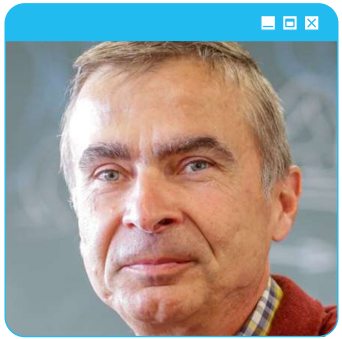
Institut
Marseille
Maladies rares

Aix*Marseille Université

TEAMS BOOKLET

1st edition - 2022



As part of MarMaRa institute's interdiscplinary approach, this first edition of our "Teams booklet" aims to offer you a whole picture of our research laboratories, that are working on rare diseases. We hope this brief document will give you a glimpse on our members's main field of studies and expertise, as well as their recent innovative projects. Besides, we would like to encourage you to contact each other for more collaborations in the future, for the sake of science and rare diseases patients! We wish you a pleasant and an insightful surfing!

BRUE THIERRY
PUPH

MarMaRa

TEAM BOOKLET MAP

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Steering committee

Thierry BRUE
Director - Scientific
& Technical Manager

Frédérique MAGDINIER
Deputy Director for Research

Denis PUTHIER
Deputy Director for Education

Cécile BERNARD
Project Manager

Laurence COLLEAUX
Tenders Manager

Rodolphe MOREAU
MMG Unit
Administrative Manager

Involved structures

13 Laboratories

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)

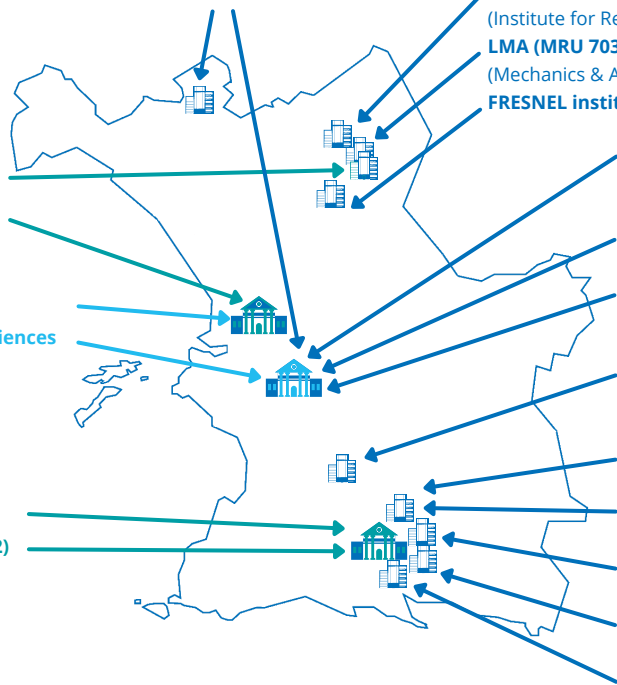
I2M (MRU 5295)
(Institute of Mathematics of Marseille)

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)



4 Doctoral Schools (DS)

Engineering sciences (DS 353)

Mathematics & Informatics (DS 184)

Life and health sciences (DS 62)

Physics and matter sciences (DS 352)

2 Faculties

Faculty of science

Faculty of medical & paramedical sciences

RU: Research Unit
MRU : Mixed Research Unit

MarMaRa in a nutshell/ page 2

Our actions

2020 - 2022

Education

- **PhD program 2022 with** Rare diseases trainings & cross-cutting trainings
- **Mentoring program**
- **13 funding / scholarships «master»** (internships grants)
- **5 funding / scholarships «training»** (acquire new skills)
- **Summer schools**
- **15 funding / scholarships «end of thesis»** (extension up to 6 months)
- **Tutored seminars**

Research

- **Interdisciplinary research group "3M" with the institute SoMuM** (Mediterranean Societies in Transition)
- **Annual symposium**
- **5 funding / scholarships «incentive action»** (support innovative & high-quality projects from different research units)
- **4 funding / scholarships «research year»** (1 year of research for medical & paramedical students)
- **8 funding / scholarships «mission»** (participation to scientific events or undertake short to mid-term scientific visits to collaborators)
- **14 funding / scholarships «publication»** (support dissemination of the research)
- **4 funding / scholarships «post-doc»** (up to 10 months)
- **3 funding / scholarships «invited researcher»** (to host an invited research form 1 week to 3 months)

MarMaRa in a nutshell/ page 3

C2VN/ LALEVÉE team/ page 5

CRCM/ LACHAUD team/ page 6

IBDM/ FASANO team/ page 7

IBDM/ HELMBACHER team/ page 8

IBDM/ KELLY team/ page 9

INMED/ MUSCATELLI team/ page 10

MMG/ AgiPreC team/ page 11

MMG/ BARTOLI team/ page 12

MMG/ BAUDOT team/ page 13

MMG/ BENSIMON-BRITO team/ page 14

MMG/ BRUE team/ page 15

MMG/ LESCROART team/ page 16

MMG/ MAGDINIER team/ page 17

MMG/ ROCHAIS team/ page 18

MMG/ VILLARD team/ page 19

MGG/ ZAFFRAN team/ page 20

TAGC/ BALLESTER team/ page 21

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TAGC/ CHEVILLARD team/ page 23

TAGC/ GONZÁLEZ team / page 24

TAGC/ MARQUET team / page 25

TAGC/ PUTHIER team/ page 26

TAGC/ RIHET team / page 27

TAGC/ SPICUGLIA team/ page 28

TAGC/ VAN HELDEN team / page 29

C2VN

> CARDIOVASCULAR TOXICITY, DYSIMMUNITY AND INFLAMMATION

Heart Failure (HF) is a chronic, progressive condition in which the heart is no longer able to ensure a sufficient blood flow to meet the body's oxygen needs. The role of the immune system in HF has been recognized for over 20 years. Pre-clinical studies have described both positive and negative effects of immune activation, revealing a complex pathophysiology that is not fully understood. Our group seeks to **identify markers of poor clinical prognosis in cardiomyopathies related to inappropriate immune and inflammatory responses** and to **decipher the pathophysiological mechanisms leading to the most severe forms of these diseases**.

FIELDS OF STUDY

- **Signaling pathways of heart failure**
- **Cardiotoxicity of cancer treatments**
- **Immune-mediated myocarditis**
- **Septic cardiomyopathy**

STRENGTHS

•Our project is based on the implementation of **translational approaches** in which the integration of biological and clinical data allows a better understanding of the pathophysiological mechanisms at the origin of cardiomyopathies.

•We work with **induced pluripotent stem cells (hiPSCs, MaCS platform, MMG) generated from patients followed in our care centres** and in **relevant preclinical murine models** with an **integrative approach ranging from cellular electrophysiology to functional genomics**, and study of **the cardiac function *in vivo*.**

FUTURE PRIORITIES

•To unravel the **signalling pathways of cardiotoxicities induced by anti-cancer treatments and during 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 cardiomyopathies.

NOTABLE COLLABORATIONS

•Our work on immune-related cardiac adverse events in cancer treatment-induced cardiotoxicities is carried out in collaboration with **the Medi-CO centre of the North Hospital** (see https://www.gmedico.fr/).

•We work with **the groups of L. Pradel and D. Puthier at TAGC** to unravel the genomic and epigenomic mechanisms of cardiomyopathies, supported by the expertise of the **TGML platform co-directed by B. Loriod and D. Puthier**.

•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 toxic cardiomyopathy.

SOURCE

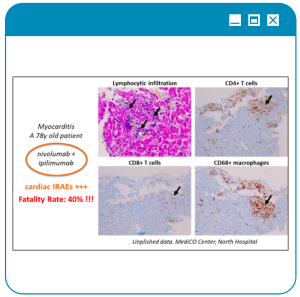
•https://publons.com/researcher/2224946/nathalie-lalevee/
•DOI: 10.1371/journal.pgen.1007502
•DOI: 10.1186/s40635-019-0263-0

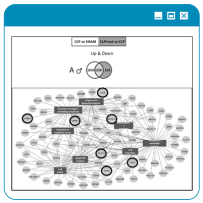
GROUP LEADER

LALEVEE Nathalie, CR (PhD, HDR)
nathalie.lalevee@univ-amu.fr

GROUP MEMBERS

BRUZZESE Laurie (IGE, PhD)
CAUTELA Jennifer (PhD student, PH)
CONTE Samantha (PhD student)
FROMONOT Julien (MCU-PH)
GUIOL Claire (PhD student)
LEONE Marc (PU-PH)
REBAOUI Zohra (PhD student)
THUNY Franck (PU-PH)
TRAN Thi Thom (IGR, PhD)





CRCM

> DNA INTERSTRAND CROSSLINK LESIONS AND BLOOD DISORDER

Many rare diseases are caused by mutations in genes involved in **DNA damage response (DDR) genes** causing **genome instability**, a hallmark of **cancer**.
DDR genes are crucial for maintaining genome stability, mutations in these genes may increases risk of cancer. Hence, **understanding the biology of rare DNA repair diseases** can help improving the diagnosis of patient at risk for cancer.
In our laboratory, we focus in **DDR genes that prevent genome instability in blood** and that are **mutated in rare genetic diseases**.

TEAM LEADER

LACHAUD Christophe (CRCN, Ph.D.)
Christophe.lachaud@inserm.fr

GROUP MEMBERS

AUDOLY Gilles (IR1, Ph.D.)
BALSALOBRE Elena Martinez (Post-doc)
GUERVILLY Jean-Hugues (CRCN, Ph.D.)
HICHERI Yosr (MD.)
LEE Lara (IE)

FIELDS OF STUDY

•Genome stability, rare genetic diseases with defect in DNA repair:
-Fanconi Anemia
-Neurodevelopmental disorder involving the UFM1 pathway

STRENGTHS

•We developed and patented state of the art technology to measure DNA repair in cells.
•We combine clinical genetics and animal models.

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 defect in DDR**.

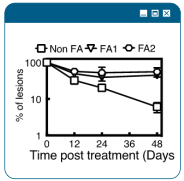
NOTABLE COLLABORATIONS

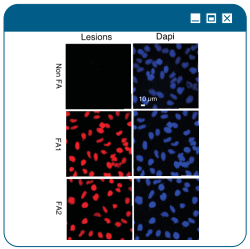
•To determine how the UFM1 pathway prevents Neurodevelopmental disorder, we collaborate with **Yogesh Kulathu (UK)** for the biochemistry part of the work, **Victor Mulero (Spain)** to generate Zebrafish model and **Estelle Colin (France)** to identify patients.

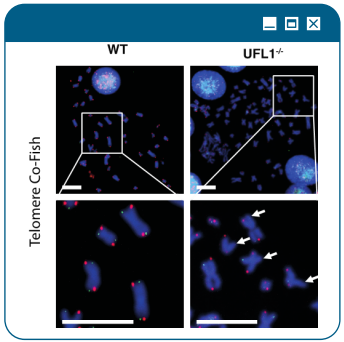
•Concerning our work on Fanconi Anemia, we collaborate with **Jean Soulier (France) Ana Belen Perez Oliva (Spain)** to identify patients and new diagnosis protocols.

SOURCE

•www.crcm-marseille.fr/en/teams/research-teams/christophe-lachaud/







IBDM

> 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

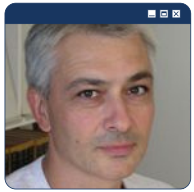
•When development goes awry: exploring the origin of disease(s): ASD & CAKUT
•Choosing a fate: how do cells acquire their identity?

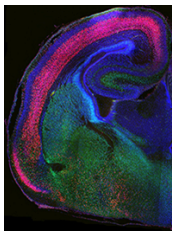
STRENGTHS

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 (MGG) 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.

GROUP LEADER

FASANO Laurent – DR2 (PhD, HDR)
Laurent.fasano@univ-amu.fr

GROUP MEMBERS

CAUBIT Xavier (MCU, PhD, HDR)
FATMI Ahmed (IE)
HAD Laurence (MCU, PhD, HDR)
MOLITOR Jordan
(PhD student - co-supervised by X. CAUBIT (Fasano Team) & P. GUBELLINI (Kerkerian - LE GOFF team (IBDM))

SOURCE

•www.ibdm.univ-mrs.fr
•Caubit X et al., Targeted Tshz3 deletion in corticostriatal circuit components segregates core autistic behaviors. Transl. Psychiatry. 2022 PMID 35292625
•Sanchez-Martin I et al., Haploinsufficiency of the mouse Tshz3 gene leads to kidney defects. Human Molecular Genetics 2021PMID 34919690

IBDM

> DEVELOPMENT AND PATHOLOGIES OF NEUROMUSCULAR CIRCUITS

Research in our team aims to understand **processes that control the development of neuromuscular circuits**, and to uncover **how alterations of these developmental processes** lead to devastating **human neuromuscular pathologies**.

TEAM LEADER

HELMBACHER Françoise
(Researcher)
francoise.helmbacher@univ-amu.fr

GROUP MEMBERS

FRAGANO Dominique
(Technical staff)

FIELDS OF STUDY

- **Neuromuscular development**
- **Muscle Regeneration**
- **Facioscapulohumeral muscular dystrophy (FSHD)**
- **Retinal angiogenesis**

STRENGTHS

- We combine **modern techniques** of **mouse genetics**, **imaging**, **bioinformatics** and **functional genomics**.
- We have teamed up with **human geneticists** and **pathologists**, so as to **design murine models of human neuromuscular pathologies** such as FSHD.

FUTURE PRIORITIES

- **Identify molecules involved in the assembly of neuromuscular connectivity**. We focus in particular on **signaling cues** and their **receptors**.
- **Distinguish the actions of complementary signaling molecules** on the various cell types involved in the neuromuscular construction, by using advanced molecular genetics.
- **Identify mechanistic nods that qualify as optimal therapeutic targets for FSHD**.
- **Identify means of preventing the appearance of fibro-adipose infiltrations in muscular pathologies** in which they occur.

SELECTECTED PUBLICATIONS

•Helmbacher F. ***"Astrocyte-intrinsic and extrinsic Fat1 activities regulate astrocyte development and angiogenesis in the retina"***. Development (2022), January 20 | doi:10.1242/dev.192047 | PDF | PMID: 35050341 |

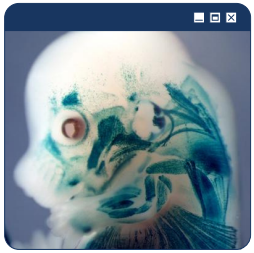
•Pastushenko I. et al. ***"Fat1 deletion promotes hybrid EMT state, tumour stemness and metastasis"***. Nature, (2021) January 21 | PMID: 33328637 | Epub 2020 Dec 16.

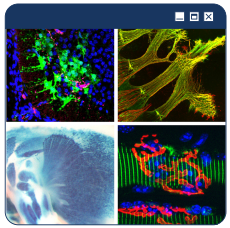
•Francoise Helmbacher#, Sigmar Stricker#. "***Tissue cross talks governing limb muscle development and regeneration" (Review article)***. Seminars in Cell and Developmental Biology, (2020), June 7 |PMID: 32517852 | #: co-corresponding | PDF: Helmbacher & Stricker 2020 |

•Helmbacher F. ***"Tissue-specific activities of the Fat1 cadherin cooperate to control neuromuscular morphogenesis"***. PLOS Biology (2018) 16(5) e2004734 | PMID: 29768404 | doi: 10.1371/journal.pbio.2004734 | previously posted as preprint: https://doi.org/10.1101/207308 |

•Puppo F. et al. ***"Identification of variants in the 4q35 gene FAT1 in patients with a Facioscapulohumeral dystrophy (FSHD)-like phenotype"***. Human Mutation (2015) 23 Jan | PMID : 25615407 | DOI: 10.1002/humu.22760

•Caruso N et al. ***"Deregulation of the protocadherin gene FAT1 alters muscle shapes: implications for the pathogenesis of facioscapulohumeral dystrophy"***. PLoS Genet. (2013) Jun;9(6):e1003550. | PMID: 23785297 | doi: 10.1371/journal.pgen.1003550 |





SOURCE

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

IBDM

> 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

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

SELECTED PUBLICATIONS

- De Bono et al.***"T-box genes and retinoic acid signaling regulate the segregation of arterial and venous pole progenitor cells in the murine second heart field"***. Hum Mol Genet. 2018 27

- Adachi et al.***"Cardiopharyngeal mesoderm origins of musculoskeletal and connectivetissues in the mammalian pharynx"***.Development.2020147:dev185256.

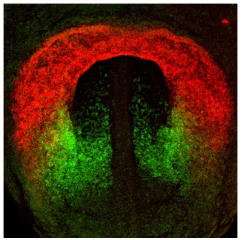
- Choquet C et al.***"Nkx2-5 defines distinct scaffold and recruitment phases during formation of the murine cardiac Purkinje fiber network"***.NatCommun.202011:5300.

TEAM LEADER

KELLY Robert – (Researcher)
robert.kelly@univ-amu.fr

TEAM MEMBERS

BERTRAND Nicolas (University lecturer)
BOULGAKOFF Lucie (PhD student)
COUDERC Marie (Technical staff)
DUMAS Camille (PhD student)
GUIJARRO CALVO Clara (PhD student)
MICHEL Louise (PhD student)
MIQUEROL Lucile (Researcher)
ROUSSET Celia Rousset (MSc student)
STURNY Rachel (Technical staff)
VAHDAT Julliette (PhD student)



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

SOURCE

- www.ibdm.univ-mrs.fr

INMED

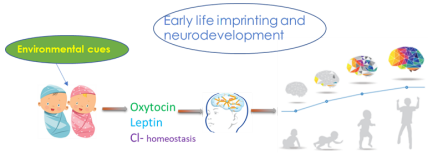
> EARLY LIFE IMPRINTING AND NEURODEVELOPMENTAL DISORDERS

Our team aims at understanding some factors that translate **the early life environment** into lasting physiological and behavioral responses, to better understand, diagnose and treat **rare neurodevelopmental disorders (Prader-Willi syndrome, Schaaf-Yang syndrome)**. Our research focuses mainly on **two hormones (oxytocin, leptin)** and **the control of chloride homeostasis** as critical neuromodulators closely connected with environment, controlling the maturation of neurons and the neural wiring and offering possible therapeutic options.

FIELDS OF STUDY

•When development goes awry: exploring the origin of disease(s): ASD & CAKUT

•Choosing a fate: how do cells acquire their identity?



STRENGTHS

•Neurodevelopment, Rare neurodevelopmental diseases, Neurohormones, Mouse behavior, Genetics, Functional neuroanatomy, Electrophysiology, Physiology, Cellular and molecular pathways.

FUTURE PRIORITIES

I) Hormonal imprinting and chloride homeostasis shape neural circuitries of physiological behaviors

1-OT-system in neural circuitry of neonatal thermo-sensory reactivity.

2-OT-system in neural circuitry of sucking activity of normal and pathological mice.

3-Implication of the OT-system for the physio-pathology of the central cardiorespiratory coupling .

II) Testing pharmacological treatments

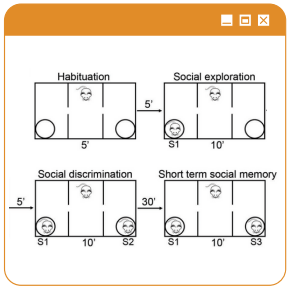
1-Modeling complex autistic-like behavior in mice (Schaller).

2-Targeting the adipocyte hormone leptin to treat Rett Syndrome.

3-A rare case of monogenic KCC2-related autistic spectrum disorder: a new benchmark for the validation of causality and treatment screening.

SELECTED PUBLICATION

Bertoni A, Schaller F, Tyzio R, Gaillard S, Santini F, et al. 2021. ***"Oxytocin administration in neonates shapes hippocampal circuitry and restores social behavior in a mouse model of autism".***Mol Psychiatry. DOI: 10.1038/s41380-021-01227-6



TEAM LEADER

MUSCATELLI Françoise - DR
francoise.muscatelli@inserm.fr

TEAM MEMBERS

Principal Investigators

GAIARSA Jean-Luc (CNRS, DR)
MEDYNA Igor (INSERM, DR)
MENUET Clement (INSERM, CRCN)
MATARAZZO Valery (AMU, PU)
PORCHER Christophe (AMU, PU)
GESTREAU Christian (AMU, MCU,)

PhD Students

BELAÏDOUNI Yasmine
BROSSET-HECKEL Mélanie
BURON Julie
HAMZE Mira
JULIA Adrien
LINOSSIER-BENKEMOUN Ambre
RICHARDEAU Maxime
ZAYAN Ugo

Technicians

DABIRA Diabé (TC INSERM)
KABORÉ Idrisse (IE INSERM)
SCHALLER Fabienne (IE, INSERM)
TYZIO Roman (IR INSERM)

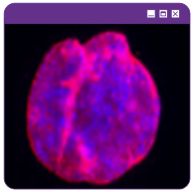
SOURCE

•www.inmed.fr/en/neurodevelopment-and-prader-willi-syndrome
•https://www.nature.com/articles/s41380-021-01227-6

MMG

> AgiPreC (AGING, PRENYLATION & CANCER)

Since 20 years, our team's research has focused on the discovery and the pathophysiology of premature aging and metabolic disorders, mainly linked to Lamin A/C mutations, including Hutchinson-Gilford Progeria, for which we identified the causative gene in 2003, towards the identification of therapeutic approaches. Other research axes include cancer mechanisms linked to Lamins A/C, as well as the pathophysiological bases of male infertility, linked to nuclear envelope proteins. Our translational research is based on the development and use of preclinical tools like patients' primary cell cultures, iPS cells and genetically modified mouse models.



FIELDS OF STUDY

- **Hutchinson-Gilford Progeria**
- **Other Premature aging syndromes**
- **MADaM syndrome** (Mandibuloacral dysplasia associated to MTX2)
- **Cancer mechanisms linked to Lamins A/C**
- **Male infertility**

STRENGTHS

Our team has always had and maintained a strong collaborative link with the Department of Medical Genetics and Cell Biology at the University Hospital la Timone, including the Biological Ressource Center, in order to establish the best bed-to-bench and bench-to-bed translatable avenues. Specific disease preclinical models were implemented by our team (i.e. the *Lmna*$^{G609G/G609G}$ mouse model for Progeria) and are now widely used for research studies in the world. Our research and medical center have become **a reference center for diagnosis and research on premature aging disorders linked to Lamins A/C**.

FOCUS

- **Molecular diagnosis**
- **Gene discovery and disease pathophysiology**
- **Cellular & mouse models preclinical use for translational research**
- **Gene therapy / pharmacological approaches**

NOTABLE COLLABORATIONS

In order to identify the genetic and molecular bases of a novel Mandibuloacral dysplasia progeroid syndrome (MADaM syndrome) sharing pathophysiological mechanisms with Hutchinson-Gilford Progeria, we established a **very large collaborative consortium involving clinicians, researchers and industrial partners from all over the world (Singapore, Ecuador, India, Turkey, Egypt, Germany, France...)**.
The fruitful collaborations established will allow to further unveil the molecular bases of this disorder towards the identification of therapeutic approaches.
(Elouej et al., Nature Communications 2020 ; PMID: 32917887).

SOURCE

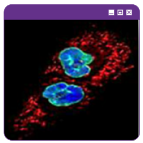
•https://publons.com/researcher/2504057/nicolas-levy/publications/
•www.marseille-medical-genetics.org/en/ageing-prenylationand-cancers/
•http://fr.ap-hm.fr/service/departement-de-genetique-medicale-hopital-timone
•http://fr.ap-hm.fr/site/crb-centre-de-ressources-biologiques

TEAM MEMBERS

AIRAULT Coraline (AI)
AL DALA ALI Maha (PhD student)
BADACHE Ali (CR)
BADENS Catherine (PU-PH)
BARTOLI Catherine (IE)
BONELLO-PALOT Nathalie (PH)
CERINO Mathieu (MCU-PH)
COLLEAUX Laurence (DR1 CNRS)
COSTE Solène (PhD student)
DESGROUAS Camille (MCF)
FABRE Alexandre (PU-PH)
FRANKEL Diane (MCU-PH)
GRANDVAL Philippe (PU-PH)
GUIGUE Philippe (IR - CDD ANR)
HARHOURI Karim (Post-doc - AFM)
KASPI Elise (MCU-PH)
LONGEPIED Guy (IE)
MITCHELL Michael (DR)
METZLER-GUILLEMAIN Catherine (PU-PH)
TOURY Léa (PhD student)
VERDIER-PINARD Pascal (CR-CN)
WINKLER Jérôme (CCA/PhD student)

CONTACT

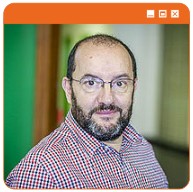
DE SANDRE-GIOVANNOLI Annachiara (PH)
Annachiara.DESANDRE@ap-hm.fr
ROLL Patrice (PU-PH)
patrice.roll@univ-amu.fr



MMG

> TRANSLATIONAL NEUROMYOLOGY

Our team is organized in **two axes**, one axis is focused on **myopathies and muscular dystrophies** , **inherited peripheral neuropathies** and the second one on **inherited peripheral neuropathies and ataxias groups of diseases**. These diseases are part of the large family of **neuromuscular disorders (NMD)**, a set of hereditary diseases ultimately leading to muscle dysfunction, due to muscle or nerve abnormalities. Although quite different in terms of affected genes and pathways, these diseases are defined by a strong genetic heterogeneity leading to complex physiopathological pathways.
Improving **diagnosis** of these diseases, the understanding of the **pathomechanisms** 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

FUTURE PRIORITIES

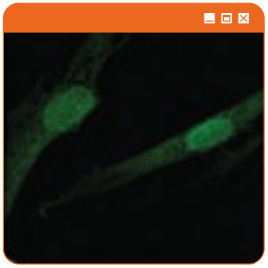
- **Identify new defective genes/proteins in NMD diseases.**
- **Develop a new hiPSC-based in vitro model** as a new tool for functional and preclinical therapeutic studies.
- **Develop novel therapeutic approaches,** based on particular clinical observations and mutational data from our large cohort of patients.
- **Pursue our previous work towards further preclinical testing of therapeutic strategies** developed by our group in particular: **transcript rescue strategies**.
- **Define 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.

TEAM LEADER

BARTOLI Marc - DR2 (PhD, HDR)
marc.bartoli@univ-amu.fr

TEAM MEMBERS

ALARY Bénédicte
ATTARIAN SHAHRAM (PUPH)
AUDIC FREDERIQUE (PH)
CAMPANA / SALORT EMMANUELLE (PH)
CASTRO CHRISTEL (AI)
COURRIER SEBASTIEN (IE)
DA SILVA NATHALIE (AI)
DELAGUE VALERIE (DR2)
GADACHA Jihane
GOROKHOVA SVETLANA (PH)
HAMZE ZEINAB (PhD student)
KRAHN MARTIN (PUPH)
MAUES DE PAULA ANDRE (MCUPH)
QUINTANA PATRICE (Post-doc)
TREVISIOL ROECKEL NATHALIE (TCH)



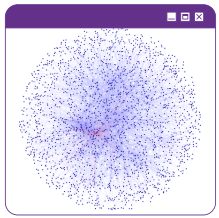
SOURCE

- www.marseille-medical-genetics.org/en/m-bartoli/

MMG

> NETWORKS AND SYSTEMS BIOLOGY FOR DISEASES (NSBD)

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



FIELDS OF STUDY

- **Methodological developments: Systems Biology and Network Theory**
- **Integrative Biology: -omics data integration**
- **Dynamical Network Modeling**
- **Applications to better understand common and rare human disorders** as well as **disease relationships and comorbidities**

STRENGTHS

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

PRIORITIES

- **Develop tools** to analyse and integrate biological data.
- **Develop predictive mathematical models** to study the dynamics of biological systems (genes and proteins functioning) in healthy or diseased contexts.
- **Develop diagnosis tools** based on network approaches, for instance to rank variants according to their proximities with genes whose mutations lead to diseases with similar phenotypes.
- **Work on drug repurposing strategies**, leveraging networks to integrate the many-to-many relationships between drugs and targets.
- **Investigate disease-disease molecular and comorbidity relationships**, in the context of the rare and common diseases.

NOTABLE COLLABORATIONS

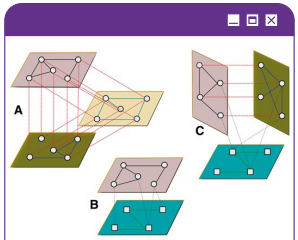
We have worked on several complementary national and international projects with **I2M**.
In 2018, we built an advanced three-layer multiplex network to predict candidate genes for the **Wiedemann – Rautenstrauch syndrome**, and to explore the network vicinity of the **SHORT syndrome**.
In 2021, we were able to identify cellular processes perturbed in **Facio-Scapulo-Humeral muscular Dystrophy**, by integrating RNA-seq expression data with a multiplex biological network, thanks to MOGAMUN, a multi-objective genetic algorithm.

TEAM LEADER

BAUDOT Anais - (DR CNRS)
anais.baudot@univ-amu.fr

TEAM MEMBERS

BAPTISTA Anthony (PhD student)
BEN BOINA Nadine (PhD student)
CHEVALIER Celine (IE)
HIRST David (PhD student)
KAUSAR Samina (IR)
LAMBERT Judith (PhD student)
OZISIK Ozan (Post-Doc)
TEREZOL Morgane (IE)



Multiplex, heterogeneous & multiplex-heterogeneous graphs

SOURCE

•www.marseille-medical-genetics.org/a-baudot/
•Valdeolivas et al. (2019). Random walk with restart on multiplex and heterogeneous biological networks. Bioinformatics (Oxford, England), 35(3), 497–505. https://doi.org/10.1093/bioinformatics/bty637
•Novoa-Del-Toro et al. (2021). A multi-objective genetic algorithm to find active modules in multiplex biological networks. PLoS computational biology, 17(8), e1009263. https://doi.org/10.1371/journal.pcbi.1009263

MMG

> CARDIOVASCULAR CALCIFICATION, MECHANISMS AND THERAPIES

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 understanding the **mechanisms of cardiovascular calcification (CVC)**, which is characterised by the progressive deposition of calcified matrix in blood vessels, cardiac valves and other heart tissues, causing impaired blood circulation. We also work on **finding new therapies** for this multifactorial disorder.

FIELDS OF STUDY

- **Cardiovascular calcification (CVC).**
- **Cardiac Valve Regeneration.**

STRENGTHS

- A young open-minded group with an advanced knowledge about the cadiovascular system and a huge interest in zebrafish models.
- Various *in vivo* and *in vitro* experimental models (genetic models, zebrafish ...)

PRIORITIES

- **Study CVC using zebrafish** as a new model for the direct observation of the calcification progress via live-imaging microscopy at single-cell resolution.
- Study multiple genetic models to **characterise cells** contributing to calcification and identify new molecular factors regulating this process.
- Explore the **functional impact** of calcification in the tissue, and how it affects blood circulation.
- Identify **new therapeutic approaches** to alleviate the impact of CVC.

European Research Council
Established by the European Commission

NOTABLE PROJECT

The ERC Starting Grant 2021 project, "CARDIOCALC"

Aim 1:
Use a broad array of zebrafish genetic models to characterise the cellular dynamics, molecular mechanisms and functional impact of CVC in vivo.

Aim 2:
Identify new local and systemic therapeutic strategies to block/ reverse CVC.

SOURCE

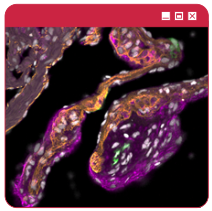
- www.marseille-medical-genetics.org/a-bensimon-brito
- AMU Europe official twitter account: https://twitter.com/univAMU_Europe/status/1504412318565867527/photo/1

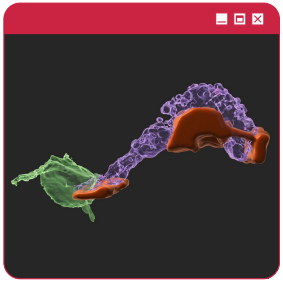
TEAM LEADER

BENSIMON-BRITO Anabela (PI, PhD)
anabela.bensimon-brito@univ-amu.fr
Twitter: @bensimonbrito

COLLABORATORS

CRISTO Inês
(Senior Postdoc, CCUL)
BEATRIZ BARBOZA Ana
(Master Student, CCUL)





MMG

> DIP-NET (DIFFERENTIATION AND PROLIFERATION OF NEUROENDOCRINE TISSUES)

The DIP-NET team is part of Marseille Medical Genetics unit (MMG). Since its creation in 2017, its members are exploring the effects of changes in shared signaling and transcriptional pathways mediating communication both within and between the diverse cell types of neuroendocrine organs, particularly the pituitary gland.

FIELDS OF STUDY

• The mechanisms of differentiation & proliferation of **neuroendocrine cells**.

• The physiological influences of molecular pathways & their abnormalities that can cause **hormone deficiencies, neuroendocrine hypersecretion or proliferative syndromes**.

• New therapeutic strategies for these disorders.

STRENGTHS

•Clinical expertise in pituitary diseases & their treatments.

•Newly reinforced expertise in experimental developmental biology.

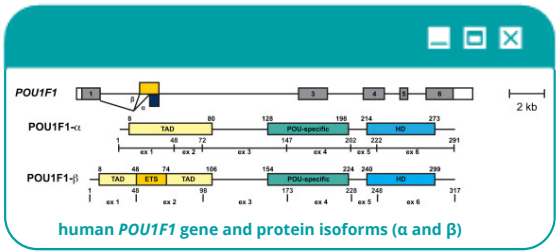
•A longstanding national & international collaborations in the field of rare diseases.

RECENT PUBLICATION

GNAS is monoallelically expressed in the normal pituitary due to methylation-based imprinting and about 40% of somatotroph tumors harbor recurrent activating GNAS mutations ("gsp oncogene"). GNAS allelic expression was analyzed using a polymorphic Fok1 cleavage site showing that 43% of gsp-negative tumors had GNAS imprinting relaxation, with lower GNAS, SSTR2 and AIP expression, indicative of lower sensitivity to somatostatin analogues and potentially aggressive behavior.

TRANSATLANTIC COLLABORATIVE STUDY

Thanks to high-throughput splicing assays, we were able to identify missense and silent splice-disruptive variants of the transcription factor *POU1F1* linked to different clinical cases of hypopituitarism.



human *POU1F1* gene and protein isoforms (α and β)

TEAM LEADER

BRUE Thierry (PUPH)
Thierry.BRUE@ap-hm.fr

TEAM MEMBERS

BARLIER Anne (PUPH)
AMODRU Vincent (PhD student)
BERNARD Cécile (Project Manager)
CASTINETTI Frederic (PUPH)
CUNY Thomas (CCA)
DUFOUR Henry (PUPH)
ETCHEVERS Heather (CRCN PhD, HDR)
FAUQUIER Teddy (IR)
FOURNEAUX Rachel (AI)
GRAILLON Thomas (MCUPH)
LAGARDE Arnaud (PhD student)
LISBONIS Christophe (AJT)
MAC THI Thom (PhD student)
MACAGNO Nicolas (MCUPH)
MARECHAL Elise (PhD student)
MONDIELLI Gregoire (IE)
MORENO Mathias (AJT)
MOUGEL Gregory (AHU)
QUERDRAY Adeline (TCH)
REYNAUD Rachel (PUPH)
ROMANET Pauline (MCUPH)
SAVEANU Alexandru (MCUPH)

SOURCE

• European Journal of Endocrinology 185, 6; 10.1530/EJE-21-0949
• Gergics, P. et al. (2021). High-throughput splicing assays identify missense and silent splice-disruptive POU1F1 variants underlying pituitary hormone deficiency. American journal of human genetics, 108(8), 1526–1539. https://doi.org/10.1016/j.ajhg.2021.06.013
• Romanet et al. (2021). Somatotroph Tumors and the Epigenetic Status of the GNAS Locus. International journal of molecular sciences, 22(14), 7570. https://doi.org/10.3390/ijms22147570

MMG

> 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.

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**.

SOURCE

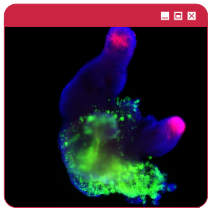
•www.marseille-medical-genetics.org/en/f-lescroart/
•Lescroart F., et al. (2018). Defining the earliest step of cardiovascular lineage segregation by single cell RNA-seq. Science . doi: 10.1126/science.aao4174

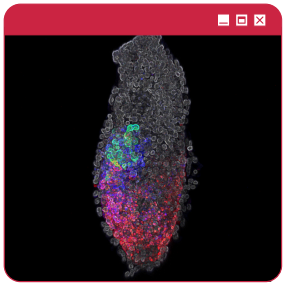
TEAM LEADER

LESCROART Fabienne (CRCN Ph.D.)
fabienne.lescroart@univ-amu.fr

TEAM MEMBERS

CHOQUET Caroline (Post-Doc)
NANDKISHORE Nitya (Post-Doc)
GHATA Adeline
(50%, Assistant engineer, INSERM)





MMG

> EPIGENETICS, CHROMATIN AND DISEASE MODELING

The involvement of epigenetic variability in the context of rare diseases still remains poorly explored. Epigenetic changes can be directly involved in diseases or contribute to symptoms variability or disease penetrance, in particular in the absence of correlation between the genetic defects and the phenotype of patients.
By combining different approaches and exploration of patient's samples, our team aims at understanding how epigenetic mechanisms contribute to rare diseases.

FIELDS OF STUDY

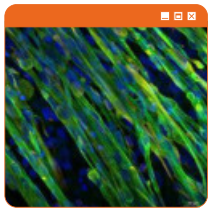
•Rare genetic diseases, exploration of biological pathways regulated by epigenetic processes:
DNA methylation, chromatin structure, chromatin topology, repetitive DNA sequences

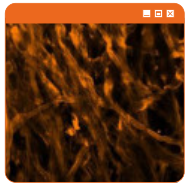
STRENGTHS

We developed tools and expertise for exploration of epigenetic mechanisms in human samples and tissues including through hiPSC-based disease modeling.

PRIORITIES

•The development of cellular models and tools for the exploration of **patho-mechanisms** associated with **neuromuscular diseases**.
•The exploration of epigenetic alterations in rare genetic diseases with a strong focus on diseases linked to **subtelomeric imbalance** including **Facio-Scapulo-Humeral muscular Dystrophy (FSHD)**.





NOTABLE COLLABORATION

Thanks to our continuous and close collaboration with **AP-HM services**, we have access to large collections of biological samples that can be exploited experimentally, in particular through the production of induced pluripotent cells (hiPSCs) and the development of new methods for the targeted differentiation of these cells and disease modeling.

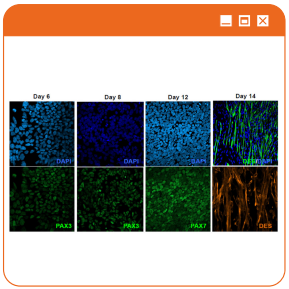
We also develop innovative molecular biology approaches for genomic analysis of complex genomic regions such as subtelomeres, in the context of diseases.

DIRECTOR & TEAM LEADER

MAGDINIER Frederique - DR2
frederique.magdinier@univ-amu.fr

TEAM MEMBERS

BERNARD Rafaëlle (PH)
CARON Leslie (Post-doc)
CHEVALIER Rafaëlle (PhD student)
DELOURME Megane (PhD student)
DUVERT Lucas (PhD student)
FUCHS Robert (DREM)
FUJII Shingo (CRCN)
MURCIA Victor (Post-doc)
NGUYEN-PHONG Karine (PUPH)
PERRIN Pierre (IE)
ROBIN Jerome (CRCN)
TRANI Jean-Philippe (PhD student)
VAN GILS Julien (PhD student)



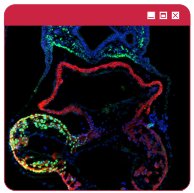
SOURCE

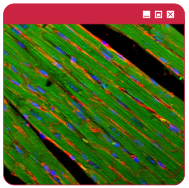
• www.marseille-medical-genetics.org/en/f-magdinier/

MMG

> HEART DEVELOPMENT AND CARDIAC REGENERATION

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.

NOTABLE COLLABORATION

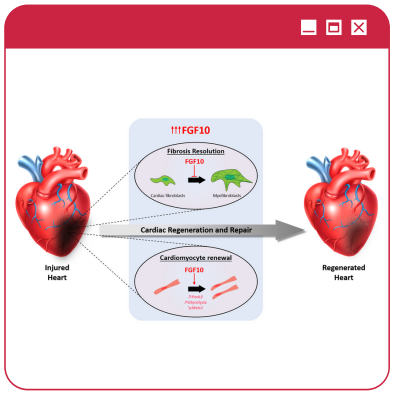
By combining experimental mouse model of myocardial infarction, advanced mouse genetics and unique human samples, we recently uncovered that the Fibroblast Growth Factor 10 (FGF10) promotes cardiac regeneration and repair. We demonstrate that FGF10 promotes cardiomyocyte proliferation and directly prevents 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).

TEAM LEADER

ROCHAIS francesca - DR (PhD, HDR)
francesca.rochais@univ-amu.fr

TEAM MEMBERS

BOUCHARD Laetitia (PhD student)
EHRHARD Morgane (PhD student)
EUDES Nathalie (Research Assistant AMU)
HUBERT Fabien (Post-Doc)
PELCE Edeline (PhD student)
PORADA Corentin (PhD student)
THEVENIAU-RUISSY Magali (CRHC, PhD, HDR)



SOURCE

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

MMG

> HUMAN NEUROGENETICS

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 Encephalopathies**
- **Rett syndrome**
- **Syndromic forms of intellectual disabilitry**

STRENGTHS

We combine clinical genetics and pediatric neurology expertise in collaboration with two departments of Marseille University Hospital, neurophysiology, cellular and molecular biology, animal models and behavioral analysis.

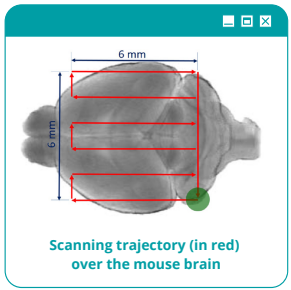
We will also soon add new expertise in electrophysiology.

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.



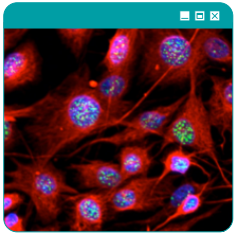
Scanning trajectory (in red) over the mouse brain

TEAM LEADER

VILLARD Laurent (PhD - HDR)
laurent.villard@univ-amu.fr

TEAM MEMBERS

BRUN Lucile (PhD student)
BUSA Tiffany (PH)
FELIX Marie-Solenne (Post-doc)
LOUIS Jordane (IE)
MIGNON RAVIX Cécile (IR)
MILH Mathieu (PUPH - HDR)
MISSIRIAN Chantal (PH)
MOLINARI Florence (CR)
RICCARDI Florence (PhD student)
ROUX Jean-Christophe (DR - HDR)
VIEMARI Jean-Charles (CR)



SOURCE

•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
•www.marseille-medical-genetics.org/l-villard/
•www.germaco.net

MMG

> GENETICS & DEVELOPMENT OF CARDIAC DEFECTS

Our laboratory is interested in the **molecular and cellular mechanisms of heart development and disease**. We use experimental embryological, genetic and molecular approaches to analyze the development of the cardiovascular system.

FIELDS OF STUDY

- **Congenital Heart Diseases**
- **Aortopathy**
- **Valvulopathy**
- **Hypertrophic cardiomyopathy**

STRENGTHS

We use **state-of-the-art genetic technologies**, including whole exome sequencing, as well as **new experimental models** (knockout mice, zebrafish and iPSC-derived organoids...) to discover and understand the function of new genes linked to less-studied congenital heart defects, such as bicuspid aortic valve or syndromic heart anomalies in rare malformation syndromes.

FUTURE PRIORITIES

•Elucidate the genetic mechanisms of Congenital Heart Diseases using mouse and in vitro models such as organoids. This will contribute to better understand the etiology of Congenital Heart Diseases and ultimately develop novel therapies aimed at healing impaired human hearts.

•Uncover the role of hemodynamism during valve development and disease such as calcific aortic valve.

•Develop mini-heart as organoids model system to study mechanism of hypertrophic cardiomyopathy.

•Develop iPSC-derived vascular smooth muscle cell model to study the pathophysiology of rare aneurysm disease.

•Uncover the contribution of different lineages in valve development and disease.

RECENT COLLABORATION

In collaboration with **Pr. Caroline OVAERT, pediatric-cardiologist, from La Timone University Hospital (AP-HM)**, we conducted a clinical and genetic investigation of a pediatric case with an early-onset dilated-LVNC (Left Ventricular Non-Compaction Cardiomyopathy).

Our study revealed compound heterozygous mutations affecting cardiac calcium homeostasis key regulator gene, encoding the Striated Muscle Enriched Protein Kinase (SPEG). They involved a *de novo* variant and caused dilated-LVNC without neuropathy or centronuclear myopathy.

Our findings also support the fact that the common SPEG; p.(Pro2687Thr) variant is functionally relevant and may act as a risk allele in the presence of the rare SPEG variant.

SOURCE

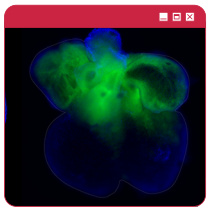
•www.marseille-medical-genetics.org/s-zaffran/
•www.zaffranlab.com
•Jaouadi et al. Dilated-Left Ventricular Non-Compaction Cardiomyopathy in a Pediatric Case with SPEG Compound Heterozygous Variants. Int J Mol Sci. 2022 May 6;23(9):5205.

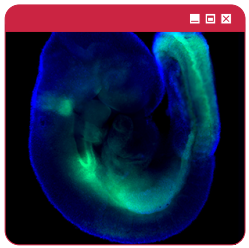
TEAM LEADER

ZAFFRAN Stephane - DR2 (PhD, HDR)
stephane.zaffran@univ-amu.fr

TEAM MEMBERS

ARGIRO Laurent (IR PhD)
AVIERINOS Jean-François (PUPH)
BAL Laurence (PH MD)
ETCHEVERS Heather (CRCN PhD, HDR)
GASTE Amélie (PhD Student)
JAOUADI Hajer (Post-Doc)
MACAGNO Nicolas (MCUPH)
MARECHAL Elise (PhD Student)
OVAERT Caroline (PUPH)

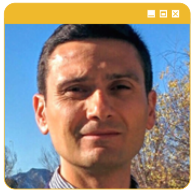




TAGC

> REGULATORY BIOINFORMATICS

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.



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.

TEAM LEADER

BALLESTER Benoit (Inserm CR – HDR)
benoit.ballester@inserm.fr

GROUP MEMBERS

BERGON Aurélie (IR)
CAMPOS Andreia (Master Student)
DE LANGEN Pierre (PhD student)
HAMMAL Fayrouz (PhD student)
LOPEZ Fabrice (IR)

SOURCE

- 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/

TAGC
> NETWORK BIOLOGY

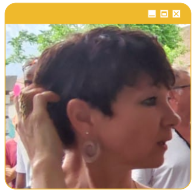
FIELDS OF STUDY
•Protein function from a network perspective
•Protein-protein and protein-RNA interaction network analyses
•Impact of genetic variations on protein networks
•Methods in Data integration, Graph partitioning and visualization

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.



RECENT PUBLICATIONS

•**Saha S.**, Perrin L., Röder L., **Brun C. and Spinelli S.** Epi-MEIF, a flexible and efficient method for detection of high order epistatic interactions from complex phenotypic traits. In review.

•Fabre B., **Choteau S.A.**, Duboé C., Pichereaux C., Montigny A., Korona D., Deery M.J., Camus M., **Brun C.**, Burlet-Schiltz O., Russell S., Combier J.P., Lilley K.S. and Plaza S. (2022) In depth exploration of the alternative proteome of Drosophila melanogaster. **Front Cell Dev Biol**. 10, 901351.

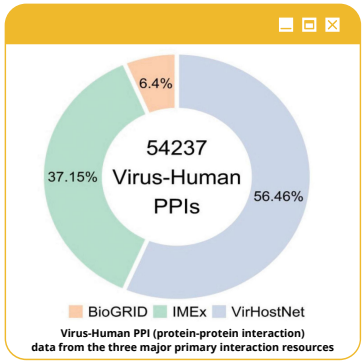
•**Saha D.**, Iannuccelli M., **Brun C.**, **Zanzoni A.** and Licata L. (2022) The intricacy of the viral-human protein interaction networks: resources, data and analyses. **Frontiers in Microbiology**,13: 849781.

•**Choteau S.**, **Wagner A.**, Pierre P., **Spinelli L.** and **Brun C.** (2021) MetamORF: A repository of unique short Open Reading Frames identified by both experimental and computational approaches for gene-level and meta-analysis. **Database**, baab032.

TEAM LEADER

BRUN Christine (DR, CNRS)
christine.brun.2@univ-amu.fr

GROUP MEMBERS
BOUJEANT Mégane (Engineer)
CHOTEAU Sébastien (PhD Student)
FERNANDEZ MACGREGOR Jaime (PhD Student)
PERRIN Jeremie (PhD Student)
SAHA Deeya (Postdoc)
SPINELLI Lionel (Research Engineer)
ZANZONI Andreas (MCU)



SOURCE
•https://tagc.univ-amu.fr/en/users/brun-christine

TAGC

> 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.

FIELDS OF STUDY

- **Chagas disease**
- **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.**

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.

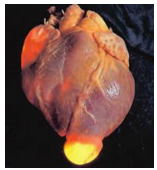
- Ouarhache M et al. ***Rare Pathogenic Variants in Mitochondrial and Inflammation-Associated Genes May Lead to Inflammatory Cardiomyopathy in Chagas Disease***. J Clin Immunol. 2021 Jul;41(5):1048-1063. doi: 10.1007/s10875-021-01000-y. Epub 2021 Mar 3. PMID: 33660144; PMCID: PMC8249271.

TEAM LEADER

CHEVILLARD Christophe (PhD – HDR)
christophe.chevillard@univ-amu.fr

GROUP MEMBERS

ANDRIEUX Pauline (PhD student)
BROCHET Pauline (PhD student)
GALLARDO Frederic (TCH)
NUNES Joao Paulo (Post-doc)
SPINELLI Lionel (IR)
TORRES Magali (IE)

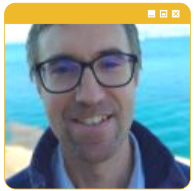


Chagas dilated cardiomyopathy

TAGC

> BIOINFORMATICS OF GENE REGULATORY SEQUENCES AND VARIANTS

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



TEAM LEADER
GONZÁLEZ Aitor
(Associate professor)
aitor.gonzalez@univ-amu.fr

TEAM MEMBERS
MICHEL Marie (PhD student)

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 (https://github.com/anthbapt/multixrank)
-VTAM
(https://github.com/aitgon/vtam/)
-pygtftk
(https://github.com/dputhier/pygtftk)
-TAGOOS
(https://tagoos.readthedocs.io/en/latest/)

FUTURE PRIORITIES

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

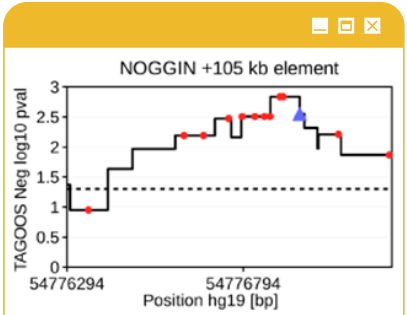
SELECTED PUBLICATIONS

- Aitor Gonzalez, Vincent Dubut, Emmanuel Corse, Reda Mekdad, Thomas Dechatre, et al.. ***VTAM: A robust pipeline for validating metabarcoding data using internal controls***. 2021. ⟨hal-03144831⟩

- Aitor Gonzalez, Marie Artufel, Pascal Rihet. ***TAGOOS: genome-wide supervised learning of non-coding loci associated to complex phenotypes***. Nucleic Acids Research, Oxford University Press, 2019, ⟨10.1093/nar/gkz320⟩. ⟨hal-02119716⟩

- Fabrice Lopez, Guillaume Charbonnier, yasmina Kermezli, Mohamed Belhocine, Quentin Ferré, et al.. ***Explore, edit and leverage genomic annotations using Python GTF toolkit***. Bioinformatics, Oxford University Press (OUP), 2019, ⟨10.1093/bioinformatics/btz116⟩. ⟨hal-02078147⟩

- Abibatou Mbodj, E. Hilary Gustafson, Lucia Ciglar, Guillaume Junion, A. Gonzalez, et al.. ***Qualitative Dynamical Modelling Can Formally Explain Mesoderm Specification and Predict Novel Developmental Phenotypes***. PLoS Computational Biology, Public Library of Science, 2016, 12 (9), pp.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

SOURCE

- https://tagc.univ-amu.fr/en/users/gonzalez-aitor

TAGC

> 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.

FIELDS OF STUDY

- **Identify susceptibility genes for severe malaria (cerebral malaria, severe anemia)**
- **Define the transcriptomic signatures of cerebral malaria**
- **Identify 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** (genetics, bulk and single-cell transcriptomics, gene reporter assays, CRIPR-Cas9 genome editing and flow cytometry).

FUTURE PRIORITIES

- **Decipher the common pathogenic mechanisms between cerebral malaria and neurodegenerative disorders.**
- **Identify new molecular mechanisms involved in susceptibility to severe malaria susceptibility.**
- **Further study 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.**

NOTABLE COLLABORATIONS

- Thanks to our collaborations with **Ogobara Doumbo (DEAP, Bamako, Mali)**, **Delmiro Fernandez-Reyes (London, UK and Ibadan, Nigeria)** and **Sandrine Nsango (Centre Pasteur, Yaoundé, Cameroon)**, we have access to several study cohorts essential to our projects.

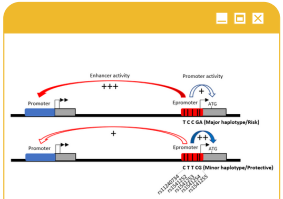
- A recent collaboration with **Antoine Claessens (UMR5235, Montpellier)**, **Antoine Berry and Nicolas Blachard (UMR1291, Toulouse)** and **Sandrine Nsango (Centre Pasteur, Yaoundé, Cameroon)**, whose expertise is complementary, allows us to develop a multidisciplinary project to disentangle both parasite and host factors on the same samples and using state-of-the-art technologies.

TEAM LEADER

MARQUET Sandrine (CNRS CRHC)
sandrine.marquet@univ-amu.fr

TEAM MEMBERS

ADJEMOUT Mathieu
(PhD student)
BERGON Aurélie (IR)
ESCANDELL Amélie
(Master student)
FARAH Gaëlle
(Master student)
NGUYEN HUU Hong Thu
(Master student)
POUVELLE Bruno (IR)
RIHET Pascal (PR)
TORRES Magali (IE)



Regulation of ATP2B4 gene by an Epromoter containing 5 SNPs associated with severe malaria

SOURCE

- https://tagc.univ-amu.fr/en/users/marquet-sandrine
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9101746/pdf/ijms-23-04849.pdf

TAGC

> 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).

TEAM LEADER

PUTHIER Denis
(Associate Professor HDR)
denis.puthier@univ-amu.fr

GROUP MEMBERS

BAVAIS Julie (PhD student)
CHEVALLIER Jessica (PhD student)
CONTE Samantha (PhD student)
GARD Charlyne (Engineer)

STRENGTHS

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

FOCUS

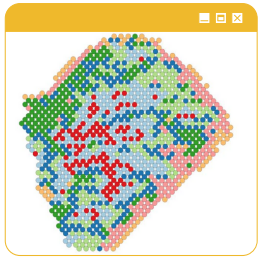
•We are currently developing, in collaboration with **TGML facility**, **spatially resolved transcriptomics** to analyse the **regulatory events occuring in the thymus**. This ongoing project with **M. Irla (CIML) and Arnauld Sergé (LAI)** aims at elucidating the **molecular mechanism** driving T-cell 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)**.

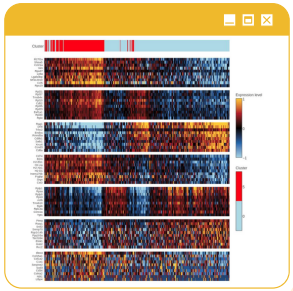
FUTURE PRIORITIES

•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).**





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

SOURCE

•https://tagc.univ-amu.fr/en/users/puthier-denis

TAGC

> MALARIA & SEPSIS TEAM

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

- **Malaria and sepsis**
- **Dysregulation of gene expression in pathogenic conditions**

STRENGTHS

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

FOCUS

- **Mapping malaria and sepsis genes in humans or mice using a positional cloning approach.**
- **Characterising transcriptional signatures associated with clinical phenotypes.**
- **Identifying cis-regulatory variants perturbing gene networks and causing the disease.**

FUTURE PRIORITIES

- **Developing a bioinformatic approach to identify genetic regulatory variants in immune cells**
- **Assessing the regulatory effect of genetic variants using classical and massive gene reporter assays**
- **Looking for genetic regulatory variants modulating gene expression in immune cells and protecting against malaria or sepsis**

NOTABLE COLLABORATIONS

- **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

- Nisar et al.. ***Identification of ATP2B4 Regulatory Element Containing Functional Genetic Variants Associated with Severe Malaria***. International Journal of Molecular Sciences, MDPI, 2022, 23 (9), pp.4849. (10.3390/ijms23094849). (hal-03690258)

- Rosier et al.. ***Transcriptional Response in a Sepsis Mouse Model Reflects Transcriptional Response in Sepsis Patients***. International Journal of Molecular Sciences, MDPI, In press, 23 (2), pp.821. (10.3390/ijms23020821). (hal-03528060)

- 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***. International Journal of Molecular Sciences, MDPI, 2021, 22, (10.3390/ijms22115852). (hal-03245766

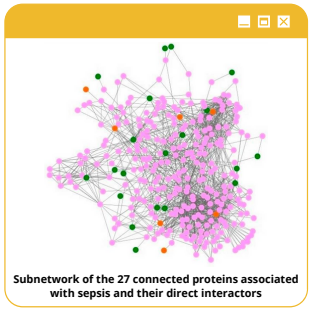
- Aitor Gonzalez et al.. ***TAGOOS: genome-wide supervised learning of non-coding loci associated to complex phenotypes***. Nucleic Acids Research, Oxford University Press, 2019, (10.1093/nar/gkz320). (hal-02119716)

TAGC DIRECTOR & TEAM LEADER

RIHET Pascal (Professor, researcher)
pascal.rihet@univ-amu.fr

TEAM MEMBERS

ADJEMOUT M. (PhD student)
COSTELLO R. (PU-PH)
CRETIN J. (M2 student)
GALLARDO F. (TCH)
GONZALEZ A. (MCU)
NGUYEN HUU H. (M2 student)
MARQUET S. (CR)
MICHEL M. (PhD student)
NGUYEN C. (DR)
PAUL P. (CR)
POUVELLE B. (IR)
PRADEL L. (MCU)
TORRES M. (IE)



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

SOURCE

- https://tagc.univ-amu.fr/en/users/rihet-pascal

TAGC

> 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.**

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

SOURCE

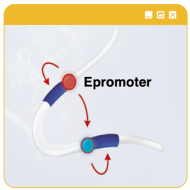
- https://canceropole-paca.com/propulser-vos-recherches/acceder-aux-technologies-expertises/
- https://www.enhpathy.eu/
- https://doi.org/10.1038/s41467-021-26861-0
- https://doi.org/10.1038/ncomms7905

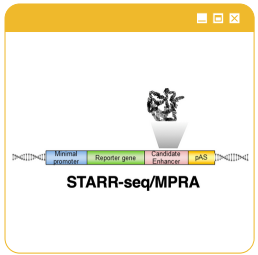
TEAM LEADER

SPICUGLIA Salvatore (inserm, DR2)
Salvatore.spicuglia@inserm.fr

GROUP MEMBERS

ABAD José David (Research Engineer)
ADOUNI Nori (Research Engineer)
CAVALIERI Davide (Project Manager)
FAN Yannan (Post-doc)
HUSSAIN Saadat (Research Engineer)
LEONETTI Francesco (PhD student)
MALFAIT Juliette (PhD student)
MANOSALVA Iris (Research Engineer)
VAN OUWERKERER Antoinette (Post-doc)
WAN Jing (PhD student)





TAGC

> RSAT (REGULATORY SEQUENCE ANALYSIS TOOLS)

Our research activities are dedicated to the **conception, implementation, evaluation and application of bioinformatics approaches** to **analyse genome regulation and biomolecular networks**. Since 1997, Professor VAN HELDEN lead the Regulatory Sequence Analysis Tools (RSAT, http://rsat.eu/), a software suite for the detection of regulatory elements in non-coding DNA sequences. He also developed bioinformatics approaches relying on graph theory (path finding, subgraph extraction), to infer metabolic pathways from sets of functionally related genes (operons, co-expression clusters, phylogenetic profiles, ...).

TEAM LEADER

VAN HELDEN Jacques (Professor)
jacques.van-helden@univ-amu.fr

TEAM MEMBERS

THOMAS-CHOLLIER Morgane (RSAT developper, FR)
MEDINA-RIVERA Alejandra (RSAT developper, MX)
CASTRO-MONDRAGON Jaime (RSAT developper, NO)
NGUYEN Nga Thi Thuy (RSAT developper, FR)
CONTRERAS MOREIRA Bruno (RSAT developper, ES)
SANTANA GARCIA Walter Santana (RSAT developper, FR)
SAND Olivier Sand (RSAT developper, FR)
DEFRANCE Matthieu (RSAT developper, BE)

FIELDS OF STUDY

•Development, evaluation and applications of algorithms for the analysis of regulatory sequences and biological networks.

STRENGTHS

•Since 2017, Pr VAN HELDEN ensures the **co-direction of the Institut Français de Bioinformatique** (IFB; https://www.france-bioinformatique.fr/), a national infrastructure federating 36 bioinformatics platforms to support research in life sciences. The IFB is also **the French node of the European bioinformatics infrastructure ELIXIR** (https://elixir-europe.org/).

FOCUS

•Our current research focuses on **integrative approaches to genomic regulation based on multi-omics data.**

SELECTED PUBLICATIONS

•Santana-Garcia et al. (2022). **RSAT 2022: regulatory sequence analysis tools**. Nucleic Acids Res. 2022 (Web Server issue), doi:10.1093/nar/gkac312. [Full text]

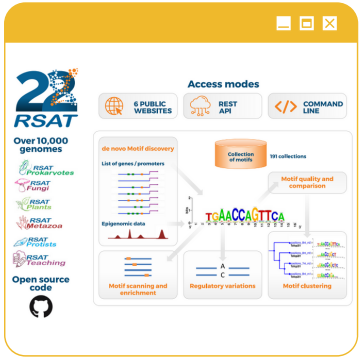
•Jacques van Helden et al. (2021). ***An appeal for an objective, open, and transparent scientific debate about the origin of SARS-CoV-2***. The Lancet, Elsevier, 2021, 398 (10309), pp.1402-1404. ff10.1016/S0140-6736(21)02019-5ff. ffhal-03358748f

•Sallard, Halloy, Casane, Decroly, & van Helden. (2021). ***Tracing the origins of SARS-COV-2 in coronavirus phylogenies: a review***. Environmental chemistry letters, 1–17. Advance online publication. https://doi.org/10.1007/s10311-020-01151-1

•Nguyen et al. (2018). ***RSAT 2018: regulatory sequence analysis tools 20th anniversary***. Nucleic Acids Res., gky317, doi:10.1093/nar/gky317. [Full text]

•Thomas-Chollier et al. (2008). ***RSAT: regulatory sequence analysis tools***. Nucleic Acids Res. [Pubmed 18495751] [Full text]

•van Helden, J. (2003). ***Regulatory sequence analysis tools***. Nucleic Acids Res. 2003 Jul 1;31(13):3593-6. [Pubmed 12824373] [Full text] [pdf]



SOURCE

•https://orcid.org/0000-0002-8799-8584
•http://rsat-tagc.univ-mrs.fr/rsat/people.php
•https://scholar.google.com/citations?hl=en&user=P9OSQpwAAAAJ&view_op=list_works&sortby=pubdate

FRESNEL Institute/ Mosaic group/ page 31

I2M/ MABioS team/ page 32

IRPHE/ DEPLANO team/ page 33

LMA/ Medical Ultrasound group/ page 34

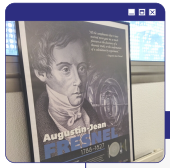
LP3/ ALLONCLE team/ page 35

Maths & physics/ page 30

FRESNEL INSTITUTE

> MOSAIC GROUP

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.

FOCUS ON THE CELL MORPHOGENESIS & POLARIZED MICROSCOPY LABS

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.**

RECENT PUBLICATION

Vaz Rimoli et al "***4polar-STORM polarized super-resolution imaging of actin filament organization in cells***"
Nature Communications 13, 301 (2022)

CONTACT

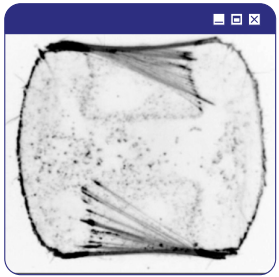
BRASSELET Sophie (Team leader): sophie.brasselet@fresnel.fr
MAVRAKIS Manos (Team leader): manos.mavrakis@fresnel.fr

DIRECTOR

RIGNEAULT Herve - CNRS Research Director (DR1)
herve.rigneault@fresnel.fr

GROUP MEMBERS

ALONSO Miguel (Professor-Researcher)
BAFFOU Guillaume (Researcher)
BRASSELET Sophie (Researcher)
CHAIGNE Thomas (Researcher)
DUBOISSET Julien (Professor-Researcher)
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)



SOURCE

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

I2M (MATHEMATICAL INSTITUTE OF MARSEILLE)

> MABioS (*Mathématiques & Algorithmique pour la Biologie des Systèmes*)

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).

Mathématiques
Algorithmique pour la
Biologie des
Systèmes

TEAM LEADER

REMY Elisabeth (DR CNRS)
elisabeth.remy@univ-amu.fr

MEMBERS

BEN BOINA Nadine (PhD Student)
CHAOUIYA Claudine (MCF AMU)
MOSSE Brigitte (MCF AMU)
PANKAEW Saran (PhD Student)
SANCHEZ-VILLANUEVA José Antonio (Postdoc)
TICHIT Laurent (MCF AMU)
ZACCAGNINO Francesca (Postdoc)

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

PRIORITIES

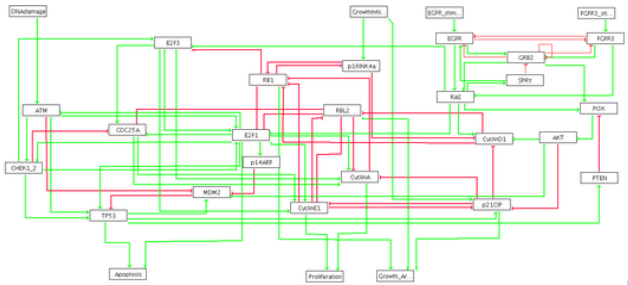
The research developed by MABioS team focuses on **the mathematical modeling of biological interaction networks in order to understand their transient and asymptotic behaviors.**

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)**.

SOURCE

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



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

> BIOMECHANICS TEAM

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**.

TEAM LEADER

DEPLANO Valérie (DR CNRS)
valerie.deplano@cnrs.fr

TEAM MEMBERS

BARON Cécile (CRCN CNRS, HDR)
BERTRAND Eric (IR AMU)
BRANDENBOURGER Martin (CRCN CNRS)
BOIRON Olivier (Pr ECM)
GUIVIER-CURIEN Carine (MCF AMU, HDR)

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

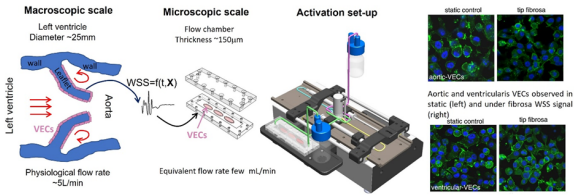
- **Complex biomimetic numerical modelling**
- **Biomimetic *in vitro* modelling of macro and micro blood circulation**
- **Controlled *in vitro* ultrasound stimulation of cells to investigate cell mechanotransduction**
- **Metrology :** PIV 3C-3D, microPIV, 3D digital image correlation for soft tissue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

PRIORITIES

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

RECENT PUBLICATIONS

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**.



Credit : V. Deplano

SOURCE

- Faure, E., Bertrand, E., Gasté, A., Plaindoux, E., Deplano, V.*, Zaffran, S.*. ***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

LMA (MECHANICS & ACOUSTICS LABORATORY)

> WAVES AND IMAGING TEAM

> 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

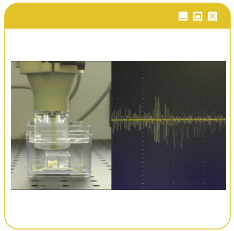
•**Ultrasound imaging techniques** for the detection of breast cancer and bone pathologies.
•**Ultrasound characterization techniques** to extract quantitative measures describing intrinsic acoustic properties and structures of scanned tissues such as bone tissue, blood and tumors.

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

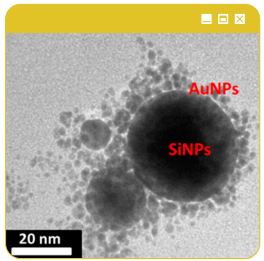
In collaboration with **LP3**, **the Fresnel Institute** and the russian lab PhysBio, we synthesized nanostructures consisting of a Silicon (Si) core covered with small gold (Au) nanoparticles (NP), thanks to the use of laser and chemical modifications. The produced Si@Au core-satellite nanocomposites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

GROUP MEMBERS

BRUNET Elena (PhD Student)
DEBIEU Eric (Engineer)
DOVERI Elise (PhD Student)
FRANCESCHINI Emilie (HDR)
GUILLERMIN Régine (Engineer)
LASAYGUES Philippe (HDR)
MENSAH Serge (HDR)
METWALLY Khaled (Post-doc, Engineer)
PAYAN Cédric (HDR)
POULAIN ZARCOS Marie (Post-doc, IMI)

CONTACT

MENSAH Serge
mensah@lma.cnrs-mrs.fr



SOURCE

• www.lma.cnrs-mrs.fr/spip/spip.php?page=theme&id_mot=22&lang=en
• Al-Kattan A, Tselikov G, Metwally K, Popov AA, Mensah S, Kabashin AV. 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 (LASER PLASMA AND PHOTONIC PROCESSES)

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 ...)

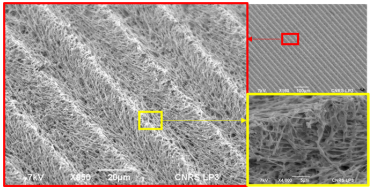
•**Laser-induced transfer processes and application** (organic-electronic, bioprinting, tissue engineering, ...)

•**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)

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

SOURCE

• www.lp3.fr

DIRECTOR

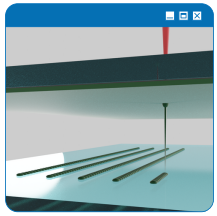
UTÉZA Olivier (DR, PhD, HDR)
olivier.uteza@univ-amu.fr

GROUP MEMBERS

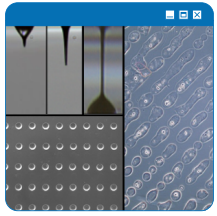
AL-KATTAN Ahmed (PhD, MCF)
ALLONCLE Patricia (PhD, CRHC)
CASANOVA Adrien (PhD, MCF)
DUVERT Lucas (PhD student)

CONTACT

ALLONCLE Patricia
patricia.alloncle@univ-amu.fr



Laser-induced forward transfer (LIFT) process



ADES / LE COZ team/ page 37

CEReSS/ AUQUIER & BOYER team/ page 38

ADES (Anthropology, law, ethics & health)

> TEAM N°2 - "BODY, NORMS, HEALTH" (CORPS, NORMES, SANTÉ)

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.

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.

TEAM LEADER

LE COZ Pierre
(Professor, AMU, ADES, EFS, CNRS)
pierre.le-coz@ univ-amu.fr

TEAM MEMBERS

CAMOIN Ariane (Doc, AMU, ADES, EFS, CNRS)
CHABROL Brigitte (Pr, AMU, ADES, EFS, CNRS)
DOUPLAT Marion (Doc, MC)
EINAUDI Marie-Ange (Doc, AMU, ADES, EFS, CNRS)
GUIVARC'H Maud (Doc, AMU, ADES, EFS, CNRS)
LUTAUD Romain (Doc)
MALZAC Perrine (Doc, AMU, ADES, EFS, CNRS)
MATHIEU Marion (Doc, AMU, ADES, EFS, CNRS)
MICHEL Fabrice (Pr, AMU, ADES, EFS, CNRS)
MERROT Thierry (Pr, AMU, ADES, EFS, CNRS)
TARDIEU Corinne (Pr)
TOSELLO Barthélémy (Pr, AMU, ADES, EFS, CNRS)

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.

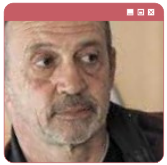
Space for ethical reflection Rhône-Alpes Region (Espace de réflexion éthique PACA Corse)

SOURCE

•Space for ethical reflection Rhône-Alpes Region: http://www.ee-paca-corse.com/
•Bulletin de l'Académie de médecine

CEReSS

The Center for Studies & Research on Health Services & Quality of Life (CEReSS) is a **public health research unit** under the direction of Pr Pascal Auquier and Laurent Boyer, 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).



DIRECTORS

AUQUIER Pascal (PU-PH)
pascal.auquier@univ-amu.fr
BOYER Laurent
laurent.boyer@univ-amu.fr

GROUP MEMBERS

BAUMSTARCK Karine (PH)
BERBIS Julie (MCU-PH)
BERNARD Cécile (Med doc)
HAMIDOU Zeinab (PhD)
LOUNDOU Anderson (Biostatistician)
VERCASSON Camille (Biostatistician)

FIELDS 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

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).

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. doi: 10.1016/j.jaci.2016.08.027.

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.

Tinland et al. ***Effectiveness of a housing support team intervention with a recovery-oriented approach on hospital and emergency department use by homeless people with severe mental illness: a randomised controlled trial***. Epidemiol Psychiatr Sci. 2020 Sep 30;29:e169.

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.

AMU WEBSITE

www.univ-amu.fr/marmara

COMMUNICATION DOCUMENTS

2020- 2022

ONLINE PRESENCE

NEWSLETTERS

internal & external NLs

TWITTER

@marmara_amu

VIDEOS

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

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

CONTACT DETAILS

Institut-marmara-contact@univ-amu.fr

www.univ-amu.fr/MarMaRa

Thank you for your collaboration!

Created by : BERNARD Cécile & SAID Rima

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