBDM)** showed that two groups of neurons control autism-like traits in Tshz3 mouse models.
- Our collaboration with the **laboratories of Adrian S. Woolf (Royal Manchester Children's Hospital, Manchester University, UK)**, **Petra Zürbig (Mosaiques diagnostics, Germany)** and **Joost P. Schanstra (U1297 Toulouse University III)** showed that Tshz3 haploinsufficiency leads to abnormalities in the adult mouse kidney.

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SELECTED PUBLICATIONS

- Molitor J et al., Altered striosome-matrix distribution and activity of striatal cholinergic interneurons in a model of autism-linked repetitive behaviors. bioRxiv 2024.05.23.595498; https://doi.org/10.1101/2024.05.23.595498
- Sanchez-Martin I et al., Haploinsufficiency of the mouse Tshz3 gene leads to kidney defects. Human Molecular Genetics 2022 PMID 34919690
- Caubit X et al., Targeted Tshz3 deletion in corticostriatal circuit components segregates core autistic behaviors. Translational Psychiatry. 2022. PMID 35292625.
- Caubit X et al., Camk2a-Cre and Tshz3 expression in mouse striatal cholinergic interneurons: implications for autism spectrum disorder. Frontiers in Genetics. 2021. PMID: 34349780
- Chabbert D et al., Postnatal Tshz3 Deletion Drives Altered Corticostriatal Function and Autism Spectrum Disorder-like Behavior. Biol Psychiatry. 2019 Aug 15;86(4):274-285. doi: 10.1016/j.biopsych.2019.03.974. Epub 2019 Mar 28. PMID: 31060802
- Caubit X et al., TSHZ3 deletion causes an autism syndrome and defects in cortical projection neurons. Nat Genet. 2016 Nov;48(11):1359-1369. PMID: 27668656

Computational Biology

The IBDM Computational Biology team works on integration of -omics data, focusing primarily on mitochondria. They have developed the mitoXplorer tool (https://mitoxplorer3.ibdm.univ-amu.fr) for the mitochondria-centric integration of data. They are also developing a sister platform, ataxiaXplorer, for deep data mining of single-cell RNA-seq data from cerebellar ataxias.

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https://www.ibdm.univ-amu.fr/team/computational-biology/
https://sites.google.com/view/habermannlab/publications

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FIELDS OF STUDY

- Computational biology
- Mitochondria
- Metabolism
- Biological networks
- Metabolic modelling

FOCUS

- Mitochondrial metabolism and biology
- computational biologY
- Data integration and visualisation

STRENGTHS

We use computational techniques including visual data mining, networks, and constraint-based modelling to study mitochondrial metabolism.
We develop user-friendly web-based tools for non-computational expert for effective data mining.

FUTURE PRIORITIES

- Enabling multi-omics data integration in mitoXplorer and ataxiaXplorer, to allow integration of metabolomic, fluxomic and expression (protein/RNA) data.
- Extending mitoXplorer to enable metabolic modelling using our mitoMammal mitochondrial model;
- Using machine-learning techniques to classify mitochondrial states based on expression data (single- and bulk RNA-seq)
- Establishing sister platforms to mitoXplorer, such as the ataxiaXplorer web platform for rare disease models

NOTABLE COLLABORATIONS

- Laurent Tichit (I2M Marseille): multi-layer network for the mitochondrial interactome
- Frank Schnorrer (IBDM Marseille): metabolic modelling of the Drosophila indirect flight muscle during development
- Rafael Arguello (CIML Marseille): single-cell metabolic characterisation of human glioblastoma
- Ronan Sicre (LIS Marseille): mitoLearner – characterizing mitochondrial states using deep learning
- Helene Puccio (INMG / PGNM, FRM-funded): establishment of the ataxiaXplorer interactome
- Olivier Pourquie (Harvard Medical School): characterisation of in vitro differentiated human BA cells

SOURCES

- Lucas M, Morris A, et al., Inferring cell cycle phases from a partially temporal network of protein interactions. Cell Rep Methods. 2023 Feb 1. doi:10.1016/j.crmeth.2023.100397
- Marchiano F, Haering M, et al., The mitoXplorer 2.0 update: integrating and interpreting mitochondrial expression dynamics within a cellular context. Nucleic Acids Res. 2022 May 7;50(W1):W490-9. doi: 10.1093/nar/gkac306.
- Haering M, Habermann BH, et al., RNfuzzyApp: an R shiny RNA-seq data analysis app for visualisation, differential expression analysis, time-series clustering and enrichment analysis. F1000Research. 2021;10:654. doi: 10.12688/f1000research.54533.2
- Meiler A, Marchiano F, et al., AnnoMiner is a new web-tool to integrate epigenetics, transcription factor occupancy and transcriptomics data to predict transcriptional regulators. Sci Rep. 2021 Jul 29;11(1):15463. doi: 10.1038/s41598-021-94805-1
- Pierrelée M, Reynders A, et al., Introducing the novel Cytoscape app TimeNexus to analyze time-series data using temporal MultiLayer Networks (tMLNs). Sci Rep. 2021;11:13691. doi: 10.1038/s41598-021-93128-5
- Yim A, Koti P, et al., mitoXplorer, a visual data mining platform to systematically analyze and visualize mitochondrial expression dynamics and mutations. Nucleic Acids Res. 2020 Jan 24;48(2):605-632. doi: 10.1093/nar/gkz1128

Research in our team focuses on neuromuscular circuits. We originally studied mechanisms driving morphogenesis of muscles and associated motor circuits during development. We recently moved to the study of mechanisms underlying adult muscle homeostasis and regeneration in healthy and pathological contexts. We explore interactions between muscle-resident connective tissue cells called Fibro-adipogenic progenitors (FAPs) and myogenic cells during injury-induced muscle regeneration, and the dysfunction of FAPs in pathological contexts such as muscular dystrophies, leading to Fibrosis and adipose infiltrations in muscles. See the two recent reviews on limb muscle development and regeneration (**Helmbacher & Stricker, 2020**), and on FAPs in physiological adipogenesis and Intermuscular adipose tissue (IMAT) remodelling (**Flores-Opazo et al 2024**)).

FIELDS OF STUDY

- Muscle morphogenesis and regeneration
- Fibro-adipogenic progenitors
- Intermuscular adipose tissue formation and remodelling in healthy and pathological muscles

STRENGTHS

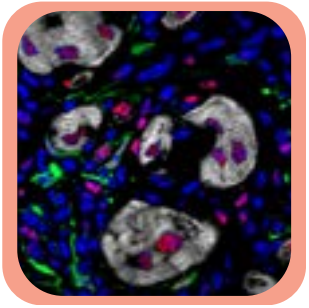
We design and use mouse models combining the power of genetics and AAV-delivered tools to manipulate the processes of muscle regeneration, via CRISPR gene editing approaches. This is combined with quantitative imaging, histology, and omic studies, and will also benefit from non-invasive bioluminescent imaging of live animals, as well as work with human iPS cells.

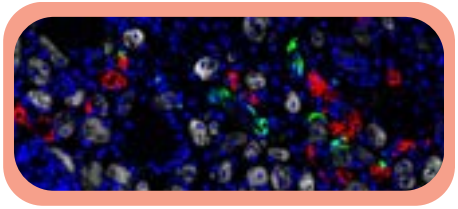
FUTURE PRIORITIES

- Design Genetic/AAV/CRISPR mouse models to **Identify and functionally validate modulators of fibro-adipogenic differentiation**
- Design models to **follow longitudinally lesion-induced fibrosis and IMAT formation using non-invasive imaging of live animals**
- **Design interventions capable of blocking or delaying progression of fibroadipose infiltrations in muscular dystrophies**

NOTABLE COLLABORATIONS

We collaborate with the **MAGDINIER and BARTOLI teams (MMG)**, to design approaches based on **human IPS Cells from healthy individuals or neuromuscular patients**, in order to study FAPs and their dysfunctions. We also collaborate with the KELLY team (IBDM) on muscle and motor neuron subtype development.





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SOURCES

http://helmbacherlab.org/
https://www.ibdm.univ-amu.fr/team/development-and-pathologies-of-neuromuscular-circuits/

- https://doi.org/10.1016/j.mam.2024.101277
- https://doi.org/10.1016/j.semcdb.2020.05.005
- https://doi.org/10.1371/journal.pbio.2004734

Genetic control of heart development

Our team studies heart development in order to identify biological mechanisms underlying organogenesis, regeneration and congenital disease.

FIELDS OF STUDY

Our group addresses how different progenitor cell populations contribute to the spatial and functional diversity of cardiomyocytes in the mouse heart. An in depth knowledge of heart development is essential to understand the origins of congenital heart defects (CHD) and to promote the repair of damaged heart tissue.
We focus on:

- Second heart field (SHF) progenitor cell development.
- The emergence of specialized cardiomyocytes of the ventricular conduction system (VCS).

STRENGTHS

We use mouse models to study gene function and lineage contributions during heart development, together with quantitative imaging, embryo and explant culture, and transcriptomic approaches.

FUTURE PRIORITIES

- Address the currently poorly understood mechanisms by which atrial and ventricular septal structures arise at the interface between TBX1 and TBX5 expressing progenitor populations.
- Address how divergent myogenic fates arise within this cardiocraniofacial developmental field.
- Study the development of specialized VCS cardiomyocytes, with a focus on the development of trabeculae, transient sponge-like myocardial projections in the fetal heart.

NOTABLE COLLABORATIONS

- the Zaffran and Lescroart' groups (MMG) on early cardiac progenitor cell lineages and head muscle development
- Nathalie Lalevee (C2VN) for electrophsyiological investigation of links between form and function in the cardiac conduction system.

SOURCES

www.ibdm.univ-mrs.fr

- Dumas et al., "Retinoic acid signalling regulates branchiomeric neck muscle development at the head/trunk interface". Development 2024 151:dev202905.
- Boulgakoff et al., "Participation of ventricular trabeculae in neonatal cardiac regeneration leads to ectopic recruitment of Purkinje-like cells". Nature Cardiovascular Research 2024 3:1140-1157.
- Guijarro et al., "Single-cell morphometrics reveals T-box gene-dependent patterns of epithelial tension in the Second Heart field". Nature Commun. 2024 15:9512.

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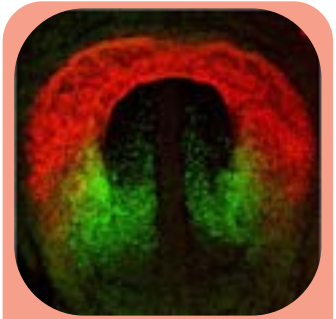


RNAscope fluorescent in situ hybridisation of a mouse embryo at embryonic day 7.5 showing early cardiomyocytes (red) and cardiopharyngeal mesoderm (green)

Molecular basis and Physiopathology of Cortical Development Disorders

*Our team aims at **understanding brain development and function in health and diseases.** We are particularly interested in the characterization and the targeting of pathogenic alterations that occur early in the developing brain and that have severe consequences on brain function.*

FIELDS OF STUDY

We study the **mechanisms controlling brain development** and maturation and involved in the **pathophysiology of neurodevelopmental disorders** sharing common features such as **cortical malformations, epilepsy, intellectual disability** or **autism spectrum disorders.**

STRENGTHS

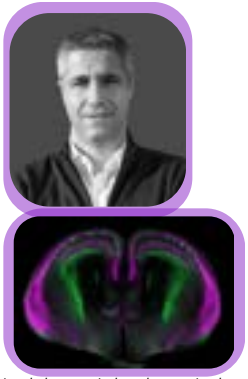
We use complementary and multi-level approaches that include multi-omics analyses, molecular and cell biology, immune-phenotyping, electrophysiology, relevant genetic (mTOR, Flna, Fat1, Dcx, NeuroD2) and non-genetic rodent models (CMV infection), in vivo imaging and behavioral analyses.

FOCUS

One of the main aim is to identify specific and/or common molecular and morpho-electrical signatures in rodent models of grey matter heterotopia (GMH) by using a 'multi-omics' approach, combining morphology, electrophysiology and transcriptomics. Indeed, distinct histological subtypes of GMH have been described, yet a systematic and comparative description of their neuronal cell composition is crucially lacking. This may help improving classification and diagnosis of GMH subtypes, and be instrumental for revealing new therapeutic targets.

FUTURE PRIORITIES

1. Investigate cellular and molecular alterations, and their functional consequences in Malformation of Cortical Development (MCD) rodent models.
2. Uncover ligand-receptor pairs that regulate cortical lamination and synaptic connectivity.
3. Understand the contribution of brain immune alterations in MCD disorders.



Projection thalamocorticale embryonnaire dans un modèle de malformation du développement corticale (Eml1cKO). Green: NetrinG1a, Pink: Tbr1. Aurélien Fortoul

NOTABLE COLLABORATION

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- Dr. F. Helmbacher IBDM on the role of FAT1 in brain development.
- Dr. P. Barbry - Nice, and Dr. L. Telley-Switzerland, on single cell RNA seq analysis and spatial transcritpomics.
- Dr B. Loriod, TAGC/TGML; Dr R. Rua, CIML; Dr H. Luche, CIPHE; Dr A. Etzerodt, Denmark; Pr T. Stamminger and Pr M. Messerle, Germany on CMV related developmental neuropathogenesis.

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SOURCES

https://www.inmed.fr/migration-neuronale-et-pathologies-du-developpement-cerebral

- Falace A, et al., FLNA regulates neuronal maturation by modulating RAC1-Cofilin activity in the developing cortex. Neurobiology of Disease, 2024; 198:106558
- Pineau L et al., Pathogenic MTOR somatic variant causing focal cortical dysplasia drives hyperexcitability via overactivation of neuronal GluN2C N-methyl-D-aspartate receptors. Epilepsia, 65(7):2111-2126.
- Vermoyal JC et al., Grey matter heterotopia subtypes show specific morpho-electric signatures and network dynamics. Brain, 2024; 147(3):996-1010.

Early life Imprinting and neurodevelopmental disorders

Brain functioning depends on the organization of neuronal circuits that are established during development under the influence of genetic programs and environmental signals. Our team aims at understanding some factors that translate, through brain signalling, the early life environment into lasting physiological and behavioral responses.

FIELDS OF STUDY

Our research focuses mainly on two hormones (oxytocin, leptin) and the control of chloride homeostasis as critical neuromodulators involved in different neurodevelopmental disorders (Prader-Willi, Schaaf-Yang, Rett, KCC2 pathogenic variants).

STRENGTHS

We aim to perform longitudinal studies on behavioral, physiological, neural connectivity, cellular and molecular impairments in several mouse models of neurodevelopmental diseases.We use a large panel of in vivo and ex vivo techniques.

FUTURE PRIORITIES

Investigate questions such as the cellular and network dynamics supporting physiological behaviors (using common genetic tools and the CircuitPhotonics platform) and perform longitudinal behavioral studies (using IA approaches). Thus, we will further study the effects of pharmacological treatments with a large panel of tools.

FOCUS

Perinatal oxytocin in normal and pathological brain development

Oxytocin (OT) is mainly produced by hypothalamus and plays important roles, regulating physiological and social functions, acting in periphery or in the brain. OT-system deficiency is involved in neurodeveloppmental diseases notably Prader-Willi (PW) and Schaaf-Yang (SY) syndromes, that are associated with MAGEL2 gene. Preclinical studies on Magel2-KO mouse model showed phenotypes reminiscent of PW and SY syndromes and a peripheral OT-administration in the first week of life restores normal phenotype from infancy to adulthood (patent Muscatelli et al.). Our studies suggest that OT, at critical developmental stages, plays key role(s), in shaping/regulating neural circuits involved in different physiological functions throughout the individual lifespan and can be an early life safety and efficient treatment.

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SELECTED PUBLICATIONS

- Buron J., ..., Menuet C. bioRxiv 2023.09.26.559512.
- Caccialupi Da Prato L, ..., Matarazzo V. 2022. Neuropsychopharmacology.
- Bertoni A, ...,Muscatelli. 2021. Dec;26(12):7582-7595.Mol Psychiatry

Bertoni A et al. 2021 Mol Psychiatry; Muscatelli F et al. 2018 Curr Top Behav Neurosci; Schaller F et al. 2010 Hum Mol Genet; Caccialupi Da Prato et al. 2022 Neuropsychopharmacology; Meziane H et al. 2015 Biol Psychiatry; Tauber M et al. 2017 Pediatrics.

Our research team is the result of convergent expertise in endocrine disorders, specifically tumors and deficiencies affecting the pituitary gland, and in the impacts of mutations on neural crest (NC) stem cells and their derivatives in congenital syndromes. Together, we focus on the influences of non-endocrine cells and tissues on the pathogenesis of functional pituitary diseases.

FIELDS OF STUDY

Syndromic or isolated rare pituitary diseases, including pituitary deficiencies and tumors, and the roles of neural crest-derived cells in mosaic and/or congenital disorders

STRENGTHS

- National Reference Center for Rare Pituitary Disorders at AP-HM (CRMR HYPO, directed by Prof. T. Brue) ·
- Large human DNA and tumor collection of pituitary disorders associated with clinical databases · Human embryo and early fetal tissue collection for research (HuDeCA) · Giant congenital melanocytic nevus tissue collection for research ·
- Long-standing national & international collaborations in rare diseases and developmental biology ·
- New experimental models, specifically iPSC-derived pituitary organoids, directed iPSC differentiation and novel murine genetic crosses

FOCUS

We model a range of rare pituitary hypo- and hyperplasic pathologies based on strengthening basic research into pituitary development, cellular states, composition and function before and after birth in animal models, in addition to multiple engineered or patient-derived hiPSC lines. We address molecular mechanisms of pituitary disorders involving mosaicism, focusing initially on Multiple Endocrine Neoplasia type 1 (MEN1), particularly its Pituitary NeuroEndocrine tumor (Pit-NET) component. We decipher the impacts of activating mutations in effectors of the MAPK signaling pathway on neural crest cell differentiation and the multisystemic congenital disorders that arise as a result.

FUTURE PRIORITIES

We continue to refine the hiPSC pituitary 3D organoid model, used initially to explore pituitary deficiency disorders, to also explore hyper-secretory states. Our group continues to develop original mouse models that conditionally manipulate gene expression to understand pathogenetic mechanisms. We also make use of opportunities provided by new technologies in single-cell/spatial transcriptomics and multiplexed immunofluorescence in human embryology and disease.

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NOTABLE COLLABORATIONS

- CRMR HYPO is a European Reference Center within the ERN for pituitary diseases and genetic endocrine tumor syndromes.

It works closely with the APHM Molecular Biology Department, which coordinates the national genetic networks TENGEN and FIRENDO for rare endocrine diseases.

- The Horizon Europe MELCAYA project supports collaborations across Europe, particularly with partners in Barcelona.
- Funding from AFM-Téléthon and patient advocacy groups enables access to MMG technological platforms and fosters national and international collaborations, including with the University of California, San Francisco.

SOURCES

- European Journal of Endocrinology. 185, 6; 10.1530/EJE-21-0949.
- Gergics P, et al., High-throughput splicing assays identify missense and silent splice-disruptive POU1F1 variants underlying pituitary hormone deficiency. Am J Hum Genet. 2021;108(8):1526–1539. https://doi.org/10.1016/j.ajhg.2021.06.013
- Romane, et al., Somatotroph Tumors and the Epigenetic Status of the GNAS Locus. Int J Mol Sci. 2021;22(14):7570. https://doi.org/10.3390/ijms22147570

Translational neuromyology

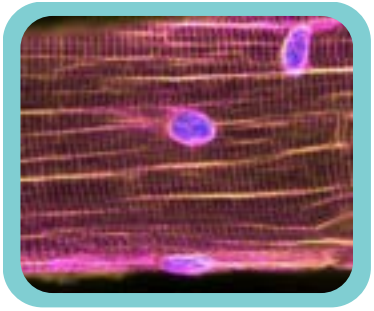
Our team is organized in two axes, one axis is focused on muscular dystrophies, and the second one on inherited peripheral neuropathies groups of diseases. Improving diagnosis of these diseases, the understanding of the patho-mechanisms and defining new treatments are primary goals that we want to achieve.

FIELDS OF STUDY

- Translational Genomics in Neuromuscular Disorders
- Genetics and Physiopathology of Inherited Peripheral Neuropathies
- Biotherapies Targeted to Neuromuscular Disorders

STRENGTHS

- A considerable expertise in Translational Genomics
- An access to a large national and international cohorts
- New in vitro and in vivo experimental models



SELECTED PUBLICATION

- El-Bazzal et al., (2019). **Loss of Cajal bodies in motor neurons from patients with novel mutations in VRK1**. Human molecular genetics, 28(14), 2378–2394. https://doi.org/10.1093/hmg/ddz060

FOCUS & FUTURE PRIORITIES

- **Identify new defective genes/proteins in NMD diseases.**
- **Develop a new hiPSC-based in vitro model** as a new tool for functional and preclinical therapeutic studies.
- **Develop novel therapeutic approaches,** based on particular clinical observations and mutational data from our large cohort of patients.
- **Pursue our previous work towards further preclinical testing of therapeutic strategies** developed by our group in particular: **transcript rescue strategies**.
- D**efine the best strategy using preclinical models** to assay efficacy of considered approaches to alleviate neuromuscular diseases.
- **Establish partnerships** at national & international level, to accelerate implementation of innovation.

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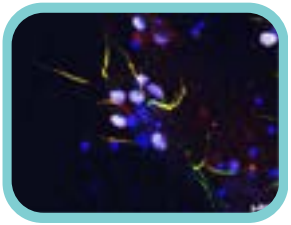


Technological advances and the associated accumulation of biomedical datasets are yielding unprecedented opportunities to better understand biological systems in healthy and pathological states. The Systems Biomedicine team aims to exploit these large-scale data to better understand genetic diseases. To this goal, the team develops and applies numerical approaches for the analysis and integration of multimodal biological data.

FIELDS OF STUDY

- Development of novel algorithms and approaches for multimodal data integration
- Applications to better understand genetic diseases

STRENGTHS

Computational Biology : An extensive experience in the development of computational methods to extract the knowledge contained in biological data.

FOCUS

- We recently developed a transfer learning algorithm for multi-omics data integration with matrix factorization
- We investigate graph representation learning strategies for drug repurposing
- We conducted system biology studies to better understand the cellular role of proteins involved in myopathies and premature aging diseases

FUTURE PRIORITIES

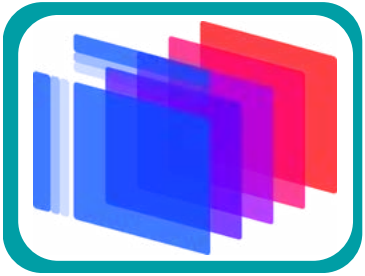
- Embedding of Knowledge graphs
- Building digital twins of organoids

NOTABLE COLLABORATIONS

We are fostering collaborations with scientists in:

- mathematics e.g., with I2M,
- computational biology e.g., with the BSC
- biology/clinics e.g., at MMG.

- Involved in the ERDERA partnership and in several national and international projects.



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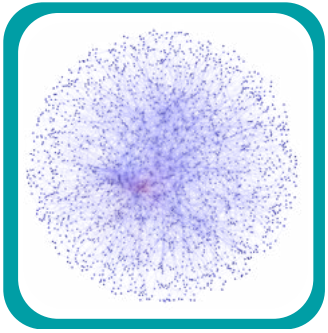

Single-Cell Heterogeneity Exploration via Machine Learning and Inference Methods (SCHEMA)

Our group develops computational methods and mathematical models to decipher single-cell heterogeneity within developing biological tissues from large sequencing and imaging datasets.

FIELDS OF STUDY

Our fields of study cover computational biology, machine learning, mathematical modeling and biophysics. In particular, we focus on multi-modal data integration, spatial network models and data-driven statistical models.

STRENGTHS

Our main strength is to be able to work in close collaboration with experimentalists on biological data while developing new methodology and mathematical models. Our expertise covers various types of data, from microscopy imaging to single-cell sequencing.

FOCUS

One of the main axis of the team is the question of data integration, we have developed machine learning methods for the integration of multiple types of images (FISH and live imaging) and are currently adapting the integration of unpaired multi-omics dataset for investigating rare diseases.

FUTURE PRIORITIES

In the future, we would like to focus on multi-modal data integration, and more generally machine learning methods to explore large and heterogeneous datasets. Our main objective is to develop these methods for spatial multi-omics in the context of rare diseases.

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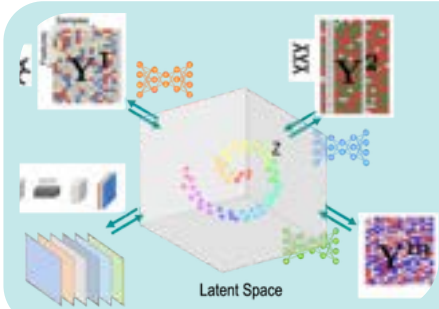
NOTABLE COLLABORATIONS

- We collaborate with the Kelly lab at IBDM on the study of second heart field,
- the Baudot team at MMG on data integration.

SOURCES

https://bioml.lis-lab.fr

https://scholar.google.fr/citations?hl=en&user=uaK6xaYAAAAJ&view_op=list_works&sortby=pubdate



Multi-modal data integration – the various types of datasets can be matched in a common latent space for improved subtyping or trajectory inference

Normal & pathophysiological specification of cardio-pharyngeal mesoderm

Our team is part of the MMG unit. It has been funded by the ATIP-avenir program since 2019. Our work is mainly focused on the understanding of diseases that affect the heart and/or skeletal muscles of the head.

FIELDS OF STUDY

- Cardiopharyngeal mesoderm (CPM) giving rise to muscles of the head and the heart
- Gastrulation and cardiac progenitors (CP) specification
- Defects of heart morphogenesis (congenital heart diseases)
- Rare diseases affecting both the head and heart (22q11.2DS)

STRENGTHS

- Various in vivo and in vitro experimental models
- (knockout mice, gastruloids 3D in vitro models...)
- Advanced knowledge about how the heart is built from distinct progenitors ...
- Expertise in gastrulation and early embryonic development.

FOCUS & PRIORITIES

Our next challenges are now to understand how cardiac progenitor heterogeneity affects their cellular and regional fate by:

- Defining the molecular program or "Heart-code" driving cardiac progenitor specification, with a particular focus on homeodomain genes.
- Understanding the different types of cell behavior during cardiac progenitor migration.
- Identifying the different environmental signals affecting the different cardiac progenitor populations.

NOTABLE PUBLICATION

We identified distinct populations of Mesp1 cardiovascular progenitors (CPs) that correspond to progenitors committed to different cell lineages and regions of the heart, identifying the molecular features associated with early lineage restriction and regional segregation of the heart at the early stage of mouse gastrulation.

SELECTED PUBLICATION

- Lescroart F., et al., (2018). Defining the earliest step of cardiovascular lineage segregation by single cell RNA-seq. Science . doi: 10.1126/science.aao4174

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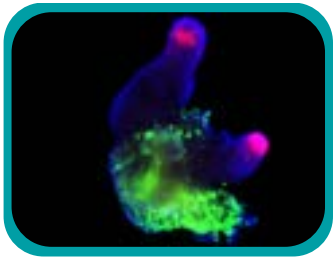
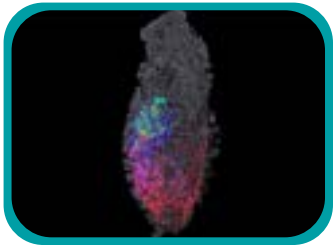




Epigenetics, chromatin and disease modeling

Alterations in chromatin organization as well as modifications of the nuclear shape are hallmarks of many pathologies including several rare genetic diseases such as FacioScapuloHumeral dystrophy (FSHD) or premature ageing syndromes (PAS).

The goal of the "Epigenetic and nucleoskeleton dynamics in rare diseases" are:

- *Investigate the molecular cause and molecular mechanisms of selected rare diseases; in particular diseases characterized by epigenetic alterations*
- *Identify potential druggable pathways and therapeutic targets*
- *Ameliorate healthcare for patient suffering of rare genetic diseases*

FIELDS OF STUDY

Through the exploration of patient's samples together with the development of in vitro (primary cell lines and induced pluripotent stem cells) and in vivo models, our projects will address fundamental questions aimed at understanding the chromatin-nucleus-cytoskeleton interplay, identifying key actors involved in this dynamic and the cross-talks between chromatin organization, nuclear structure in rare genetic diseases.

STRENGTHS

- Access to patient's samples; translational research
- Expertise in cell biology
- Expertise in epigenetics
- Expertise in stem cell research and development of cellular models using cells from patients.

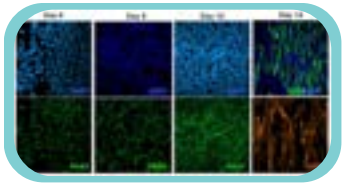
FUTURE PRIORITIES

- Decipher the complexity of the 4q35 and homologous 10q26 loci in FSHD patients with atypical genomic features using a combination of genomic approaches including long read sequencing.
- Develop integrative tools for genotype-phenotype correlations in FSHD.
- Defining the contribution of non-muscular cells in the pathogenesis of FSHD using cutting edge technologies of tissue bioengineering.
- Investigates the dynamics of DNA methylation and the role of SMCHD1 in shaping the epigenome.

FOCUS

Facioscapulohumeral dystrophy (FSHD) is an autosomal dominant muscular dystrophy characterized by selective and variable muscle weakness. Although genetically heterogeneous, it is clinically homogeneous with incomplete penetrance. Two forms have been identified: FSHD1, the most common, caused by contraction of the D4Z4 repeat array at the 4q35 locus, and FSHD2 (about 5% of cases), most often associated with mutations in the SMCHD1 gene. In both forms, disease onset is linked to D4Z4 hypomethylation, chromatin relaxation, and aberrant expression of the DUX4 gene. However, the molecular mechanisms underlying muscle weakness and tissue specificity remain poorly understood.

Our research focuses on the regulation of the D4Z4 array, the role of epigenetic mechanisms in FSHD, and the function of SMCHD1. Through close collaboration with national reference centers for FSHD, we have access to extensive patient samples and clinical data. We have developed a wide range of experimental tools, including induced pluripotent stem cell models and artificial intelligence–based approaches, to support both molecular and clinical investigations.



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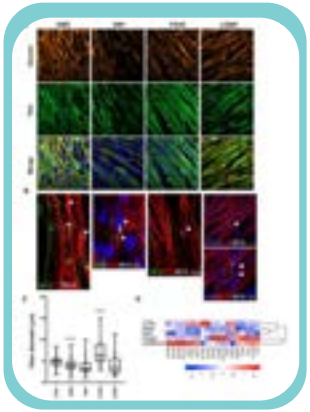
NGUYEN Karine PU-PH, AP-HM, amU
Post doc to be hired, June 2025



NOTABLE COLLABORATION

- Marseille Stem Cells core facility (MaSC)
- System in Biomedicine team - Anaïs Baudot

SOURCE

https://orcid.org/0000-0002-0159-9559

For more than 20 years, our team's research has focused on the discovery and the understanding of the pathophysiology of premature aging syndromes, mainly related to lamin A/C mutations, including Hutchinson-Gilford Progeria, for which we identified the causative gene in 2003, to identify therapeutic approaches. Another area of translational research related to our hospital activity concerns the study of lamin A/C contribution in cancer (lung adenocarcinoma). Our translational research is based on the development and use of preclinical tools such as patients' primary cell cultures, iPS cells and genetically engineered mouse models.

FIELDS OF STUDY

- Hutchinson-Gilford Progeria Syndrome (HGPS)
- MADaM syndrome (Mandibuloacral dysplasia associated to MTX2)
- Hallermann-Streiff syndrome
- Other premature aging syndromes
- Cancer mechanisms related to lamins A/C

STRENGTHS

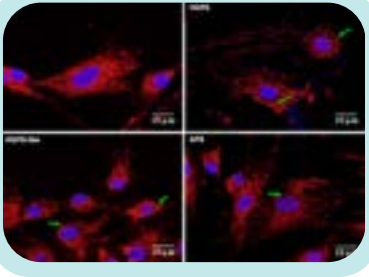
- Strong collaboration with the Departments of Medical Genetics and Cell Biology at the University Hospital la Timone, including the Biological Resource Centre, facilitates the establishment of the best bed-to-bench and bench-to-bed translational pathways.
- Robust disease-specific preclinical models available: LmnaG609G/G609G mouse model for Progeria, iPSC for Progeria and other progeroid syndromes (MADaM, Atypical Progeria Syndromes).

FOCUS

- Molecular diagnosis
- Gene discovery and disease pathophysiology
- Role of epigenetic modifications including non-coding RNAs in premature aging syndromes
- Cellular & mouse models preclinical use for translational research
- Gene therapy / Pharmacological approaches

FUTURE PRIORITIES

Improve our knowledge of the premature aging syndromes studied and develop proofs of concept paving the way to novel therapies



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COSTE Solène, PhD student
DE SANDRE GIOVANNOLI Annachiara, PH
FRANKEL Diane, MCU-PH
KASPI Elise, MCU-PH, HDR
NAEL Sara, AI
TOURY Léa, PhD student

NOTABLE COLLABORATIONS

- We maintain a close collaborative relationship with the Departments of Medical Genetics of AP-HM, the French reference centre for the molecular diagnosis of progeroid syndromes.
- We are collaborating with another MarMaRa team at the C2VN Institute to look for common epigenetic patterns (non-coding RNAs and methylation) in HGPS and lipodystrophies, which are both classified as laminopathies.
- We have long-standing collaborations with the iSTEM Institute (X. Nissan) and the "Institut de Myologie" (A. Muchir, G. Bonne). To identify the genetic and molecular bases of the recently described Mandibuloacral dysplasia progeroid syndrome (MADaM syndrome), we have established a very large collaborative consortium involving clinicians, researchers and industrial partners from all over the world (Singapore, Ecuador, India, Turkey, Egypt, Germany, France, ...).

Modeling muscular dystrophies using patients' hiPSC to explore physiopathology and therapeutic options

Our group is located at the MMG unit and is part of the team "Epigenetic and nucleoskeleton dynamics in rare diseases" led by Frédérique Magdinier. Our goal is to better understand the genetic and molecular mechanisms contributing to debilitating skeletal muscle diseases. Using innovative patients' stem cells models, we are able to identify the genes, biological pathways and functional properties affected in various neuromuscular diseases. HiPSC-based models also support the development of innovative treatments for muscle conditions and may open the door for preclinical screening of a personalized panel of drug candidates to improve these debilitating disorders.

FIELDS OF STUDY

- Neuromuscular diseases, undiagnosed muscular dystrophies, Laminin 2 related muscular dystrophy.
- Human Pluripotent stem cells models.
- Translational science

STRENGTHS

We use patient's induced pluripotent stem cells (hiPSC) models that we combine to state-of-the-art molecular and functional technologies (CRISPR/Cas9 gene editing, multi-omics, NGS, calcium imaging and MEA) to study and characterize neuromuscular disorders.

FOCUS

One of our main focuses is deciphering the mechanisms contributing to Undiagnosed Muscular Dystrophies (UMDs) in order to facilitate their classification and orient the patients' diagnoses. In the long term, this study will provide innovative leads for the development of new therapies.
Another specific focus is deciphering the patho-mechanisms of Laminin a2 deficiency related muscular dystrophy (LAMA2-RD), an ECM-related neuromuscular disorder and one of the most common congenital muscular dystrophies for which there exists no cure.

PRINCIPAL INVESTIGATOR

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GROUP MEMBERS

BEN DAOUD Imane, PhD student
AKSOY Defne, IE

NOTABLE COLLABORATION

For the LAMA2-RD project, we closely collaborate with Dr Valérie Allamand from the Center of Research in Myology (Sorbonne University, Paris) and Dr Marc Bartoli (MMG).
At the European level, we are involved in the Lama2-Europe Network

FUTURE PRIORITIES

- Identification of novel disease-causing genes in MD patients in diagnosis deadlock.
- Identify pathomechanisms and biological pathways involved in various NMD, including LAMA2-RD.
- Development of innovative therapeutic approaches for these NMD.
- Using our patients' hiPSC-based preclinical cellular models to test new therapeutic options

SOURCES

https://www.marseille-medical-genetics.org/fr/f-magdinier/

- Caron et al., 2022 Induced Pluripotent Stem Cells for Modeling Physiological and Pathological Striated Muscle Complexity. J Neuromuscul Dis. 2023 ;10(5):761-776.

Nowadays, there is growing interest in developing alternatives to animal testing for disease modeling. Tissue engineering, which combines expertise from various disciplines, stands out as one of the most promising fields for replicating the morphological and biological complexity of human tissues and organs. By combining stem cells, 3D bioprinting, and laser-ablation techniques, our team aims to recreate the architecture and biological niche of skeletal muscl

PRINCIPAL INVESTIGATOR

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GROUP MEMBERS

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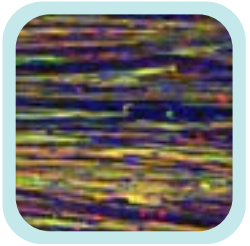
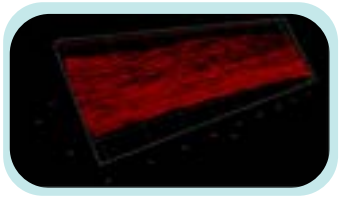
PERRIN Pierre, IE





FIELDS OF STUDY

- Skeletal muscle
- tissue engineering
- stem cells,
- neuromuscular disease modelling,
- 3D bioprinting

STRENGTHS

We are a young, multidisciplinary, and dynamic team with strong expertise in cellular biology, skeletal muscle tissue engineering, and biomedical engineering.

FOCUS

The research focuses on developing complex models of human skeletal muscle tissue to achieve a high level of structural organization, maturation, and functionality. These models will serve as a platform for studies on skeletal muscle tissue under both physiological and pathological conditions, offering a reliable and ethical alternative to animal models, fully aligned with the 3Rs principles.

NOTABLE COLLABORATION

- Given the multidisciplinary nature of our research, we have established a close and fruitful collaboration with the “Lasers, plasmas et procédés photoniques” department (LP3, UMR 7341), exploring the possible applications of laser procedures on tissue engineering.
- More recently, we have undertaken new collaborations with the “Marseille cancer research centre” (CRCM) to study the mechanisms involved in muscle tissue atrophy during cachexia syndrome.

FUTURE PRIORITIES

- Development of advanced human preclinical models for the study of neuromuscular diseases.
- Development of complex co-culture models to study the influence of cancer in the development of skeletal muscle atrophy.
- Development of patient-specific models for personalized medicine applications.
- Development of macrofluidic devices for modeling vascularized tissues.

SOURCES

https://www.marseille-medical-genetics.org/fr/f-magdinier/
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Spermatogenesis and genome stability

Our group using next generation sequencing (NGS) to identify genetic causes of male infertility Pathogenic genetic variants identified in infertile men, are validated and studied through creation of mouse models to explore effect on spermatogenesis, mode of inheritance, and impact on gamete quality, including genome stability.

FIELDS OF STUDY

- The genetic basis of human male infertility – gene variants and modes of inheritance (e.g. digenic).
- Molecular genetics as a tool to study spermatogenesis in the mouse.
- Genome integrity in cases of male infertility linked to de-repression of transposable elements.

STRENGTHS

- Our group works in both clinical and mouse genetics.
- Creation of a mouse model to identify proteins contributing to germ-line transposon repression.
- Creation of mouse models revealing functional redundancy during spermatogenesis.

FOCUS

Genes involved in piRNA-mediated transposable element (TE) silencing in germ cells are frequently found mutated in cases of male infertility. piRNAs are micro-RNAs that bind to PIWI proteins, targeting them to TE transcripts, where they silence TEs by epigenetic modification of TE promoters or by TE transcript degradation. We aim to identify proteins involved in TE silencing and define the consequences of ectopic TE activity for genome stability and gamete quality.

FUTURE PRIORITIES

- **Use NGS to identify genes and processes involved in the silencing of TEs** during mammalian spermatogenesis: in infertile men with TE expression (exome), and in our mouse model where an unknown factor required for TE silencing is absent (whole genome).
- Define the consequences of TE expression for the stability of the genome and the epigenome.
- Develop diagnostic tools to identify TE silencing failure in infertile men.

RECENT COLLABORATIONS

- Valérie Delague: GBiM - Genomics and Bioinformatics platform at MMG, Marseille.
- Ramesh Pillai: University of Geneva, Switzerland. Characterisation of failed piRNA-mediated transcriptional repression of TEs causing infertility in our mouse model (publication pending).
- WARD Monika: University of Hawaii, USA. Role of the Y chromosome in gamete production.

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GROUP MEMBERS

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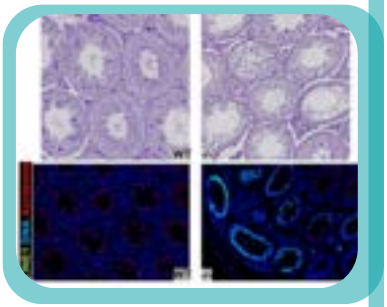
LONGEPIED Guy, IE
IBRAHIM Marie Charbel, PhD student

SOURCES

- Al Dala Ali M et al., (2024). Nucleoporin NUP210L and BAF-paralogue BAF-L together ensure microtubule organization and nuclear integrity in spermatids. BioRxiv://doi.org/10.1101/2024.05.16.5945802024.
- Al Dala Ali M et al., (2024). Spermatozoa in mice lacking the nucleoporin NUP210L show defects in head shape and motility but not in nuclear compaction or histone replacement. Clin Genet. 2024;105(4):364-75. doi: 10.1111/cge.14468.
- Auguste Y et al., (2018). Loss of Calmodulin- and Radial-Spoke-Associated Complex Protein CFAP251 Leads to Immotile Spermatozoa Lacking Mitochondria and Infertility in Men. Am J Hum Genet. 2018;103(3):413-20. doi: 10.1016/j.ajhg.2018.07.013.



Heart developpement and cardiac generation

Cardiovascular diseases including congenital heart defects are the leading cause of mortality. Despite significant advances, conventional treatments do not correct the defects in myocyte numbers and the prognosis of congestive heart failure remains poor.
Our team aims to ***uncover the developmental origins of rare congenital heart diseases*** *and to* ***identify novel therapeutic targets for heart regeneration and repair****.*

FIELDS OF STUDY

- Heart development
- Congenital heart diseases
- Cardiac regeneration and repair

STRENGTHS

Our project relies on an interdisciplinary approach which integrates multiple competencies including advanced mouse genetics, highly relevant pathological animal models, state of the art transcriptomics, developmental biology, stem cell biology, cardiac physiology and imaging.

FUTURE PRIORITIES

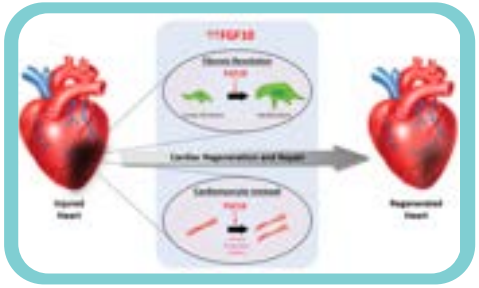
- Identify molecular mechanism controlling cardiac progenitor cell deployment and regulatory steps controlling cardiomyocyte proliferation during heart development.
- Uncover the developmental origins of congenital heart diseases.
- Unveil clinically relevant targets for cardiac regeneration and repair.

SOURCE

www.marseille-medical-genetics.org/f-rochais/

NOTABLE COLLABORATION

By combining experimental mouse model of myocardial infarction, advanced mouse genetics and unique human samples, we recently uncovered that the Fibroblast Growth Factor 10 (FGF10) promotes cardiac regeneration and repair. We demonstrate that FGF10 promotes cardiomyocyte proliferation and directly prevents scar-promoting myofibroblast activation, thus identifying FGF10 as a clinically relevant therapeutic target for heart regeneration in humans. (Hubert et al., Cardiovascular Research, 2021; Patent: Rochais, B2624PC00 2017).



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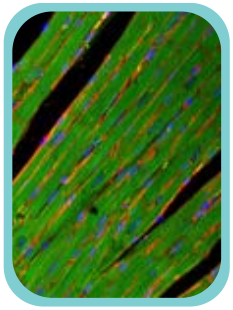
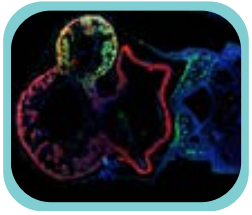
PELCE Edeline, PhD student
PORADA Corentin, PhD student
THEVENIAU-RUISSY Magali, CRHC, PhD, HDR



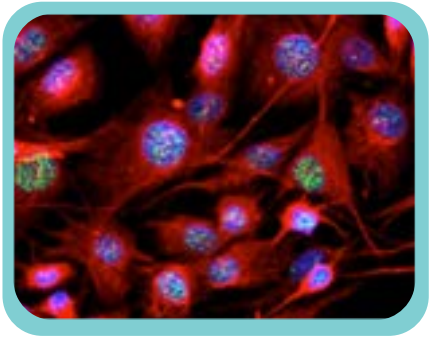


Our team has been studying ***the genetics of neurodevelopmental disorders*** *for more than 15 years,* ***with a focus on sporadic, progressive, and pharmacoresistant diseases****.*

We identify new genes, study their role, develop pre-clinical models and new therapeutic approaches.

FIELDS OF STUDY

- Developmental and Epileptic Encephalopathie
- Rett syndrome
- Syndromic forms of intellectual disabilitry



STRENGTHS

We combine a clinical expertise in collaboration with two departments of Marseille University Hospital with neurophysiology, cellular and molecular biology, animal models, behavioral analysis and electrophysiology.
We will also soon add new expertise in electrophysiology.

FOCUS

- Diagnosis of neurodevelopmental diseases
- Neurophysiology
- Cellular and mouse model characterization
- Gene therapy / pharmacology

NOTABLE COLLABORATION

Our recent collaboration with **LMA UMR 7031** and two labs of the Paris-Saclay Uni showed that opening the blood-brain barrier (BBB) by **ultrasound** improves the viral vector-based gene delivery in the entire murine brain. **Focused ultrasound (FUS)** appears to be a safe and promising approach to treat patients with neurological diseases affecting large areas of the brain.

SOURCES

www.marseille-medical-genetics.org/l-villard/

www.germaco.net

- Felix M-S, et al., Ultrasound-Mediated Blood-Brain Barrier Opening Improves Whole Brain Gene Delivery in Mice. Pharmaceutics. 2021; 13(8):1245. https://doi.org/10.3390/pharmaceutics13081245

PRINCIPAL INVESTIGATOR

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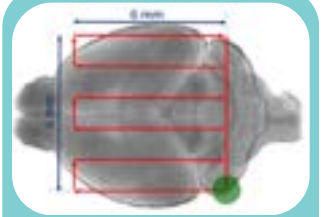
MOLINARI Florence, CR
ROUX Jean-Christophe, DR - HDR
SAUREY Manon, PhD student
TOUBAS Manon, TCN
VIEMARI Jean-Charles, CR
WILLIAMS Maya, Post-doc



Scanning trajectory (in red) over the mouse brain

Genetics of cardiac diseases

Congenital heart defects *(CHD) are the most common type of birth defect, occurring in about 1% of all births. Our main goal it to better understand the genetic basis and developmental origin of CHD.*
We use embryological, genetic, and molecular approaches to analyze the development of the cardiovascular system. Using in vivo and in vitro models, we aim to decipher mechanisms that control heart development and disease. Our goal is to establish relationships between signaling pathways and transcription factors that control progenitor identity and contribute to cardiac malformations.

FIELDS OF STUDY

- Cardiovascular Development,
- Congenital Heart defects,
- Genetics, iPSC,
- Organoids, aortic and valve diseases.

STRENGTHS

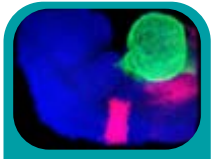
- Through our collaboration with clinicians, we develop translational approaches using clinical data, patient samples and in vivo or in vitro models.
- Integrating animal models, hiPSC-derived models, and imaging techniques, we aim to enhance our understanding of the underlying pathophysiological mechanisms of rare diseases affecting cardiac and head muscles.
- Based on our expertise we create 3D models using human iPSC-derived cells as rare diseases models to explore cellular and environmental interactions and identify molecules as potential therapeutic targets.

NOTABLE COLLABORATION

- the teams of Robert Kelly (IBDM) and Fabienne Lescroart (MMG) to study the development of early cardiac progenitor cells & the role of the retinoic acid signal during the formation of the pharyngeal region.
- the teams of Valérie Deplano (IRPHE) and Frédérique Magdinier (MMG) for the study of the cellular response to hemodynamics (wall shear stress) of valvular and aortic cells.

FUTURE PRIORITIES

- Identify novel genes involved in cardiac disease using genetic screening.
- Deciphering the role of the retinoic acid (derivative of the vitamin A) pathways in heart and valve development.
- Address ageing mechanisms of valve disease and regeneration in mouse and zebrafish genetic models.
- Develop powerful vascular organoid model as a 3D model to screen molecules repressing aortic disease.
- Use gastruloids as a model to study rare diseases affecting cardiac and head muscle lineages.



Wholemount RNAscope in situ hybridization on E8.5 embryo with probe for Hoxb1 and Tnnt2

Cross-sectional H&E images showing normal aortic valve (left; three leaflets) and bicuspid aortic valve (right)

PRINCIPAL INVESTIGATOR

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JAOUDI Hager - Postdoc
LE GALLO Coralie - AI
MARCHESE Damien - Postdoc
OVAERT Caroline - Pr. Pediatric-Cardiology
SEDDIK Amel - PhD Student
VALERIO Nuno - PhD Student

RECENT PUBLICATIONS

- Argiro L, Chevalier C, et al., Gastruloids are competent to specify both cardiac and skeletal muscle lineages. Nat Commun. 2024 Nov 23;15(1):10172. ßCo-Senior authors.
- Odelin G, Faucherre A, et al., Variations in the poly-histidine repeat motif of HOXA1 contribute to bicuspid aortic valve in mouse and zebrafish. Nat Commun. 2023;14:1543.
- Jaouadi H, Jopling C, et al., Expanding the phenome and variome of the ROBO-SLIT pathway in Congenital Heart Defects: Toward improving the genetic testing yield of CHD. J Transl Med. 2023 Feb 28;21(1):160.
- Faure E, Bernard E, et al., Side-dependent effect in the response of valve endothelial cells to bidirectional shear stress. Int J Cardiol. 2021 Jan 15;323:220-228.

*Our research group focuses on **the identification and analysis of non-coding/regulatory regions** using large scale integration of high-throughput sequencing data. How those barely annotated regulatory elements shape the expression and the dynamics of our genomes is the main goal of our research.*

PRINCIPAL INVESTIGATOR

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GROUP MEMBERS

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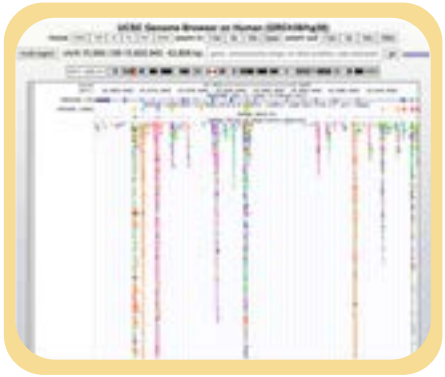
CAMPOS Andreia, Master Student
DE LANGEN Pierre, PhD student
HAMMAL Fayrouz, PhD student
LOPEZ Fabrice, IR

FIELDS OF STUDY

- Large scale regulatory elements identification
- Transcription of regulatory elements
- Impact of transposable elements in TF binding
- Intragenic enhancers detection

STRENGTHS

We address our research by creating unique genomic catalogs built from large scale integration of available regulatory omic data. These catalogs of 1000 Pol2 or 15000 TF ChIP-seq (ReMap) are at the foundation of the biological question we address.
Our strength reside in bioinformatics/genomics expertise for the analyses of regulatory datasets.



FUTURE PRIORITIES

- As regulatory elements are numerous and possibly redundant in our genome, our research will progress towards **detecting the "active" or "key" regulatory elements in different biological system**.
- We also will focus on **how the regulatory code in tightly interlaced with genome plasticity/evolution**.

NOTABLE COLLABORATIONS

- Our long term collaboration with **the JASPAR team in NCMM Norway** allow us to improve the definitions of thousands of **Transcription Factor Binding sites (TFBS)**.
- **The UCSC Genome Browser** has released our **ReMap catalogue** as a native regulatory track.

SOURCES

ReMap 2022: https://remap.univ-amu.fr/
ReMap 2022, NAR: "*ReMap 2022: a database of Human, Mouse, Drosophila and Arabidopsis regulatory regions from an integrative analysis of DNA-binding sequencing experiments*". https://doi.org/10.1093/nar/gkab996
UCSC : https://genome.ucsc.edu/

FIELDS OF STUDY

- Protein function from a network perspective
- Protein-protein and protein-RNA interaction network analyses
- Impact of genetic variations on protein networks
- Methods in Data integration, Graph partitioning and visualization

STRENGTHS

Interdisciplinarity (Biology, Bioinformatics, Physics, Statistics, Computer Science)

FOCUS

- Network perturbations in host-pathogen relationships
- functions of novel small peptides.

FUTURE PRIORITIES

- Signaling and decision-making,
- functions of proteins encoded by neogenes,
- network perturbations mediated by pathogens vs. commensal bacterial effectors.

NOTABLE COLLABORATIONS

Pascal Falter-Braun, INET, Helmholtz Zentrum, Munich, Germany;
Patrick Aloy, IRB, Barcelona, Spain;
Olivier Destaing, IAB, Grenoble, France;
Renaud Vincentelli, AFMB, Marseille, France;
Anne-Ruxandra Carvunis, University of Pittsburgh, PA, USA
Erich Baurnberg-Bauer, University of Müenster, Germany

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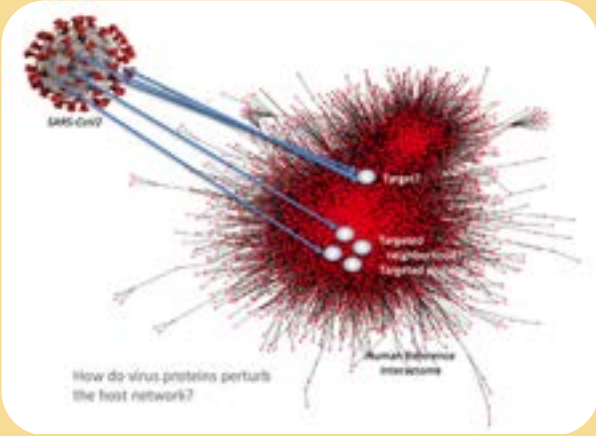
STOSSKOPFF Thomas, Engineer
ZANZONI Andreas, MCU



SOURCES - RECENT PUBLICATIONS

- Hoteau SA, Cristianini M, et al., mimicINT: a workflow for microbe-host protein interaction inference. bioRxiv. 2022.11.04.515250.
- Kim DK, et al., A proteome-scale map of the SARS-CoV-2 human contactome. Nature Biotech. 2023;41:140-149. doi: 10.1038/s41587-022-01475-z.
- Young V, et al., A gut meta-interactome map reveals modulation of human immunity by microbiome effectors. bioRxiv. 2023.09.25.559292.
- Slivak M, Choteau SA, et al., InteractORF, predictions of human sORF functions from an interactome study. bioRxiv. 2024.06.10.598216.
- Lopez F, Spinelli L, et al., Clust&See3.0: clustering, module exploration and annotation. F1000Research. 2024;13:994.

Genetic landscape of cardiomyopathies

The main aim of our group is to decipher the pathogenic process associated to the development of severe cardiomyopathies. The alternative aims are the identification of biomarkers and the identification of targets for drugs development.

PRINCIPAL INVESTIGATOR

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NUNES Joao Paulo, Post-doc
SPINELLI Lionel, IR
TORRES Magali, IE

FIELDS OF STUDY

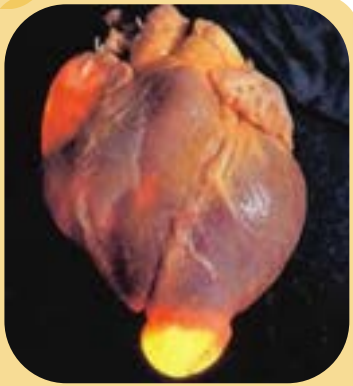
- Chagas diseas
- Diabetis
- Severe dilated cardiomyopathies
- Hypertrophic cardiomyopathies
- Arrhythmia
- LVNC

STRENGTHS

- Heart tissue collection
- OMIC profiling and multi-OMIC analysis
- Genetic variants of susceptibility (GWAS and Exome sequencing)
- Functional variants characterization (CRISPR/CAS9, IPS-cardiomyocytes)
- Bioinformatic analyses (variant priorisation)

FOCUS

- Knock in/out on IPS derived cardiomyocytes from cases and controls.
- Develop heart organoids model system to study pathogenic variant effects.
- Characterise the involvement of mitochondria in pathologies.
- Elucidate the effect of pathogenic variants in drosophila model.



Chagas dilated cardiomyopathy

NOTABLE PUBLICATIONS

- Nunes JPS et al., *Co-Exposure of Cardiomyocytes to IFN-γ and TNF-α Induces Mitochondrial Dysfunction and Nitro-Oxidative Stress: Implications for the Pathogenesis of Chronic Chagas Disease Cardiomyopathy*. Front Immunol. 2021 Nov 11;12:755862. doi: 10.3389/fimmu.2021.755862. PMID: 34867992; PMCID: PMC8632642.
- Teixeira PCet al., *Impairment of Multiple Mitochondrial Energy Metabolism Pathways in the Heart of Chagas Disease Cardiomyopathy Patients*. Front Immunol. 2021 Nov 12;12:755782. doi: 10.3389/fimmu.2021.755782. PMID: 34867990; PMCID: PMC8633876.
- Ouarhache M et al., *Rare Pathogenic Variants in Mitochondrial and Inflammation-Associated Genes May Lead to Inflammatory Cardiomyopathy in Chagas Disease*. J Clin Immunol. 2021 Jul;41(5):1048-1063. doi: 10.1007/s10875-021-01000-y. Epub 2021 Mar 3. PMID: 33660144; PMCID: PMC8249271.

Bioinformatics of gene regulatory sequences and variants

*Our group is studying **gene regulation** in **Drosophila** and **human**, using **different computational approaches**.*

FIELDS OF STUDY

- Analysis of gene regulatory sequences and variants
- Human genetics and complex diseases
- Software development

STRENGTHS

Assistant Professor GONZÁLEZ has contributed to 17 peer-reviewed articles, 2 preprints and 2 reviews (h-index=11).

Latest software:

- MultiXrank (Our group is studying gene regulation in Drosophila and human, using different computational approaches.)
- VTAM (Our group is studying gene regulation in Drosophila and human, using different computational approaches.)
- pygtftk (Our group is studying gene regulation in Drosophila and human, using different computational approaches.)
- TAGOOS (Our group is studying gene regulation in Drosophila and human, using different computational approaches.)

FUTURE PRIORITIES

- Computational prioritization of genetic variants.
- Undersand the molecular basis of pleiotropic variants.
- Collaborate with experimentalists to develop innovative high-throughput experimental methods.

PRINCIPAL INVITIGATOR

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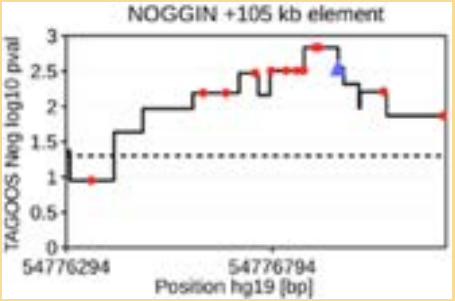
SELECTED PUBLICATIONS

- Gonzalez A, Dubut V, et al., VTAM: A robust pipeline for validating metabarcoding data using internal controls. 2021. ‹hal-03144831›.
- Gonzalez A, Artufel M, et al. TAGOOS: genome-wide supervised learning of non-coding loci associated to complex phenotypes. Nucleic Acids Res. Oxford University Press, 2019. ‹10.1093/nar/gkz320›. ‹hal-02119716›.
- Lopez F, Charbonnier G, et al., Explore, edit and leverage genomic annotations using Python GTF toolkit. Bioinformatics. Oxford University Press, 2019. ‹10.1093/bioinformatics/btz116›. ‹hal-02078147›.
- Mbodj A, Gustafson EH, et al., Qualitative Dynamical Modelling Can Formally Explain Mesoderm Specification and Predict Novel Developmental Phenotypes. PLoS Comput Biol. 2016;12(9):e1005073. ‹10.1371/journal.pcbi.1005073›. ‹hal-01619081›.



TAGOOS prediction of genetic variants in the+105 kb NOGGIN regions (hg19,chr17:54,776,180-54,777,328) including the previously validated variant rs227727 in blue. doi: 10.1093/nar/gkz320

Genetics and functional genomics of human malaria

Malaria *kills half a million children a year, yet most Plasmodium falciparum infections remain asymptomatic while about 10% of infections progress to fever. Of these, only a small fraction develops severe clinical manifestations with* ***cerebral malaria (CM)*** *and* ***severe anaemia (SA)*** *being the two most frequent forms.* ***By combining genetics, transcriptomics, and functional genomics approaches****, we aim to* ***identify the molecular dysfunctions responsible for CM and SA****. We are also* ***studying the host-pathogen interaction at the single-cell level in asymptomatic individuals****, who serves as a reservoir for the parasite, a major challenge for malaria eradication.*

FIELD OF STUDY

- Identify susceptibility genes for severe malaria
- Define the transcriptomic signatures of cerebral malaria
- Identify and characterize functional variants and cis-regulatory elements involved in pathogenic mechanisms of severe malaria
- Discover predictive biomarkers of infection outcome (symptomatic, asymptomatic, short and long-lasting infections)

STRENGTHS

We combine epidemiological, bioinformatics and experimental approaches to disentangle both
parasite and host factors using state-of-the-art technologies.

- Sample collection from Africa (Mali, Nigeria, Cameroon)
- Genetic variants of susceptibility/resistance
- Functional genomics (gene reporter assays, CRISPR-Cas9 genome editing, flow cytometry)
- Multi-OMICS analysis (bulk and single-cell transcriptomics, ATACseq)
- Bioinformatics analysis

FOCUS

- Decipher the common pathogenic mechanisms between cerebral malaria and neurodegenerative disorders.
- Identify new molecular mechanisms involved in severe malaria
- Study of common polymorphisms and rare mutations in the ATP2B4 and PIEZO1 genes to determine their molecular effects and physiological consequences.
- Perform integrative single-cell multi-omics analysis to decipher host-pathogen interactions and discover predictive biomarkers of infection outcome.

PRINCIPAL INVESTIGATOR

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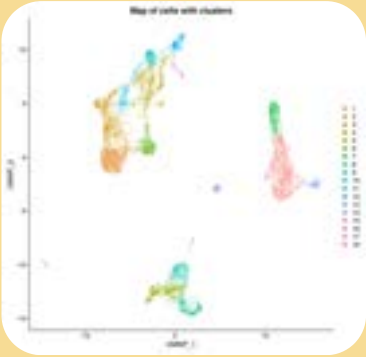
POUVELLE Bruno, IR
QUATREVILLE Loréna, PhD student
RIHET Pascal, PR
TORRES Magali, IE

NOTABLE COLLABORATIONS

- Antoine Claessens, UMR5235, Montpellier, France
- Antoine Berry and Nicolas Blanchard, UMR1291, Toulouse, France
- Sandrine Nsango, Centre Pasteur, Yaoundé, Cameroon
- Delmiro Fernandez-Reyes, University College London, London, United Kingdom



SOURCES

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9101746/pdf/ijms-23-04849.pdF
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10404997/pdf/main.pdf
https://biorxiv.org/cgi/content/short/2024.03.18.585566v1

Genetics and functional genomics of complex diseases such as sepsis, malaria and T-cell acute lymphoblastic leukemia

The main objective of our projects is to identify non-coding sequences regulating genes involved in disease development.

FIELDS OF STUDY

Expertise in inflammation processes, cancer development, mechanisms of gene deregulation and epigenetic.

STRENGTHS

- Systematic experimental approach to identify regulatory sequence variants and genes involved in complex diseases
- High-throughput sequencing (Chip-Seq, RNA-seq...), bioinformatics analysis (variant prioritization), functional analysis (reporter assays, qPCR, CRISPR/Cas9)
- Functional studies on human and mouse cell lines and mouse models
- Studies from human patient samples

FUTURE PRIORITIES

- Identification of variants and deciphering of processes involved in the development of severe forms of sepsis using a massive parallel rapporter assay
- Identification of new markers of severe sepsis using epigenetic data and RNA sequencing
- Identification of new genes and mutations involved in the development of T-ALL using epigenetic data and RNA sequencing.

NOTABLE COLLABORATION

- Nathalie Lalevée and Marc Leone on a Sepsis project,
- Sandrine Marquet and Pascal Rihet for the Malaria project
- Salvatore Spicuglia for T-ALL projects.

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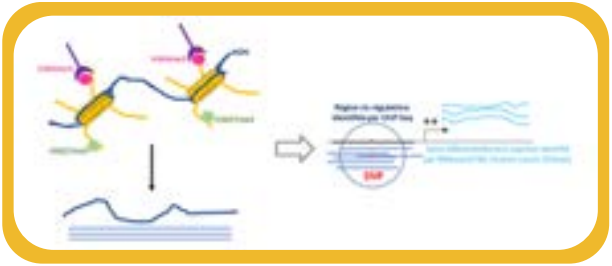


SELECTED PUBLICATIONS

- Wan J, van Ouwerkerk A, et al., Comprehensive mapping of genetic variation at Epromoters reveals pleiotropic association with multiple disease traits. Nucleic Acids Res. 2024 Dec 27:gkae1270. doi: 10.1093/nar/gkae1270.
- Rosier F, Nuñez NF, et al., Transcriptional Response in Sepsis Patients Reflects Transcriptional Response in a Sepsis Mouse Model. Int J Mol Sci. 2022 Jan 13;23(2):821. doi: 10.3390/ijms23020821.
- Belhocine M, Simonin M, et al., Dynamics of broad H3K4me3 domains uncover an epigenetic switch between cell identity and cancer-related genes. Genome Res. 2022 Jul;32(7):1328-1342. doi: 10.1101/gr.266924.120.
- Rosier F, Brisebarre A, et al., Genetic Predisposition to the Mortality in Septic Shock Patients: From GWAS to the Identification of a Regulatory Variant Modulating the Activity of a CISH Enhancer. Int J Mol Sci. 2021 May 29;22(11):5852. doi: 10.3390/ijms22115852.
- Santiago-Algarra D, Dao LTM, et al., Recent advances in high-throughput approaches to dissect enhancer function. F1000Res. 2017 Jun 19;6:939. doi: 10.12688/f1000research.11581.1.
- Baaklini S, Afridi S, et al., Beyond genome-wide scan: Association of a cis-regulatory NCR3 variant with mild malaria in a population living in the Republic of Congo. PLoS One. 2017 Nov 9;12(11):e0187818. doi: 10.1371/journal.pone.0187818.
- Navarro JM, Touzart A, et al., Site- and allele-specific polycomb dysregulation in T-cell leukaemia. Nat Commun. 2015 Jan 23;6:6094. doi: 10.1038/ncomms7094.

Bioinformatics of transcriptional regulation in T-cells

*Our group is interested in understanding the **transcriptional mechanisms that drive T-cell development in the thymus**. This encompasses the implementation of **(multi-) omics methods** to perform single-cell or spatially resolved large-scale analyses of coding and non-coding transcriptome or epigenome. These molecular methods are coupled with the development of **bioinformatic tools** that implement **dedicated statistical frameworks** (e.g Python GTF Tool Kit, OverLap Of Genomic Regions Analysis using Monte Carlo).*

STRENGTHS

- Large scale (spatially/single cell resolved) transcriptome analysis, epigenetics.
- Bioinformatic methods and tools development (e.g. Python GTF Tool Kit, OLOGRAM, OLOGRAM-MODL, SciGeneX).
- Co-leader of the TGML (Transcriptomics and Genomics Marseille Luminy) facility.

FOCUS

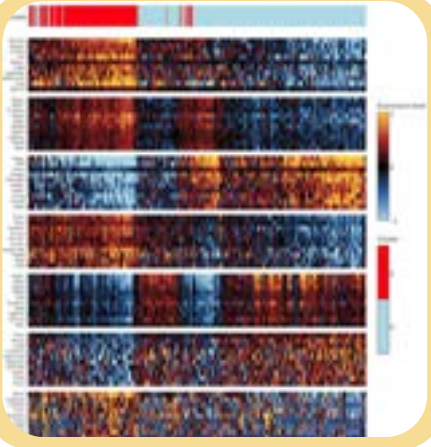
We are currently developing, in collaboration with TGML facility, spatially resolved transcriptomics to analyse the regulatory events occuring in the thymus. This ongoing project with M. Irla (CIML) and Arnauld Sergé (LAI) aims at elucidating the molecular mechanism driving T-cell and epithelial cell development in the thymus (cross-talk). This project is coupled with the development of partitioning approaches implemented in the Scigenex R package that is currently developed in collaboration with L. Spinelli (CIML).

FUTURE PRIORITIES

- One of our main goal is to implement **molecular and bioinformatics methods** to **produce spatially resolved multi-omics map of the thymus.**
- Develop **statistical and machine-learning methods** to **foster multi-omics integration.**

NOTABLE COLLABORATIONS

- Long term collaboration with **Salvatore Spicuglia (TAGC)** on elucidating the role of non-coding RNA in developing T-cell and the role of promoter with enhancer activity (ePromoters).
- Our group has been collaborating for several years with **the group of Saadi Khochbin and Sophie Rousseau (IAB, Grenoble).**



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GROUP MEMBERS

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CHEVALLIER Jessica, PhD student
CONTE Samantha, PhD student
GARD Charlyne, Engineer

SELECTED PUBLICATIONS

- Ferré et al.,(2019). *"OLOGRAM: Determining significance of total overlap length between genomic regions sets"*. Bioinformatics (Oxford, England), btz810. Advance online publication. https://doi.org/10.1093/bioinformatics/btz810
- Lopez et al., (2019). *"Explore, edit and leverage genomic annotations using Python GTF toolkit"*. Bioinformatics (Oxford, England), 35(18), 3487–3488. https://doi.org/10.1093/bioinformatics/btz116
- Dao et al., *"Genome-wide characterization of mammalian promoters with distal enhancer functions"*. Nat Genet 49, 1073–1081 (2017). https://doi.org/10.1038/ng.3884

*Malaria and sepsis. Our research mainly focuses on **malaria and sepsis**. The overall objective is to **identify genes, gene networks and their variations** involved in the control of infection and the onset of clinical disease.*

FIELDS OF STUDY

Dysregulation of gene expression in sepsis and malaria

STRENGTHS

We combine bioinformatic approaches with genetics and transcriptomics approaches in human populations, and in animal and cell models.

FOCUS

- Characterising transcriptional signatures associated with clinical phenotypes.
- Assessing the regulatory effect of genetic variants using classical and massive gene reporter assays
- Identifying cis-regulatory variants perturbing gene networks and causing the disease

FUTURE PRIORITIES

- Looking for genetic regulatory variants modulating gene expression in immune cells.
- Assessing the effect of regulatory variants on the activation of immune cells at the single-cell level using cytometry and a new microimmunotest developed by our collaborator (LAI).

NOTABLE COLLABORATIONS

Collaboration with O Theodoly (Adhesion and Inflammation Laboratory)

Collaborations in Africa:

- F Ntoumi, Brazzaville University, Congo
- A Dieye, B Mbemgue, R Ndiaye, Cheikh Anta Diop University, Dakar, Senegal
- A Thiam, Institut Pasteur de Dakar, Senegal -S Sawadogo, Ouagadougou University, Burkina Faso

SELECTED PUBLICATIONS

- Adjemout et al., From GWAS to functional variants: ARL14 cis-regulatory variants are associated with severe malaria. 2024; Mar 26:jiae159. Journal of Infectious Diseases.
doi: 10.1093/infdis/jiae159. -

- Adjemout et al., Concurrent PIEZO1 activation and ATP2B4 blockade effectively reduce the risk of cerebral malaria and inhibit in vitro Plasmodium falciparum multiplication in red blood cells.Genes Dis. 2023 Mar 27;10(6):2210-2214.
doi: 10.1016/j.gendis.2023.02.029

- Madaci et al., Diseases. The Contribution of Multiplexing Single Cell RNA Sequencing in Acute Myeloid Leukemia. 2023 Jul 12;11(3):96.
doi: 10.3390/diseases11030096.

- Cretin et al., A Non-Coding Fc Gamma Receptor Cis-Regulatory Variant within the 1q23 Gene Cluster Is Associated with Plasmodium falciparum Infection in Children Residing in Burkina Faso. Int J Mol Sci. 2023 Oct 28;24(21):15711.
doi: 10.3390/ijms242115711.

- Rosier et al., Transcriptional Response in a Sepsis Mouse Model Reflects Transcriptional Response in Sepsis Patients. Int J Mol Sci. 2022 Jan 13;23(2):821.
doi: 10.3390/ijms23020821.

- Rosier et al., Genetic Predisposition to the Mortality in Septic Shock Patients: From GWAS to the Identification of a Regulatory Variant Modulating the Activity of a CISH Enhancer. Int J Mol Sci. 2021 May 29;22(11):5852.
doi: 10.3390/ijms22115852.

PRINCIPAL INVESTIGATOR

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PAUL P, CR
POUVELLE B, IR
PRADEL L, MCU
TORRES M, IE
ZHOU Y, Post-doc

Subnetwork of the 27 connected proteins associated with sepsis and their direct interactors

Functional genomics of normal development and leukemia

The laboratory brings together an interdisciplinary team of researchers and engineers with a wide range of skills (cellular and molecular biology, genomics, bioinformatics, genetics). The team has a long-standing experience in genome-wide approaches to decipher ***epigenetic regulation*** *at play* ***during normal and pathological cell differentiation, including cancer****. By developing* ***Massively Parallel Reporter Assays (MPRA)****, they study* ***cis-regulatory elements*** *in* ***different cell types and stimulatory conditions*** *to disentangle* ***new type of regulatory mechanisms****.*

FIELDS OF STUDY

- Molecular basis of gene regulation, with a focus on enhancer function
- Impact of genetic variation on cis-regulatory activity
- Epigenetic dysregulation in Leukemia

STRENGTHS

- Discovered a novel type of cis-regulatory elements, named Epromoters, which harbor both promoter and enhancer activity.
- Developed high-throughput approaches to study cis-regulatory activity genome-wide.
- CRISPR-based screens to systematically assess enhancer function at the endogenous location.
- Co-leader of the regional CRISPR screen platform, leveraging functional genomic screening.

FUTURE PRIORITIES

- Set-up systematic approaches to study the impact of regulatory variants using MPRA.
- Develop new types of massive reporter assays using an integrative approach.
- Combine synthetic biology & machine learning approaches to unravel the genetic determinants of enhancer versus promoter activity of Epromoters.

SOURCES

- https://canceropole-paca.com/propulser-vos-recherches/acceder-aux-technologies-expertises/
- https://www.enhpathy.eu/
- https://doi.org/10.1038/s41467-021-26861-0
- https://doi.org/10.1038/ncomms7905

NOTABLE COLLABORATION

- S. Spicuglia is coordinator of **ENHPATHY**, a **multidisciplinary science consortium** created in the frame of **the MSCA - European Training Networks** and regrouping 12 academic and 3 non-academic European organisations in the continuum of **basic, translational and clinical research on enhancers and associated diseases**.
- ENHPATHY aims to **identify key deregulated enhancers and regulatory mechanisms, and provide new biomarkers and therapeutic avenues for enhanceropathies**.

To achieve this goal, ENHPATHY has set up an innovative, integrated and disease-focused research programme that brings together European leaders in enhancer biology, computational biology and human genetics.

ENHPATHY
MOLECULAR BASIS OF HUMAN ENHANCEROPATHIES

PRINCIPAL INVESTIGATOR

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*Mosaic is an **interdisciplinary research group** aiming at unravelling **life science problems** using **advanced photonic tools**. Mosaic principal investigators are physicists and biologists working together at the cross roads between advanced optical imaging, nanophotonics and tissue morphogenesis. In parallel, the Mosaic group is involved in collaborative projects related to the fields of developmental biology, immunology, neurosciences and biomedical research.*

FIELDS OF STUDY/ LABS

- Cell & Tissue Morphogenesis
- Nanobiophotonics
- Polarized microscopy
- Wavefront shaping in scattering media
- Thermoplasmonics
- Quantitative phase microscopy for Biology & Nanophotonics
- Non-linear optics for label-free microscopy & molecular spectroscopy
- New fiber probes for biosensing and imaging
- Mathematical optics
- Photoacoustic imaging for neurobiology

STRENGTHS

- **Development of cutting-edge optical microscopy techniques.**
- **Highly multi- and interdisciplinary research.**
- **Rich scientific production since 2002** (5160 peer-reviewed publications, 12 book chapters, 2 books, 14 patents and 1 patented software).
- **National and international collaborations** with public research organizations and private industries.

RECENT PUBLICATIONS

- Vaz Rimoli et al, "*4polar-STORM polarized super-resolution imaging of actin filament organization in cells*" Nature Communications 13, 301 (2022)
- Martins et al, "Genetically encoded reporters of actin filament organization in living cells and tissues" bioRxiv (2024) https://doi.org/10.1101/2024.04.26.591305

FOCUS

The Cell Morphogenesis and Polarized Microscopy Labs are headed by Manos Mavrakis and Sophie Brasselet, respectively. Manos, Sophie and their collaborators are developing molecular and optics instrumentation tools to study **the interplay between the higher-order organization and function of cytoskeletal proteins and molecular assemblies in cells and tissues, including actin filaments and myelin.**

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www.fresnel.fr
https://sites.google.com/view/cell-morphogenesis-lab/welcome

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HEUKE Sandro, Researcher
LE-GOFF Loic, Researcher
MAVRAKIS Manos, Researcher
MONNERET Serge, Researcher
OMI MASSIEAU Shizue, Engineer
RIGNEAULT Herve, Researcher
SAVATIER Julien, Engineer
WENGER Jerome, Researcher

MABioS is an interdisciplinary I2M group. It is involved in the CENTURI Institute convergence (Turing Centre for Living Systems) in the Luminy campus of Aix-Marseille Université. Two of its members are part of CENTURI committees, and are actively implicated in the elaboration of an interdisciplinary (Biology/Mathematics/Computer Science/Physics) graduate school, called CMB (Computational and Mathematical Biology).

FIELDS OF STUDY/ LABS

- Discrete modeling of dynamical regulatory networks (Keywords: Boolean networks, graphs, discrete dynamical systems, Boolean functions)
- Analysis of large-scale interaction networks (Keywords: graphs, modularity, classification, communities, active modules, random walks, network embedding, dimension reduction)

STRENGTHS

- Complementary expertise within the group(((bio)mathematics, computer science and bioinformatics)
- Solid and complementary collaborations on interdisciplinary projects at local and international level

FUTURE PRIORITIES

The research developed by MABioS team focuses on **the mathematical modeling of biological interaction networks in order to understand their transient and asymptotic behaviors.**

SOURCES

www.i2m.univ-amu.fr
mabios.math.cnrs.fr
centuri-livingsystems.org/about-us/#governance

NOTABLE COLLABORATIONS

Along our different collaborations, we have developed several Boolean models of regulatory networks to provide mechanistic explanations of the functioning of biological processes. Analysis and simulations of the models allow us to identify the key components controlling the dynamics, and to make predictions about behavior in altered situations. We jointly develop mathematical methods to analyze large Boolean systems.
Previous applications on cancer have explained the observed co-occurring and mutually exclusive mutations or synergies between anti-cancer drugs used in targeted therapy. We apply this modelling to decipher and characterize the specific functioning of **rare diseases**, through collaborations with **NSBD teams (Anaïs Baudot)**.

Mathématiques Algorithmique pour la Biologie des Systèmes

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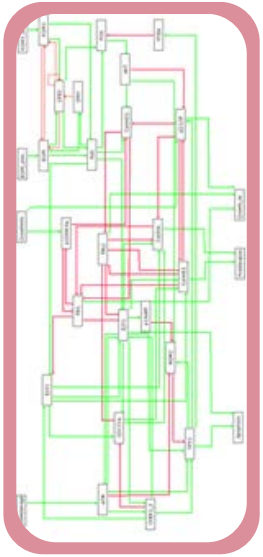

IRPHE is a CNRS, Aix-Marseille University (AMU), Centrale Marseille joint laboratory associated to the Institute for engineering and systems sciences (INSIS, CNRS), ***specialized in the modelling of complex macroscopic systems*** *coupling* ***experimental, analytical, and numerical tools****. Specialist in* ***biofluids mechanics****, the biomechanics team of IRPHE develops* ***multi physics in silico models*** *and* ***multi modal in vitro experiments*** *to investigate* ***fluid structure interactions in biological systems****,* ***soft tissue properties*** *and* ***biological porous media behaviour*** *at different scales* ***from organ to cell****.*

FIELDS OF STUDY

- Modelling cardio-vascular pathologies: Aortic aneurysm, aortic dissection, stenosis, valvular dysfunction, RBG pathological aggregation.
- Characterization of biological soft tissue and porous media
- Modelling biomechanical behavior of soft tissue
- Experimental and numerical investigation of ultrasound interaction with biological tissues and cells.
- Modelling lymph transport in the lymphatic system.

STRENGTHS

- Complex biomimetic numerical modelling
- Biomimetic in vitro modelling of macro and micro blood circulation
- Controlled in vitro ultrasound stimulation of cells to investigate cell mechanotransduction
- Metrology : PIV 3C-3D, microPIV, 3D digital image correlation for soft tissue biomechanical characterization, microCT, rheometry, photoacoustics, quantitative imaging.

FUTURE PRIORITIES

- Cell mechanotransduction in living tissues.
- Cancer cell migration via the lymphatic system.
- Thrombus modelling.
- Prediction of the evolution of aortic pathologies.

TEAM LEADER

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BARON Cécile, CRCN CNRS, HDR
BERTRAND Eric, IR
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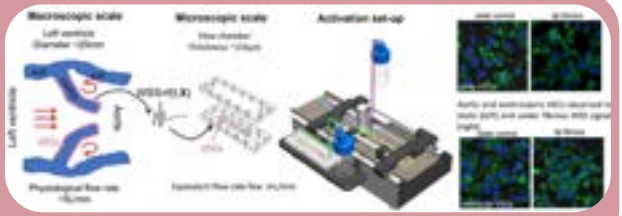
NOTABLE COLLABORATION

Our collaboration with **Stéphane ZAFFRAN Team (MMG, Marseille)** on the **mechanisms of mechano-transduction involved in valvulopathies** led to the development of **an original fluid activation device**. This *in vitro* experimental set-up generates **physio-pathological pulsatile wall shear stress (WSS)** to which valvular endothelial cells are exposed. This set up is connected to a **home-made flow chamber**, allowing **valve cell quantitative analysis** using a **3D collagen hydrogel for cells culture**.

SOURCE

- Faure, E., Bertrand, E., et al., *Side-dependent effect in the response of valve endothelial cells to bidirectional shear stress*. International Journal of Cardiology, 2021, 15;323:220-228. Doi : 10.1016/j.ijcard.2020.08.074



Credit : V. Deplano

Theme Medical Ultrasound

*Our research group is interested in **developping new ultrasound-based techniques** for the characterization and imaging of biological tissues such as the breast, bone and blood.*

FIELDS OF STUDY

- Ultrasound imaging techniques for the detection of breast cancer and bone pathologies.
- Ultrasound characterization techniques to extract quantitative measures describing intrinsic acoustic properties and structures of scanned tissues such as bone tissue, blood and tumors.

STRENGTHS

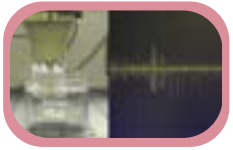
- **Different methodologies**: Ultrasound tomography, source/object location optimization, quantitative ultrasound techniques of tissue microstructures, nonlinear acoustic, signal processing.
- **A wide range of biomedical applications**: breast cancer, bone pathologies, erythrocyte aggregation, microbubbles circulating in the blood
- **Diverse national & international academic & industrial collaborations**.
- **Concrete contributions to socio-economical aspects in the Health field** (holder of patents...).

FUTURE PRIORITIES

Research progresses concern **the inverse problems in wave propagation with all the fundamental aspects involved**: the understanding of the mechanisms of interaction between wave and scatterers, the data acquisition strategy, their inversion and the image reconstruction with the quantitative character (in opposition to the qualitative character of conventional ultrasonic imaging).

NOTABLE COLLABORATION

In collaboration with **LP3**, **the Fresnel Institute** and the russian lab PhysBio, we synthesized nanostructures consisting of a Silicon (Si) core covered with small gold (Au) nanoparticles (NP), thanks to the use of laser and chemical modifications. The produced Si@Au core-satellite nanocomposites promise a major advancement of imaging & phototherapy modalities based on plasmonic properties of nanomaterials.



PRINCIPAL INVESTIGATOR

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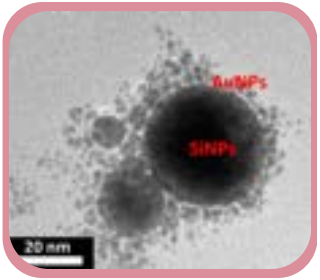
MENSAH Serge, HDR
METWALLY Khaled, Post-doc, Engineer
PAYAN Cédric, HDR
POULAIN ZARCOS Marie, Post-doc, IMI



SOURCES

WWW.LMA.CNRS-MRS.FR/SPIP/SPIP.PHP?PAGE=THEME&ID_MOT=22&LANG=EN
Al-Kattan A, Tselikov G, et al., Laser Ablation-Assisted Synthesis of Plasmonic Si@Au Core-Satellite Nanocomposites for Biomedical Applications. *Nanomaterials*. 2021; 11(3):592. https://doi.org/10.3390/nano11030592

LP3 conducts original research on the physics of pulsed laser-matter interactions and in order to develop new photonic processes.

FIELDS OF STUDY

- Laser-induced plasma,
- Elemental analysis,
- Optical probes and hard pulsed X-ray sources for time-resolved diagnostics of materials under pulsed laser excitation,
- Nano-objects for biology and medical applications,
- Additive fabrication for organic microelectronic,
- Laser bioprinting,
- Laser damage and ablation in ultrashort regime,
- Laser-induced material modifications ...

STRENGTHS

Our **skills** and **unique set of laser sources with the related equipment** (two high-tech laser platforms: ASUR for "Applications des Sources Laser Ultra-rapide" and LaMP for "Laser pour le Micro-usinage et les Procédés") allow the development of **new lasers processes,** to propose **innovative solutions for industrial, bio-medical & academic worlds.**

FOCUS

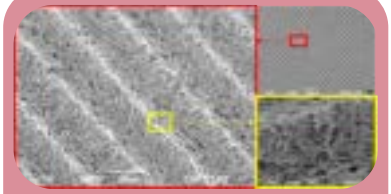
- **Laser fabrication of nano-objects and applications** (theragnostic, functionalized materials with high spatial resolution, tissue engineering ...)
- **Laser-induced transfer processes and application** (organic-electronic, bioprinting, tissue engineering, ...)
- **Laser ablation and laser-induced material modifications** (micro-structuring of semiconductors ...)
- **Laser-plasma interaction and high-resolution diagnostics** (time resolved X-ray diffraction, elemental analysis by laser-induced breakdown spectroscopy for fundamental and applied material science, food security or biological imaging)

SOURCE

www.lp3.fr

NOTABLE COLLABORATIONS

Since a few years, a collaboration has been set up with the **MMG (F. Magdinier)** and our group in order to combine cell biology and advanced laser-based techniques (laser-assisted printing, laser surface structuring, laser nanoparticle fabrication).
The objective is to **create and study 2D/3D microenvironments that best mimic the complexity and architecture of tissues *in vivo***.
In particular, we are targeting the optimization of muscle cell differentiation and the formation *in vitro* of active neuromuscular junctions. Currently, this collaboration is part of **an ANR ASTRID project** started in 2021. A co-directed **PhD thesis (Lucas Duvert) (grant AMU - AID)** has also started in October 2021.



Laser-induced micro-structuration of a layer of biopolymer for cells culture

PRINCIPAL INVESTIGATOR

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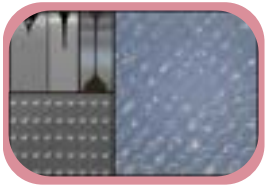
Laser-induced forward transfer (LIFT) process



Genetics, Red Cells, Biotherapy (GENGLOBE)

GENGLOBE is a team of UMR 7268 ADES (Bio-cultural Anthropology, Law, Ethics and Health), a multi-disciplinary unit directed by Pr Jacques Chiaroni.
GENGLOBE focuses on human genetics diversity in its evolutionary and functional dimensions, through the exploration of normal and pathological red blood cells and the study of blood groups and their implications for biotherapy. Research projects are organized in 3 axes: (1) Evolutionary genetics, (2) Red cells in health and disease, (3) Biotherapy.

FIELDS OF STUDY

- Hemoglobinopathies
- Red cell disorders
- Haematopoiesis and erythropoiesis

STRENGTHS

- Full expertise of in vivo and in vitro erythropoiesis
- 3D cultures mimicking the bone marrow compartment
- Real-time live cell imaging under controlled gas and temperature conditions
- Animal models
- Preclinical studies

FOCUS

The "Red cells in health and disease" axis of GENGLOBE investigates blood cells and hematopoiesis in health and disease, with a special focus on red blood cells and erythropoiesis in sickle cell disease.

FUTURE PRIORITIES

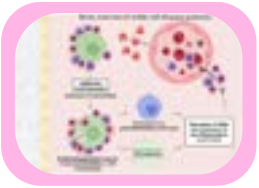
Identify new pathological pathways in hemoglobinopathies and red cell disorders to target by novel therapeutical strategies.

SOURCE https://ades.univ-amu.fr/en/research-teams/blood-cell-biology-anthropology

NOTABLE PROJECT

Our team is partner of the key networks in the field of red cells and erythropoiesis at the national and international levels, including the Laboratory of Excellence GR-Ex, the French Club of Red Cells and Iron, The European Red Cell Society and Hemocentro of Ribeirão Preto (São Paulo, Brazil).

We have established collaborations with MarMaRa partners: Christophe Lachaud (UMR 7258 CRCM) on ineffective erythropoiesis in beta thalassemia and Fanconi anemia; Pr Catherine Badens (UMR 1263 C2VN) on inherited red cell disorders and hemoglobinopathies.



PRINCIPAL INVESTIGATOR

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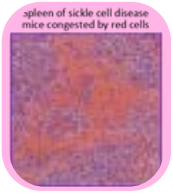
GODARD Auria (Post-doctoral fellow)
SEUTE Robert (Post-doctoral fellow)



ADES complements the medical approach to the body with a global approach, both socio-cultural and ethical. The different researches of team n°2, called "Body, norms, health" share the same double-aspect approach to the body : on the one hand, as a "body-object" and on the other hand, as a "body-subject. The growing development of "biomedicine" is changing the way the body is represented and calls for an anthropological and philosophical reflection.

FIELDS OF STUDY & STRENGTHS

- Historically invested by geneticists and paediatricians, **our field of research in ethics** deals with **subjects** such as genetics, **screening, prevention, perinatal diagnosis.**
- **A medical-oriented multidisciplinary approach to the body**: Anthropology of Health, moral philosophy, medical ethics, epistemology of medicine, health law, human and social sciences.
- **Modern premises** of 500 m², including a 130-seat conference room and a large documentation center.
- **A strategic place** located at La Timone UH, called «***Espace Ethique Méditerranéen***», welcoming **diverse research partners** (EFS, Faculty of Medical and Paramedical Sciences, AP-HM, etc.).
- **Nationally known experts** affiliated to numerous prestigious bodies.

FUTURE PRIORITIES

- The field of **clinical trials** is under acute ethical tensions between **the individual interest and the collective one**. Clinical trials carry **risks of adverse events** that are only partially predictable. The ethical questions we raise are **whether the risk is clearly assumed** and by **whom**, knowing that the collective benefit of an expected clinical trial may be significant for future generations of patients.
- Other aspects of our research relate to **scientific integrity and deontology**. Our work questions the conditions of objectivity in the production of medical knowledge.

NOTABLE PROJECT

The "Body, standards, health" team is responsible for **the IGPrare study** on **genetic information in kinship**, in response to the call for research tenders **« AMP, diagnostic prénatal, diagnostic génétique»**, (funding from **the Biomedicine Agency**, 30,000 euros). Ongoing since 2020.

PRINCIPAL INVESTIGATOR

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http://www.ee-paca-corse.com/
Bulletin de l'Académie de médecine

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TARDIEU Corinne, Pr
TOSELLO Barthélémy (Pr, AMU, ADES, EFS, CNRS

Espace de réflexion éthique PACA Corse

The Center for Studies & Research on Health Services & Quality of Life (CEReSS) is a public health research unit under the direction of Laurent Boyer, Julie Berbis and Sami Hraiech , located at the Faculty of Medical and Paramedical Sciences, Timone sector (Aix-Marseille University). The CEReSS develops a research activity on Health Services Research (HSR) with an emphasis on the contribution of patient-centered measures (Patient-Reported Outcome Measures or PROMs and Patient-Reported Experience Measures or PREMs).

FIELD OF STUDY

Our HSR projects focus on various chronic pathologies, grouped around 4 main themes:

- **Mother-child**
- **Oncology**
- **Psychiatry-neurology-precariousness and disability**
- **Resuscitation, emergency medicine & anesthesia,**
- **Clinical pharmacy**
- **Primary care**
- **Nursing science**

FOCUS

Our Health Services Research (HSR) concentrates on Quality of Life, especially in the context of chronic diseases. We are committed to developing and utilizing Patient-Reported Experience Measures (PREMs) and Patient-Reported Outcome Measures (PROMs) to capture and integrate patient perspectives into health policy decisions. Additionally, we analyze real-world data from French cohort studies and national medical-administrative databases (PMSI, SNDS) to investigate the organization and quality of healthcare delivery. This comprehensive approach ensures that our research not only enhances understanding but also contributes to tangible improvements in healthcare systems.

STRENGTHS

The unit collaborates with more than 20 research teams from different countries mainly in Europe, North America, South America and Australia.

The CEReSS is in charge of several French cohorts such as :

- cohort of childhood leukemia survivors,
- cohort of patients with a hereditary haemorrhagic disease (France Coag in conjunction with MHEMO - French rare diseases Healthcare Network : rare constitutional hemorrhagic disorders),
- cohort of patients with hereditary metabolic diseases diagnosed during their childhood and requiring a restrictive and specific diet (in connection with the G2M structure),
- GPQoL cohort (children of school age and very premature babies)
- COVID-19 cohorts (cohort of homeless people, a health data warehouse linked to
- COVID-19 with European funding from EHDEN).

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LOUNDOU Anderson, PhD Data scientist
LOUBIERE Sandrine, PhD Economist
FERNANDES Sara, PhD Psychomotrician

FUTURE PRIORITIES

- Expanding and refining **PREMs and PROMs**, particularly for chronic diseases,
- Integrating diverse data sources through advanced analytics and machine learning, and using research insights to inform health policy.
- Strengthening cross-national comparisons to better understand variations in care and patient outcomes.
- Together, these efforts aim to reinforce patient-centered research and data-driven health system improvement.

NOTABLE COLLABORATIONS

CEReSS leads major national and European projects, including EHDEN, THCS, and Horizon Europe's EU-MIND (2024), in collaboration with partners from six European countries. It has developed an innovative digital platform using computerized adaptive testing to measure PREMs and PROMs, improving understanding of patient experience and care quality. Its research covers key fields such as mother-child health, oncology, psychiatry-neurology, emergency and critical care, while expanding into clinical pharmacy, primary care, and nursing sciences, all with a strong focus on patient-reported outcomes.

RECENT PUBLICATIONS

- Barlogis et al., *Physical health conditions and quality of life in adults with primary immunodeficiency diagnosed during childhood: A French Reference Center for PIDs (CEREDIH) study*. J Allergy Clin Immunol. 2017 Apr;139(4):1275-1281.e7
- Fond et al., *Association Between Mental Health Disorders and Mortality Among Patients With COVID-19 in 7 Countries: A Systematic Review and Meta-analysis*. JAMA Psychiatry. 2021 Nov 1;78(11):1208-1217
- Kalfon et al; IPREA Study group. *A tailored multicomponent program to reduce discomfort in critically ill patients: a cluster-randomized controlled trial*. Intensive Care Med. 2017 Dec;43(12):1829-1840
- El Khamali et al., SISTRESSREA Study Group. *Effects of a Multimodal Program Including Simulation on Job Strain Among Nurses Working in Intensive Care Units: A Randomized Clinical Trial*. JAMA. 2018 Nov 20;320(19):1988-1997
- Hraiech et al., *Undocumented migrants in French intensive care units in 2011-2018: retrospective nationwide study*. Intensive Care Med. 2022 Mar;48(3):290-299

TECHNICAL FACILITIES

https://www.marseille-medical-genetics.org/#collapse-220-2

The Marseille Stem Cell facility is a facility dedicated to somatic cells reprogramming and induced pluripotent stem cells differentiation. The facility provides also training to induced pluripotent stem cells culture.

FIELDS OF TECHNOLOGY

- Rare diseases
- Stem cell technology

SERVICE/EQUIPMENT/CERTIFICATION

Services:

- PBMCs reprogramming into hIPSCs
- Fibroblasts reprogramming into hIPSCs
- hIPSCs characterization
- hIPSCs banking

Differentiation of hIPSCs into:

- sensory neurons
- cranial motor neurons
- spinal motor neurons
- fibroblasts
- cardiomyocytes
- vascular smooth muscle cells
- mesenchymal stem cells and terminal derivates

Equipment:

- 3 cell culture hoods equipped with stereomicroscope
- 3 CO2 incubators
- 1 microscope equipped with a tablet

The facility is labeled “Plateformes Aix Marseille”

NOTABLE COLLABORATIVE PROJECTS

Collaboration with MMG teams (Translational Neuromyology Team, Epigenetic and nucleosketeton dynamics in rare diseases Team, Human Neurogenetics Team, MOPED Team, Heart development and cardiac regeneration Team, Genetics of cardiac diseases Team), C2VN Team (cardiovascular toxicity, dysimmunity and inflammation led by Nathalie Lalevée), CRCM team (DNA interstrand crosslink lesions and blood disorders, led by Christophe Lachaud).
Involvement in MYOPHARM project (managed by Istem)

Last publications:

Transcriptome and acetylome profiling identify crucial steps of neuronal differentiation in Rubinstein-Taybi syndrome. Van Gils J, Karkar S, Barre A, al., Commun Biol. 2024 Oct 15;7(1):1331. doi: 10.1038/s42003-024-06939-3. PMID: 39407026

Mesenchymal stem cells derived from patients with premature aging syndromes display hallmarks of physiological aging. Trani JP, Chevalier R, Caron L, al., JD. Life Sci Alliance. 2022 Sep 14;5(12):e202201501. doi: 10.26508/lsa.202201501. PMID: 36104080

Facioscapulohumeral dystrophy weakened sarcomeric contractility is mimicked in induced pluripotent stem cells-derived innervated muscle fibres. Laberthonnière C, Novoa-Del-Toro EM, Delourme M, al., Cachexia Sarcopenia Muscle. 2022 Feb;13(1):621-635. doi: 10.1002/jcsm.12835. Epub 2021 Dec 3. PMID: 34859613

Production of Innervated Skeletal Muscle Fibers Using Human Induced Pluripotent Stem Cells. Delourme M, Broucqsault N, Mazaleyrat K, al., Methods Mol Biol. 2022;2454:231-239. doi: 10.1007/7651_2020_334. PMID: 33368020

HEAD OF THE FACILITY

BROUCQSAULT Natacha, IE Inserm

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HADADEH Ola, IR AMU
NAIT ATMANE Sara, IE AMU

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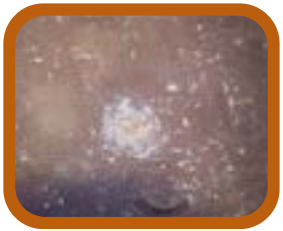

LABEL/CERTIFICATIONS

SOURCES

- https://www.marseille-medical-genetics.org/fr/plateforme-de-reprogrammation-et-differenciation-cellulaire/
- https://www.linkedin.com/showcase/marseille-stem-cell/?viewAsMember=true
- https://infrastructures.inserm.fr/Pages/ficheinfrastructure.aspx?infrastructureId=4241

Genomics and Bioinformatics (GBiM)

The Genomics and Bioinformatics Marseille (GBiM) core facility is providing state-of-the-art next generation sequencing services in the field of genomics, transcriptomics and epigenetics, to the academic researchers and private external partners.

FIELDS OF TECHNOLOGY

- Next Generation sequencing services in the field of genomics, transcriptomics, epigenomics
- Bioinformatics services for the analysis of NGS data
- Expertise in NGS in rare diseases
- Scientific support and counselling upstream and downstream the sequencing project.

SERVICE/EQUIPMENT

NGS services

We work with any species and any type of starting biological material.
On demand, we can realize any NGS project and/or bioinformatics analysis.

- Genomics: amplicons, exomes (WES), genomes (WGS), targeted sequencing
- Transcriptomics: Bulk, single cell and spatial RNA-Seq,
- Epigenomics/Epitranscriptomics: ATAC-Seq, ChiP-Seq, Methylation
- Bioinformatics: SNV, CNV, SV detection from WES/WGS, Differential Gene Expression, splicing analysis, methylation, scRNA-seq, spatial RNA-Seq, miRNA-Seq.

Equipment

- Short read Sequencing: Novaseq 6000, *Illumina*
- Long read sequencing: gridION Mk1 and PromethION, *Oxford Nanopore* sequencers
- Single Cell transcriptomics: Chromium X, *10X Genomics*
- Spatial Transcriptomics: Visium Cystassist, *10X Genomics*
- Sample Preparation: Covaris M220 ultrasonicator, Pipeting Robot, *SPT Labtech*
- Quality Control: 2100 Bioanalyzer and 4200 Tapestation , *Agilent*
- 5 High performance computing machines (CPU & GPU)

LABELS & CERTIFICATIONS

Our experiments and analysis are realized according to laboratory best practices and ISO 9001 and NFX-50 standards. In 2025, we are applying for these certifications and for the IBiSA certification.

NOTABLE COLLABORATIVE PROJECT/CONTRIBUTION

We accomplish more than 70 sequencing projects per year and we are collaborating with researchers from several MarMaRa' labs: MMG, C2VN, CRCM, IBDM, TAGC

- De Bono et al., 2025. Multi-modal refinement of the human heart atlas during the first gestational trimester. Development doi: 10.1242/dev.204555
- Argiro L, et al., 2024. Gastruloids are competent to specify both cardiac and skeletal muscle lineages. Nat Commun. 15(1):10172. doi: 10.1038/s41467-024-54466-w. * Co-last and co-corresponding authors.
- Hamzé et al., 2024. Altered NRG1/ErbB4 signaling and cholesterol metabolism dysregulation are key pathomechanisms in VRK1-related motor neuropathies and motor neuron diseases. bioRxiv 2024.02.19.581053; doi:https://doi.org/10.1101/2024.02.19.581053

SOURCE

www.marseille-medical-genetics.org/fr/genomics-bioinformatics-platform/

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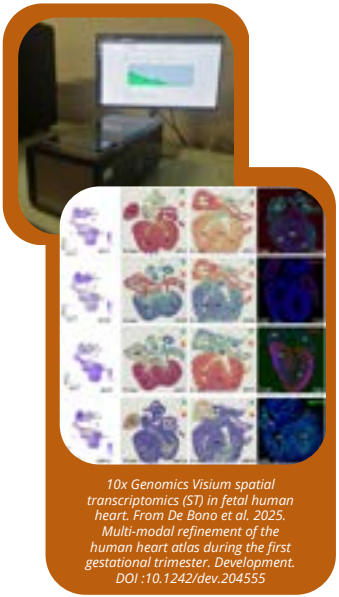

10x Genomics Visium spatial transcriptomics (ST) in fetal human heart. From De Bono et al. 2025. Multi-modal refinement of the human heart atlas during the first gestational trimester. Development. DOI :10.1242/dev.204555

Transcriptomics and genomics Marseille Luminy (TGML)

The TGML sequencing platform in Marseille is a cutting-edge facility dedicated to high-throughput sequencing and genomic analysis. Equipped with advanced technologies and expertise, it caters to diverse applications such as whole genome sequencing, transcriptomics, and epigenetics. Supporting both academic and industrial research, the platform delivers end-to-end services, from sample preparation to data analysis. This facility serves as a dynamic center for innovation and collaboration in the genomics field.

FIELDS OF TECHNOLOGY

- Transcriptomics: RNA-seq , miRNA-seq
- Genomics: Targeted re-sequencing, complete exome, SNV, small / large IndDels, etc.
- Epigenomics: CapStarr-Seq, ChIP-seq, FAIRE-seq / ATAC-seq, Mnase-seq, 3C-seq, 4C-seq
- Single Cell: scRNA-seq, scATAC-seq, sc-HiC, cell-hashing
- Spatial transcriptomics: In progress.
- Bioinformatics analysis: on demand according to the project

SERVICE/EQUIPMENT/CERTIFICATION

Equipment

- Sequencing: NextSeq 2000 (Illumina), NextSeq 500 (Illumina),
- Single-cell and Long read: Chromium X (10x Genomics),Chromium Controller (10x Genomics)
- Robots : GentleMacs Octo dissociator with heaters (Milteny), EVO 150 (Tecan), Apollo-324 (WaferGen) and Fragment Analyzer (Advanced Analytical).

Certification

The platform received the IBiSA label in 2008, and was then integrated into the distributed infrastructure of France Génomique. In 2016, the TGML received the amU technology platform label, which was renewed in 2025.

NOTABLE COLLABORATIVE PROJECT/CONTRIBUTION

DP: Denis Puthier, LB: Lisa Bargier, BL: Béatrice Loriod,
HV: Hortense Vachon, FN: Nicolas Fernandez-Nunez

- **Promoters with enhancement activity: a new regulatory mechanism:**

– PI: Salvatore Spicuglia, TAGC, Marseille. – Funding: INCa, ANR, Ligue, A*MIDEX
- Belhocine, M., et al., 2022, Genome Res. - DP
- Cieslak, A., et al., 2020, J Exp Med. - DP
– Alomairi, J et al., 2020. PLoS ONE 15, e0233191 – DP
– Gutiérrez-Reyna et al. 2020. Front. Immunol. 11, 1089 – BL, DP
– Dao, L.T.M et al, 2017. Nat. Genet. 49, 1073-1081 – DP
– Medina-Rivera, A. et al, Trends Biochem. Sci. 43, 452-468 – DP (review)

- **The H2AL2 histone variant and its role in protamine incorporation**

– PI : Saadi Khochbin & Sophie Rousseau, IAB, Grenoble. – Funding: INCa, ARC, ANR, FRM
- Wang, T., et al, 2021, Life Sci Alliance. - DP, BL
- Gao, M., et al, 2021, Cell Rep. - DP, BL
- Iuso, D. et al, 2023, Sci. Adv. - DP, BL
– Hoghoughi, N. et al, 2020. Cells – DP
– Shiota, H. et al. 2018. Cell Rep. – DP
– Barral, S. et al. 2017. Mol. Cell. – DP, FN
– Goudarzi, A et al. 2016. Mol. Cell. – DP

- **Leukemia and Sepsis**

– PI : Regis Costello, TAGC, Marseille
- Madaci, L., et al, 2023, Diseases - DP, BL
- Madaci, L., et al, 2023, Diseases - DP, BL
- Madaci, L., et al, 2022, Biomark Res - BL
- Labiad, Y., et al, 2018, Exp Hematol. - BL, FN
- Ragheb, R., et al, 2016, Arch Dermatol Res. - BL
- Venton, G., et al, 2016, Immunol Res - BL

- **Genomics of livestock animals**

– PI : Kaj Chokeshaiusaha, Rajamangala University of Technology Tawan-ok, Thailand
- Sananmuang, T., 2024, Theriogenology - DP
- Chokeshaiusaha, K., 2023, Vet World. - DP
- Chokeshaiusaha, K., 2022, Vet World. - DP
- Chokeshaiusaha, K., 2020, Vet World. - DP
- Sananmuang, T., 2020, Theriogenology - DP
- Chokeshaiusaha, K., 2018, Vet World. - DP

- **The development of medullary thymic epithelial cells.**

– PI : Magali Irla, CIML, Marseille. – Funding: A*MIDEX / PI : Arnauld Sergé, LAI, Marseill. – Funding: A*MIDEX
- Santamaria, J., et al, 2024 - DP

- Collaboration With IMBE:
  - Project LiCCOCO Pierre Henry Willard

The sea urchin, Paracentrotus Lividus, used as a model to study the cocktail effects of chlordecone and the main pesticides present in the French West Indies.
  - Project : J-P. Mevy - TETRAMEG

Toxicity of Metallic Trace Elements in Pubescent Oak in the Gardanne mining basin: genomic approaches, airborne imaging and hyperspectral reflectance.

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https://tagc.univ-amu.fr/fr/services/TGML
https://plateformes-aix-marseille.univ-amu.fr/tgml.html
https://www.france-genomique.org/platforms-and-equipments-seq

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SOURCES

Publications:
https://pubmed.ncbi.nlm.nih.gov/?term=%28LORIOD+B%5BAuthor%5D%29+OR+%28PUTHIER+D%5BAuthor%5D%29&sort=date

Newsletter
https://tagc.univ-amu.fr/sites/default/files/2025-01/N%C2%B06_Janvier_2025.pdf

The platform's strength lies in its robust model, built on strong expertise, standardized procedures, and openness to the national and international scientific community and industry. Certified ISO 9001:2015 and NFX 50-900:2016 since 2015, it is now part of theb MarMaRa' institute. Deeply engaged in teaching, the platform contributes to AMU's TIGER project and plays a central role in the RARETRIPS initiative, supporting research-based training for Master's and PhD students. For nearly a decade, its staff has also provided national and international training in bioinformatics.

Plateforme d’Imagerie Commune Site de Luminy

AMU WEBSITE

www.univ-amu.fr/marmara

COMMUNICATION DOCUMENTS

2020- 2022

NEWSLETTERS

internal & external NLs

VIDEOS

"MarMaRa - Vision, action & ecosystem"
www.youtube.com/watch?v=Nk_qV-YsYnA

"Aix Marseille Université Institut d'établissement - MarMaRa"
vimeo.com/651636329/96d5992a03

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Thank you for your collaboration!

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MarMaRa Institute - 2025