Master in Biomedical Research

2023-2024

List of potential laboratories

Other laboratories would also be accepted

(by alphabetical order using the last name of each principal investigator)

Master in Biomedical Research

2023-2024

List of potential laboratories

(the list is in alphabetical order using the last name of each principal investigator)

Note: the list of groups is orientative. Students can also find by themselves research groups (in Spain or abroad) that are not in this list, and submit the acceptance letter of the researcher responsible (principal investigator) of the group together with the rest of the documentation when they send their application to this master

See also important information about projects and groups in the next page

Admissions to the Master in Biomedical Research (BIOMED) are prioritized for students that have been accepted in a research group for their *practicum*.

If more than two students are opting to the same group, the master coordinator may recommend that some of the applicants be redirected to other groups based on their motivation profile and academic criteria.

a) If you have already been accepted to a research group for doing the master research *practicum*, please submit the acceptance letter by the group's supervisor/director. The group can be in Spain or in a foreign country.

b) If you do not have a host research group at the time of registering, you must indicate your first 5 choices, in order of preference, **from the list of groups** offered by the BIOMED master. Knowing these choices gives us additional information to assess your application.

Important:

b1) When listing your 5 choices, please write the name of the PI for each group. Don't just say "group in tumor modelling" or something like that.

Besides telling us your 5 choices from the list, you can search for a research group (in Spain or abroad) that is not in this list. You do not need to indicate that in addition to your 5 choices above.

b2) Keep in mind that indicating your choices does not mean that you will be assigned to a group automatically. You are encouraged to actively seek acceptance in a group because having a group will increase your chances of being accepted to the master.

You must contact the group you are interested in (from the list provided here or from your own searches), arrange an interview, and get the written acceptance of the investigator in charge of that group.

The next page outlines some guidelines to help candidate students to find a research group.

It also has a list of potential laboratories to which you can submit applications. This list can be updated with some new groups in the next months.

Note: **admissions to the Master in Biomedical Research (BIOMED) are prioritized for students that have been accepted to do his/her research *practicum* in a research laboratory.**

A main orientation of the BIOMED master is to continue towards a PhD thesis, and the majority of students enrolling in this master have, at the time of pre-registration, been accepted in research groups to do a PhD after they finish the master. However, there are students who have a motivation to do this master, and eventually a PhD, but who may not know how to contact a suitable laboratory.

This document contains a few guidelines to help candidate students in finding a research group, and also a list of potential laboratories to which they can submit applications. **These groups have expressed their interest for hosting a master student.**

This list is orientative, and students can do their research in another laboratory that they can find on their own. Also, this list is not just to choose a laboratory: you must contact the group you are interested in, arrange an interview, and get the written acceptance of the investigator in charge of that group.

“How to: getting accepted in a research laboratory”

1- You have to know what you would like to work on.

2- Be specific: you should be able to say what are the questions that are important to you and why.

Not very good: I want to work in neurosciences, I have always liked it.

Much better: I want to understand the processes and mechanisms that make neurons more sensitive to oxidative stress and oxygen deprivation in patients with neurodegenerative diseases such as...

Not very good: I want to work in regenerative medicine, I think that stem cells have a lot of potential to cure diseases.

Much better: I want to contribute to the identification of proteins that when expressed in a differentiated cell such as a fibroblast, can cause it to dedifferentiate and acquire functional characteristics of a pluripotent cell.

3- Find out who is working on what.

Websites of universities and research centers, PubMed searches, Google...

It takes time! (don’t wait till last minute to begin looking for your favorite lab)

4- Write to the group that interests you.

5- Contacting a group.

a) Motivation letter: tell them why you want to work with them (for this, you need to know something about what they do and about current questions in the field).

It takes time! (don’t wait till last minute to begin looking for your favorite lab)

Also tell them why you are good. Labs appreciate commitment, responsibility, ability to work in a team, ability to persevere and a strong motivation.

Ask them for an interview to show them how good you are.

Do not write a generic letter to copy-paste and send to ten different laboratories changing only the name of the group leader.

Choose your labs and send a personal, specific letter to each one.

b) Keep in mind that a person working full time in a cellular-molecular biology lab can spend more than 1000 euros/month in materials, besides a lot of time required to train you and supervise you until you begin to get solid results.

Expect that during the first 6 months it is more likely that you will produce more trouble and expenses than productive results. Laboratories are very careful with how they

spend their money because they get their funding from competitive grants that are given or denied based on productivity (that means getting results) and publications in internationally respected journals.

Do not get discouraged with rejections, learn from them to improve your application.

c) Do not forget important details in your CV:

1- Give names of senior persons that can be a reference.

Be careful with “clone” reference letters from teachers that don’t really know you and will just say general things.

2- Include your university scores. If they are not too good, you should be ready to explain why, either in your application letter or in an interview. Be honest and realistic about it. If the teaching/exam system of your university hasn’t worked for you, you will know the reasons better than anyone else, so be prepared to speak frankly about it.

University scores are not an exact indicator of who will become a successful scientist, but they say that a person has gone through 4-5 years of serious effort with a better than average performance.

Most people will interpret this as a sign of self-discipline, organization, capacity to work even if you have a bad day, and to get things done regardless of whether they are more fun or plainly boring.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Blending Biology and Chemistry to Enable Systems Pharmacology

Project supervisor (principal investigator of the laboratory/group)
Name: Patrick Aloy
eMail: patrick.aloy@irbbarcelona.org
Group name: Structural Bioinformatics and Network Biology
Institution: Institute for Research in Biomedicine (IRB Barcelona)
Webpage of the group: https://sbnb.irbbarcelona.org

Main grant associated with this project:
Principal investigator: Patrick Aloy
Agency: Ministerio de Ciencia e Innovación
Reference/ years: 2021-2024

Brief summary of the project or current research lines of the group

Large-scale small molecule bioactivity data are not routinely integrated in daily biological research to the extent of other 'omics' information. Compound data are scattered and diverse, making them inaccessible to most researchers and not suited to standard statistical analyses. The urge to couple chemical and biological data to cutting-edge machine learning has prompted us to develop new strategies for data integration and knowledge representation, especially in the form of heterogeneous networks and vector-like descriptors. In particular, we generated the Chemical Checker, which is currently the largest repository of small molecule bioactivity signatures (Duran-Frigola *et al.* 2020 Nat Biotechnol; Bertoni *et al*. 2021 Nat Commun). To complement it, we created the Bioteque, a repository of context-dependent biological signatures based on a gigantic knowledge graph representing most currently known biology (Fernández-Torras *et al*. 2022 Nature Commun). This common vector format to represent biology and chemistry helps blending the two worlds. We are now developing a generalized connectivity mapping, as a form of virtual phenotypic screening, to discover novel chemical or genetic modulators able to *revert* the specific signatures of disease and 'cancel out' the phenotypic traits of complex disorders. For instance, we have discovered compounds able to revert AD signatures *in vitro* and *in vivo*, neutralizing the cognition deficiencies in AD mouse models (Pauls *et al.* 2021 Genome Med). We now aim at finding compounds to globally modulate the activity of a specific set of targets, selected from the SARS-CoV-2 – Human contactome (Kim *et al*. 2023 Nat Biotecnol), and to design compounds that specifically kill certain pancreatic cancer cell lines, without affecting the rest. All in all, the incorporation of high-content biological and chemical descriptors to the drug discovery process will trigger the identification of novel compounds, finally enabling systems precision medicine.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: METABOLIC CONTROL OF IMMUNE RESPONSES

Project supervisor (principal investigator of the laboratory)
Name: **Jose Aramburu**
Mail: jose.aramburu@upf.edu
Group name: GENIMMUNE
Institution: Universitat Pompeu Fabra
Webpage of the group: https://www.upf.edu/web/genimmune
https://www.upf.edu/web/biomed/entry/-/-/15818/adscripcion/jose-francisco-aramburu
https://www.upf.edu/web/jose-aramburu

Main grant associated with this project:
Principal investigator: Jose Aramburu and Cristina López-Rodríguez
Agency: Plan Estatal I+D+i, Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación
Reference/ years: PID2021-128721OB-I00 (2022-2025)

Brief summary of the project or current research lines of the group

Metabolism regulates immune responses, both ensuring energy and metabolites necessary for immune functions as well as influencing gene expression and functional specialization of immune cells. Metabolism and immune response co-regulate each other, and immune cells are capable of adapting their metabolism to be able to function in different niches and even hostile conditions, while on the other hand altered metabolic conditions can lock immune cells in a detrimental functional state.

We are currently studying how metabolism influences diverse immune responses in two pathological settings, obesity and cancer. We have combined high-throughput RNA-sequencing analyses and metabolomics to identify metabolic pathways and metabolism-regulated gene signatures and functions in different populations of immune cells in these scenarios.

We offer a master position in a project that will aim at modifying specific metabolic pathways in T lymphocytes and macrophages to redirect immune responses and enhance their therapeutic effectiveness in cancer and obesity. The selected candidate will acquire conceptual fluency in current trends in immunometabolism research, in parallel with hands-on experience in diverse cellular, molecular and immune function techniques (for instance flow cytometry, CRISPR-directed deletions, gene expression, chromatin analyses, cell differentiation assays, metabolic activity, antitumor function) of primary immune cells isolated from gene-edited mice under different pathological settings.

Leading recent publications of the group:

Lunazzi et al., 2021 Journal of Immunology
Huerga Encabo et al., 2020 Journal of Experimental Medicine
Aramburu and López-Rodríguez, 2019 Frontiers in Immunology
Buxadé et al., 2018 Journal of Experimental Medicine
Tellechea et al., 2018 Journal of Immunology
Aramburu et al., 2014 Science Signaling
Berga-Bolaños et al., 2013 Proc Natl Acad Sci USA
Buxadé et al., 2012 Journal of Experimental Medicine
Ortells et al., 2012 Nucleic Acids Research

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Cell Cycle Control: Role of Alternative CDKs in S Phase Progression

Project supervisor (principal investigator of the laboratory/group)
Name: José Ayté
eMail: jose.ayte@upf.edu
Group name: Oxidative Stress and Cell Cycle
Institution: UPF
Webpage of the group: https://www.upf.edu/web/osccg/

Main grant associated with this project:
Principal investigator: José Ayté
Agency: Ministerio de Ciencia, Innovación y Universidades
Reference/ years: Pending (2023-2026)

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

In our laboratory, we are ultimately interested in deciphering the mechanisms that control cell cycle progression using fission yeast as model organism. Recently, we have started a new project to obtain a more profound understanding of how CDKs (the central core of the cell cycle machinery) are regulated. Cdc2 (CDK1) is the single CDK kinase described to regulate cell cycle progression in fission yeast, like in all other yeasts. However, despite several global phosphoproteomic and genome-wide studies to determine which are the target(s) of the CDK activity in the G1/S transition, up-to-now it is unknown which are the primary targets of Cdc2 in this cell cycle phase. We have been recently investigating the role of an alternative CDK, Pef1, which was originally described to be involved in controlling TORC1 pathway and autophagy. Interestingly, we have observed an impact on cell cycle regulation, since cells lacking Pef1 are smaller that wild type cells (11.5 μ vs 13.3 μ). Using synchronous cultures (block and release experiments), asynchronous cultures in a reporter strain developed in the laboratory or by measuring DNA content of isolated nuclei from asynchronous cultures, we can affirm that Pef1 is required for completion of mitotic S phase. We have analysed the proteome and phosphoproteome of a wild type, *Δpef1*, and a conditional Pef1 strains from asynchronous cultures and we have found several candidate proteins that seems to be phosphorylated by Pef1. The candidate will determine direct targets of Pef1 involved in cell cycle progression and in completion of S phase using some wide-range technologies, including protein purification, microscopic fluorescence quantification and cytometry.

Some related publications from the group are:

Salat-Canela et al. (2023) **Trends Cell Biol.** 33:124-137
Hummer et al. (2021) **Cell Rep.** 37:109893
Salat-Canela et al. (2021) **Cell Rep.** 37: 109951
González-Medina et al. (2019) **Nucleic Acids Res.** 47:8439-8451
Knezevic et al. (2018) **FEBS J.** 285:3870-3881
Alves-Rodrigues et al (2016) **Cell Reports** 14:885-895
Eckert et al. (2016) **PLoS Genet.** 12:e1005768
Gomez-Escoda et al. (2011) **EMBO Rep.** 12:84-89
Moldon et al. (2008) **Nature** 455:997-1000

Preventing metastasis initiation by targeting the tumor stroma

Josep Baulida, PhD - jbaulida@imim.es

Programa de Recerca en Càncer
IMIM-Institut Hospital del Mar d'Investigacions Mèdiques
Parc de Recerca Biomèdica de Barcelona
c/Doctor Aiguader, 88. 08003 Barcelona, Spain. Tel 93 3160436
http://www.imim.es/programesrecerca/cancer/en_elementsinvolved.html
Agencia Estatal de Investigación - PID2019-104698RB-I00 / 2020-23

Brief summary of project summary or current research lines

We have described that, at diagnosis, 16% of the early infiltrating breast cancers present Cancer–Associated Fibroblast with myofibroblastic activity (myoCAFs) that express the transcription factor Snail1. These patients have a worse prognosis than those presenting Snail1 negative fibroblasts.

We have demonstrated that Snail1-expressing myoCAFs generate a pro-metastatic micro-environment around tumors, as they deposit extracellular fibers, such as the fibonectin and collagen fibers, in an aligned conformation that allow an increase of the connective tissue rigidity.

We also showed that to orchestrate these changes, myofibroblasts synthetises and polymerises a special fibronectin isoform including an extra domain (EDA, for ExtraDomain A).

The master project aims to study new molecular regulatory event in myoCAFs and test strategies to inhibit them.

We propose a molecular approach to unveil new pharmacological targetable molecules on CAFs. Cell culture, biochemical techniques and mouse models for metastatic cancer will be used.

Tridimensional reconstruction of a pro-metastatic extracellular matrix.

From confocal immuno-fluorescent images of activated fibroblasts in culture.

Extracellular fibronectin fibers in red, intracellular αSMA-stress fibers in green, and nuclei in blue.

Differential response of EDA+ or EDA- fibronectin fibers to tumor cells.

Cocultures of tumor cells (white colonies) and fibroblasts (green) expressing fibronectin EDA+ or

EDA- isoforms. Tridimensional reconstructions from confocal immuno-fluorescent images.

Fibronectin fibers in green, actin fibers in white, and nuclei in red.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: The urea cycle enzymes in therapeutics: Probes and small molecules targeting the metabolic regulator argininosuccinate synthetase 1 (ASS1).

Project supervisor (principal investigator of the laboratory/group)
Name: Marta Barniol-Xicota
eMail: marta.barniol@upf.edu
Group name: Chemical Biology of Therapeutic Enzymes
Institution: Universitat Pompeu Fabra – Medicine and Life Sciences Department
Webpage of the group: https://barniolxicotalab.com/

Main grant associated with this project: Starting Funds & LaCaixa Junior Leader
Principal investigator: Marta Barniol-Xicota
Agency: UPF-MELIS & LaCaixa
Reference/years: 2022-2027

Brief summary of the project or current research lines of the group:

Citrullinemia type 1 (CTLN1) is a rare disease that mainly affects neonates and currently has no cure. This disease is caused by mutations in the structure of argininosuccinate synthetase 1 (ASS1), which is a key metabolic enzyme in the urea cycle. Mutations in ASS1 reduce its activity, causing toxic levels of ammonia in the blood. Therefore, **molecules able to rescue ASS1 activity could be of therapeutic interest for CTLN1**.
Chemical rescue of an enzyme's activity can be achieved through its allosteric modulation. This is produced thanks to the binding of small molecules to a site different from the active center. Allosteric modulation is one of the most efficient and selective ways to regulate enzyme activity, but unfortunately allosteric sites are difficult to predict and the modulators are often discovered serendipitously.
Phage display allows molecular screening of large libraries quickly and efficiently. Our group has recently developed the chemically modified phage display technique. Our technique incorporates: 1) cyclization of the peptides presented in the phage, giving them a secondary structure and, therefore, greater selectivity and 2) incorporation of warheads or electrophilic moieties that allow us to convert our molecules into covalent ones. Contrary to traditional approaches, with our technique, we do not need to know the exact structure of the protein binding site to develop a molecule. Therefore, we can find ASS1 modulators in a targeted and rational way, using the chemically modified phage display.

The goal of this project is to **prepare selective allosteric modulators of the metabolic enzyme ASS1** able to **rescue its enzymatic activity** and that can be used for the **treatment of the rare disease Citrulinemia type I**. To do so, we will use the innovative technique of chemically modified phage display.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: SARCOPENIA AND NUTRITIONAL ABNORMALITIES IN BRONCHIECTASIS PATIENTS: IMPLICATIONS IN THE CLINICS OF DIFFERENCES BETWEEN MEN AND WOMEN

Project supervisor (principal investigator of the laboratory/group)
Name: Esther Barreiro
eMail: ebarreiro@imim.es
Group name: Muscle Wasting and Cachexia in Chronic Respiratory Diseases and Lung Cancer
Institution: IMIM-Hospital del Mar, UPF
Webpage of the group: https://www.imim.es/programesrecerca/rct/en_urmar.html

Main grant associated with this project:
Principal investigator: Esther Barreiro
Agency: Instituto de Salud Carlos III, PI21/00215
Reference/ years: 2022-2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Non-cystic (non-CF) fibrosis bronchiectasis is a highly prevalent disease, since it represents the third chronic inflammatory disease of the airways after bronchial asthma and chronic obstructive pulmonary disease (COPD). Hypothesis and objectives: In bronchiectasis patients, systemic inflammation and nutritional abnormalities are relevant manifestations, which may also affect the muscle compartment. Hence, we hypothesized that the function of the respiratory and both upper and lower limb muscles may be altered in patients with bronchiectasis. The level of respiratory and limb muscle dysfunction may be associated with the degree of the patients' systemic manifestations, namely the nutritional abnormalities and systemic inflammation levels. Differences in the target parameters may exist between female and male patients. Hereafter, we further hypothesized that nutritional abnormalities, muscle dysfunction/sarcopenia, and systemic inflammation would be more severe in female than in male patients. Methods: A total of N=150 adult patients, men and women, with non-CF bronchiectasis and 20 control subjects (lung function and normal body composition) will be recruited from the outpatient Bronchiectasis Clinical Unit of the Pulmonology Department at Hospital del Mar (Barcelona). In addition, patients will have a wide-range body composition, which will allow stratification according to alterations in their nutritional status, muscle mass and function loss. In patients and control subjects, the following parameters will be determined: clinical evaluation and nutritional status, lung function, respiratory and peripheral muscle function (upper and lower limbs), and exercise capacity. In a subgroup of patients (N=20) and controls (N=10) the vastus lateralis quadriceps will be sampled. Inflammatory and nutritional parameters and damage (troponin I) will be analyzed in blood from all patients and controls, and levels of proteolysis, autophagy, apoptosis, muscle damage and regeneration, oxidative stress, cytokines, endoplasmic reticulum stress, and signaling (NF-kB and FoxO1/3 pathways), will be quantified in muscle specimens using diverse laboratory techniques. Using the corresponding statistical methods, all clinical, physiological, and biological variables and their potential relationships will be analyzed in specific stratified groups of patients. Differences between female and male patients will also be assessed.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Extra chromosomal DNA as a driver of intra-tumor heterogeneity
Project supervisor (principal investigator of the laboratory/group)

Name: Francisco Barriga, PhD
eMail: fbarriga@vhio.net
Group name: Functional Cancer Genomics
Institution: VHIO
Webpage of the group: https://vhio.net/pf/functional-cancer-genomics-group/
Main grant associated with this project:
Principal investigator: Francisco Barriga, PhD
Agency: ERC - StG
Reference/ years: 101041659 / 2023-2028

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Our group studies the function of large-scale chromosomal changes known as copy number alterations (CNAs). We combine state of the art genome engineering strategies with in vivo models of cancer to uncover the mechanisms by which CNAs enable cancer cells to propagate and resist therapies. We are particularly interested in the role of these alterations in immune surveillance, tumor heterogeneity, and cancer genome evolution. Our long-term goal is to understand the complex biology of CNAs to identify new therapeutic strategies that target cells with these chromosomal aberrations.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Studying the role of hippocampo-cortical projections in higher-order conditioning

Project supervisor (principal investigator of the laboratory/group)
Name: Arnau Busquets Garcia
eMail: abusquets@imim.es
Group name: Cell-type mechanisms in normal and pathological behavior
Institution: Institut Hospital del Mar d'Investigacions Mèdiques
Webpage of the group:
https://www.imim.cat/programesrecerca/neurociencies/en_mecanismes_cellulars.html

Main grant associated with this project:
Principal investigator: Arnau Busquets Garcia
Agency: European Research Council
Reference/ years: Grant 948217 HighMemory

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Animals and humans adapt to changes in the environment through the encoding and storage of previous experiences. Although associative learning involving a reinforcer has been the major focus in the field of cognition, other forms of learning are gaining popularity as they are likely more relevant and frequent in human daily choices. Indeed, associations between non-reinforcing stimuli represent the most evolutionarily advanced way to increase the chances of predicting future events and adapting individuals' behavior. These processes explain why individuals are very often repulsed or attracted by stimuli (persons, places, sounds), which do not have intrinsic repellent or appealing value and were never explicitly paired with negative or positive outcomes. This is called higher-order conditioning or mediated learning (ML). Importantly, these behavioral processes involve the hippocampus, are characterized by defined and accessible phases and involve several brain regions, making them perfect models to study the tight regulation of behavior by hippocampo-cortical projections. During this Master project, the student will participate in a project that is investigating the causal involvement of hippocampo-cortical projections in higher-order cognitive processes.

The candidate will use mouse sensory preconditioning and/or second-order conditioning paradigms, which will be combined with chemogenetic approaches, in order to investigate how specific hippocampo-cortical projections are involved in higher-order conditioning. Thus, the student will learn stereotaxical surgeries, behavioral procedures and imaging techniques.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Characterizing stress-induced activity changes in mouse brain and peripheral tissues.

Project supervisor (principal investigator of the laboratory/group)
Name: Arnau Busquets Garcia & Patrick Welz
eMail: abusquets@imim.es
Group name: Cell-type mechanisms in normal and pathological behavior
Institution: Institut Hospital del Mar d'Investigacions Mèdiques
Webpage of the groups:
https://www.imim.cat/programesrecerca/neurociencies/en_mecanismes_cellulars.html
https://www.imim.es/programesrecerca/cancer/en_intercellular_communication.html?t=membres&g=121

Main grant associated with this project:
Principal investigator: Arnau Busquets Garcia
Agency: European Research Council
Reference/ years: Grant 948217 HighMemory

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

When we are facing scary and/or anxious situations, we usually experience brain-dependent stressful feelings, which can be accompanied by stress-responses in peripheral organs, especially in the digestive tract. Whereas the brain circuits induced by these stressful events have been widely studied in animal models, whether the stressful situations engage peripheral tissues or peripheral-to-central circuits has not been explored into depths. In this project, we are using an inducible transgenic mouse model, which allows to express the fluorescent reporter tdTomato specifically in cells that are active at a chosen time ("trapped" cells). In other words, using these mice we are able to characterize the activated cells in a particular time window (e.g. after exposure to an stressful event), allowing us to identify cell signalling networks involved in stress-responses in the brain and in peripheral organs. The Master project will consist in characterizing the effects of acute stressors on tdTomato expression in the brain and in intestinal tissues of the reporter mice. Indeed, analysing neural activation in peripheral tissues such as the intestine could reveal unknown gut-to-brain communication circuits involved in stress and emotional states. The main techniques that will be acquired throughout the project include emotional behavioral procedures, organ perfusion, histopathology as well as immunohistochemistry techniques, and imaging analysis.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: **Unraveling the cell biology of the closest relatives of animals**

Project supervisor (principal investigator of the laboratory/group)
Name: Elena Casacuberta/Iñaki Ruiz-Trillo
eMail: elena.casacuberta@ibe.upf-csic.es/ : inaki.ruiz@ibe.upf-csic.es

Group name: MultiCellGenome Lab
Institution: Institute of Evolutionary Biology, IBE (CSIC-UPF)
Webpage of the group: https://multicellgenome.com

Main grant associated with this project: The origin of animals; A functional and biodiversity approach

Principal investigator: Elena Casacuberta /Iñaki Ruiz-Trillo
Agency: Ministerio Español de Ciencia e Innovación
Reference/ years: PID2020-120609GB-I00 2021/2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Have you ever wondered how from a unicellular organism multicellularity was evolved? How are the protists that are most closely related to animals? Any idea how researchers study emerging model organisms in the quest for evolutionary cell biology?

In our labs we are working with different protists that are phylogenetically close to animals. For three of them, the icthyosporeans *Creolimax fragantisima* and *Abeoforma whisleri*; and the corallochytrian *Corallochytrium limacisporum,* we have been developing genetic tools, from transient, to stable transfection and Crispr/Cas9. These organisms have the potential to become important models to understand the evolution of specific cell biological features, because they have different life cycles and morphologies, from the coenocytic stage of Creolimax and Corallochrytrium to an incredible diversity of shapes and stages in Abeoforma. Right now we are studying a range of different cellular behaviors and cellular mechanisms related to the evolution towards multicellularity, from movement, to cell differentiation, binary fission or coenocytic development. For pictures and videos of those taxa see: "https://www.flickr.com/people/146564503@N06/" https://www.youtube.com/user/multicellgenomeLab.

A master student would join our project to deeply study these emerging models in biology, by addressing questions about their nuclear division and their cytoskeleton understanding the transitions of their different life stages. The techniques involved in the project include basic molecular biology, cell culture, transfection, microbiology, and optical and fluorescent microscopy.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: CRISPR-Cas TO MODEL HUMAN GENETIC DISEASES IN *Caenorhabditis elegans*

Project supervisor (principal investigator of the laboratory/group)
Name: JULIAN CERON MADRIGAL
eMail: jceron@idibell.cat
Group name: Modelling human diseases in C. elegans
Institution: Bellvitge Biomedical Research Institute (IDIBELL)
Webpage of the group: www. ceronlab.com and www.idibell.cat

Main grant associated with this project:
Principal investigator: Julián Cerón Madrigal
Agency: Ministerio de Ciencia e Innovación
Reference/ years: PID2020-114986RB-I00 2020-2023(extended to 2024)
(The lab also counts with a grant to model cancer mutations in *C. elegans* until 2025, Ref WORMVUS, from Plan de Recuperación, Transformación y Resiliencia - Financiado por la Unión Europea – NextGenerationEU).

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Our lab uses the powerful genetic model C. elegans to investigate human diseases: rare diseases (Kukhtar et al, 2020) or cancer (Serrat et al, 2019). We have broad expertise in CRISPR technologies that are being applied to model human diseases (*ex. by introducing human mutations in C. elegans*). Moreover, we have an active research line on optimizing CRISPR genome editing by creating methodologies or by using distinct Cas9 enzymes (Vicencio et al, 2019; 2021). Thus, a Master's research project in our lab would include molecular biology, CRISPR, and classic genetics. The student will participate in any ongoing projects focused on modeling genetic diseases in *C. elegans* with the chance to explore innovative CRISPR methods.

Recent publications:

Mimicking of splicing-related retinitis pigmentosa mutations in C. elegans allow drug screens and identification of disease modifiers. Kukhtar D, et al. *Human Molecular Genetics* 2020 doi: 10.1093/hmg/ddz315.

CRISPR editing of *sftb-1*/SF3B1 in *Caenorhabditis elegans* allows the identification of synthetic interactions with cancer-related mutations and the chemical inhibition of splicing. Serrat X et al, *PLoS Genetics*. 2019 Oct 21;15(10):e1008464. doi: 10.1371/journal.pgen.1008464

Genome editing in animals with minimal PAM CRISPR-Cas9 enzymes. Vicencio et al, *Nature Communications.* 2022 May 12;13(1):2601. doi: 10.1038/s41467-022-30228-4.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Defining specificity traits in the class I DYRK protein kinases

Project supervisor (principal investigator of the laboratory/group)
Name: Susana de la Luna
eMail: susana.luna@crg.eu
Group name: Signaling and transcriptional regulation
Institution: Centre for Genomic Regulation
Webpage of the group: https://www.crg.eu/en/programmes-groups/de-la-luna-lab

Main grant associated with this project:
Principal investigator: Susana de la Luna
Agency: Ministerio de Ciencia e Innovación
Reference/ years: 2023-2026

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Protein kinases are central to all cellular processes in eukaryotes, and often linked to disease in humans when their activation and/or expression are altered. Our group is interested in a family of protein kinases known as DYRK (dual-specificity tyrosine-regulated kinases), whose members participate in the regulation of critical processes important for cellular viability and homeostasis. Members of the DYRK family are found in four of the five main taxa (animalia, plantae, fungi and protista), and all DYRK proteins studied to date share common structural, biochemical and functional properties with the ancestral forms represented by yeast. In mammals, there are 5 DYRK proteins (DYRK1A, DYRK1B, DYRK2, DYRK3 and DYRK4) with a highly similar kinase domain. However, very little is known on the molecular determinants defining commonalities and differences among the DYRK human kinases. Thus, although the closest paralogs DYRK1A and DYRK1B share 85% of their sequences even outside their kinase domain and are expressed mostly following the same tissue pattern, the clinical outcomes of the inactivating mutations in the corresponding genes are linked to very distinct syndromes, affecting different tissues and organs. Inactivating mutations in one DYRK1A allele have been described in patients with general growth retardation and severe primary microcephaly, defining a rare clinical syndrome, whereas missense mutations in DYRK1B in heterozygosis cause a rare form of metabolic syndrome.

The group thus aims to dissect how DYRK activities are linked to human pathology. We are particularly interested on the DYRK-associated activities that impact on the regulation of gene expression programs either directly through their recruitment to chromatin or indirectly through modulation of specific signaling pathways. Current work of the group has led to the definition of the proximity interactomes for DYRK1A and DYRK1B. Efforts are dedicated to identify docking sites in DYRK1s that could work as recruiting surfaces for different targets and evaluate their contribution as traits of specificity for these two DYRKs. We expect that this work can be used to dissect DYRK1s function in cellular processes and to foster the development of novel pharmacological approaches for these kinases.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Disentangling the molecular basis of amyotrophic lateral sclerosis using single-cell RNA sequencing and whole-transcriptome sequencing approaches

Project supervisor

Name: Oriol Dols Icardo
eMail: odols@santpau.cat
Group name: Genetics of Neurodegenerative Diseases Unit
Institution: Sant Pau Biomedical Research Institute
Webpage of the group: NA

Main grant associated with this project:

Principal investigator: Oriol Dols Icardo
Agency: Instituto de Salud Carlos III & Alzheimer's Association
Reference/ years: PI21_01395/3 years & AARF-22-924456

Brief summary of the project or current research lines of the group:

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease neuropathologically characterized by the aberrant cytoplasmic aggregation and phosphorylation of the 43-kDa transactive response DNA-binding protein (pTDP43), an RNA-binding protein, in the majority of ALS cases at postmortem evaluation (1). Beyond neurodegeneration, RNA dysfunction and neuroinflammation are key pathological features of ALS. In this context, a microglial subpopulation (Disease Associated Microglia (DAM)) has been implicated as the major regulator of neuroinflammation in ALS by our group (2). DAM express high levels of the major histocompatibility complex II class markers, which, under neurodegenerative conditions, respond to and enhance systemic inflammation, and interact with peripheral blood immune cells (PBICs) promoting their entry in the central nervous system. However, the role of PBICs has been underappreciated in ALS pathogenesis and progression (3). In this project, we will investigate the role of transcriptomic alterations (using RNA sequencing and small RNA sequencing) in 120 brain samples from ALS patients and healthy controls. In addition, for the first time in ALS, our study is focused on the identification of novel peripheral immune cell subtypes and RNA changes at the resolution of individual cells using single-cell RNA sequencing. Altogether, we will assess (through immunofluorescence, RNA scope techniques), in the brain of ALS patients, the presence, distribution and the role of the most important alterations found in PBICs and their relationship with the density of pTDP43 aggregates, glial cells and neurodegeneration. The results of this study will open new avenues to develop peripheral biomarkers and novel therapeutic strategies for ALS.

(1) Brown RH, Al-Chalabi A. Amyotrophic Lateral Sclerosis. *N Engl J Med*. 2017;377(2):162-172.

(2) Dols-Icardo O, et al. Motor cortex transcriptome reveals microglial key events in amyotrophic lateral sclerosis. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(5):e829.

(3) Prinz M, Priller J. The role of peripheral immune cells in the CNS in steady state and disease. *Nat Neurosci*. 2017;20(2):136-144.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and Life Sciences, Universitat Pompeu Fabra

Project Title: Functionalization of bacterial flagella for Biotechnology and Biomedicine.

Project supervisor (principal investigator of the laboratory/group)
Name: Ulrich Eckhard
eMail: ulrich.eckhard@ibmb.csic.es
Group name: Synthetic Structural Biology
Institution: Molecular Biology Institute of Barcelona (IBMB-CSIC)
Webpage of the group: https://www.ibmb.csic.es/en/staff-member/ulrich-eckhard/

Main grant associated with this project:
Principal investigator: Ulrich Eckhard
Agency: Ministerio de Ciencia e Innovación
Reference (years): RYC2020-029773-I (2022-2027), PID2021-128682OA (2022-2025)

Brief summary of the project or current research lines of the group:

We are seeking highly motivated students for internships and bachelor/master thesis research projects to work with us on the development of biotechnological and biological applications based on proteolytic flagellins, a recently discovered flagellin protein family with enzymatic capabilities, and nature's proof that functionalization of bacterial flagella is indeed possible. Project-specific tasks may include: molecular cloning using Golden Gate assembly, gene editing, recombinant protein expression and purification, biochemical and structural characterization, functional testing, microbial imaging, structural modelling and structure-function analysis, all under the guidance and supervision of an experienced researcher in the lab. Importantly, the lab has a strong commitment to foster a supportive environment for student training and development, and to guide them towards their next steps in their academic and/or scientific career.

About the lab: We are a recently established research team focusing on the biological impact of enzymatically active flagella, and the possibility to alter their biochemical properties for biotechnological and biomedical applications. We are located at the *Parc Científic de Barcelona*, one of the main life science research hubs in Spain, which hosts not only over 90 companies, but also major research institutes such as the Institute for Research and Biomedicine (IRB), the Institute of BioEngineering of Catalonia (IBEC), and also our institute, the IBMB-CSIC. As part of the *Structural and Molecular Biology* Department, we are in close contact with multiple high-profile research teams and have access to state-of-the-art research equipment and facilities, such as the Automated Crystallography Platform for robot-assisted protein crystallization and imaging, and have readily access to various European Synchrotrons, including ESRF in Grenoble (France), Diamond Light Source in Didcot (UK), or ALBA in Cerdanyola del Vallès. Additionally, as the lab is embedded within the highly collaborative Proteolysis Lab of Prof. Xavier Gomis-Rüth, we fully profit of a well-established and a highly productive research environment.

Candidate specifications: Motivated candidates with a keen interest in Molecular Biology, Microbiology, Biochemistry, Structural Biotechnology, and Biomedicine are encouraged to send their CV directly to Ulrich Eckhard (ulrich.eckhard@ibmb.csic.es). Fluency in English, team spirit, and good communication and problem solving skills are considered a big plus.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Pharmacological and neurophysiological profiling of novel $Ca_V2.1$ modulators to develop new therapies for Hemiplegic Migraine and related neurological disorders.

Project supervisor (principal investigator of the laboratory/group)
Name: José Manuel Fernández Fernández
eMail: jmanuel.fernandez@upf.edu
Group name: Laboratory of Molecular Physiology
Institution: Department of Medicine and Life Sciences, University Pompeu Fabra
Webpage of the group: http://www.upf.edu/fisio/

Main grant associated with this project:
Principal investigator: José Manuel Fernández Fernández
Agency: National Research Agency
Reference/ years: Call In Process

Brief summary of the project or current research lines of the group:

Human mutations in the *CACNA1A* gene (encoding the pore-forming α_{1A} subunit of the voltage-gated $Ca_V2.1$ (P/Q-type) Ca^{2+} channel) and N-hypoglycosylation induce $Ca_V2.1$ gain-of-function effects causing neuronal hyperexcitability that leads to multiple rare neurological disorders including Sporadic and Familial Hemiplegic Migraine (S/FHM), cerebellar pathologies such as congenital ataxia (CA), as well as stroke-like episodes and cerebellar syndrome associated to the most frequent form of Congenital Disorder of Glycosylation, Phosphomannomutase Deficiency (PMM2-CDG), a metabolic rare disease. Accordingly, there are pharmacological evidences suggesting that reduction of $Ca_V2.1$ activity (for example by medicinal plants) has therapeutic potential in the treatment of Hemiplegic Migraine (HM) and the relief of common migraine. At present, the $Ca_V2.1$-selective inhibitors available are peptide toxins. They are not suitable therapeutic tools due to both undesirable side effects and, as other peptides, limited utility for *in vivo* studies.
We aim to identify novel direct and indirect inhibitory modulators of the $Ca_V2.1$ channel and to check *in vitro* their capability of reversing the pathological $Ca_V2.1$ gain-of-function and subsequent neuronal hyperexcitability. For direct and selective $Ca_V2.1$ inhibition we will include in the study three novel compounds generated after chemical modifications from an existing state-dependent non-selective inhibitor of voltage-gated Ca^{2+} channels, along with sixteen commercially available small molecules selected *in silico* on basis of their expected binding to a specific region of the $Ca_V2.1$ channel and that have already shown inhibitory action on $Ca_V2.1$ in a preliminary screening. Regarding indirect inhibitory modulation of $Ca_V2.1$, we will test the pharmacologically-induced increase in the N-glycosylation pathway using inhibitors of the phosphomannose isomerase (MPI). *In vitro* studies will be done using both, cells heterologously expressing wild-type and HM/CA mutant $Ca_V2.1$ channels, as well as networks of cortical neurons in primary cultures obtained from WT and FHM-knockin (KI) mice (the latter expressing the equivalent to human $Ca_V2.1$ R192Q mutant linked to FHM).

Project Title: Tumor microenvironment and cancer invasion during epithelial tumorigenesis

Project supervisor: **Antonio García de Herreros**, Group "Epithelial to Mesenchymal Transition and Tumor Invasion", Programa de Recerca en Càncer, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Parc de Recerca Biomèdica de Barcelona, Room 298.03, agarcia@imim.es, Tel: 933160433.
Web: https://www.imim.es/programesrecerca/cancer/ubcm.html

Main grant associated with this project:
Principal investigator: Antonio García de Herreros; Ministerio de Ciencia e Innovación -Agencia Estatal de Investigación (Retos de Investigación) (ref. PID2019-104698RB-I00).

Brief summary of the project or current research lines of the group:

Our group has a long-standing interest in the study of the process of epithelial tumor invasion and its relation with epithelial-to-mesenchymal transition (EMT). Snail1 is transcriptional factor required for EMT that has been the topic of our research for many years. Besides controlling tumor invasion, Snail1 expression is required for the acquisition of chemo-resistance and for cancer stem properties. In the last years we have studied how Snail1 expression is controlled, focusing in the post-translational control by ubiquitin ligases and deubiquitinases (Lambies et al, Cancer Res 2019). We have recently characterized the control of Snail1 expression and EMT by non-canonical Wnt ligands (Villarroel et al, Cell Mol Life Sci 2020, Fuertes et al, EMBO Rep, in press).

The most recent work of the group has been focused on the relevance of Snail1 expression in the tumor microenvironment (TME). We have described that Snail1 expression is often observed in the stroma, more specifically in activated fibroblasts. Snail1 is necessary for the activation of cancer-associated fibroblasts (CAFs) by TGFb or other cytokines derived from the tumor cells. We have investigated the effect of Snail1 expression in fibroblasts on the activation by these cells on tumoral cell invasion and implantation. Our results indicate that the invasive capability of tumoral cells is markedly enhanced in the presence of CAFs, supporting the well-known effect of the TME cells on tumor development (Mestre-Farrera et al, Cancer Res 2021). Our group is also analyzing the role of Snail1 on other cells of the TME, such as endothelial cells where it is required for tumor angiogenesis (Cabrerizo et al, Theranostics, 2021). We are also studying the effect of cancer-activated adipocytes in the stimulation of CAFs and in the invasive properties of tumor cells. Finally, we are interested in the characterization of new drugs selectively affecting cells that have undergone an EMT, drugs that might be used as putative cancer therapies.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Infinite Assembly of Folded Proteins in Health and Disease.

Project supervisor (principal investigator of the laboratory/group)
Name: Hector Garcia Seisdedos
eMail: hgsbmc@ibmb.csic.es
Group name: Structural Systems Biology
Institution: IBMB-CSIC
Webpage of the group: https://www.ibmb.csic.es/en/department-of-structural-and-molecular-biology/structural-systems-biology/

Main grant associated with this project:
Principal investigator: Hector Garcia Seisdedos
Agency: Ministerio de Ciencia e Innnovacion
Reference/ years: 2022-2025

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

The cellular interior is not a mere Brownian soup of molecules; it is rather an exquisitely structured entity organized into hierarchical levels. Knowing how proteins assemble into different layers of organization, is thus fundamental to understanding the functioning of the cell.

We recently demonstrated that proteins are a few mutations, sometimes even one mutation away, to form infinite polymers –aka **supramolecular assemblies**– (Garcia-Seisdedos, *et al.* Nature 2017, Empereur-Mot, Garcia-Seisdedos, *et al.* Sci Data 2019, Garcia-Seisdedos, *et al.* Angew. Chem 2019, Garcia-Seisdedos, *et al.* PNAS 2022). They are amorphous or ordered structures resulting from the self-assembly of folded proteins.

In recent years, many studies have identified proteins that naturally (often in a condition-dependent manner, e.g. membrane-less organelles), or as a result of mutation, form supramolecular assemblies, suggesting important implications in cellular adaptation and disease.

Although it is a widespread phenomenon that is shifting the way we see the proteome organization, supramolecular assembly remains poorly understood. Its characterization will bring about important advances with implications in evolution, disease, and protein design.

The research of the lab is at the interface of Structural, Cell, and Systems Biology and aims to understand **the process by which proteins form supramolecular assemblies in the cell, as well as its role in cellular organization, adaptation, and disease.** To address these aims, we combine the power of yeast genetics and high-content microscopy with biophysical and structural techniques.

Project Title:
Molecular mechanisms of endocytic traffic in health and disease

Project supervisor
María Isabel Geli Fernández-Peñaflor
Institute for Molecular Biology of Barcelona (IBMB, CSIC)
National Research Council
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08028 Barcelona
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phone: 934020193
Web page:

Summary of current research.

Our group is interested in understanding the molecular mechanisms underlying endocytic membrane traffic in eukaryotes and in deciphering their relevance in human diseases. The endocytic pathway removes material from the cell surface in a highly regulated manner to either deliver it to degradative compartments or to other cellular organelles. Thereby, endocytic traffic spatio-temporally controls cell signalling, nutrient sensing and uptake, or cell reshaping during embryogenesis, among many other processes. Consequently, miss-function of the endocytic pathway has a major impact in a myriad of human diseases. To study endocytic traffic, we apply superresolutioni live-cell fluorescence imaging of single endocytic events, quantitative electron microscopy and *in vivo* and *in vitro* traffic assays, in *S. cerevisiae* and mammalian cells. In the recent years, we uncovered an essential role of VAP (VAMP associated Protein), ORPs (Oxysterol Binding Protein Related Protein) and type I myosins in endocytic uptake. These proteins play pivotal roles in establishing contacts between the plasma membrane and the endocplasmic reticulum, and their missfunction in humans leads to neurological and kidney diseases (Encinar del Dedo (2017) Dev Cell; Encinar del Dedo (2021) J Cell Biol). The project assigned to the students will be designed and developed in the context of this research line, trying to understand the molecular function of ER-endocytic contact sites.

J. Encinar Del Dedo, F. Z. Idrissi, I. M. Fernandez-Golbano, P. Garcia, E. Rebollo, M. K. Krzyzanowski, H. Grötsch, M. I. Geli. "ORP-Mediated ER Contact with Endocytic Sites Facilitates Actin Polymerization" (2017) ***Dev Cell****. 43:588-602.*

I. M. Fernández-Golbano, F. Z. Idrissi, J. P. Giblin, B. L. Grosshans, V. Robles, H. Grötsch, M. M. Borrás and M. I. Geli. "A cross-talk between PI(4,5)P_2 and CK2 modulates actin polymerization during endocytic uptake" (2014)* ***Dev Cell.*** *30: 746-758.*

F. Z. Idrissi, A. Blasco, A. Espinal and M. I. Geli. "Ultrastructural dynamics of proteins involved in endocytic budding" (2012) ***Proc Natl Acad Sci U S A.*** *109: E2587-94.*

H. Grötsch, J. P. Giblin, F. Z. Idrissi, I. M. Fernández-Golbano, J. R. Collette, T. M. Newpher, V. Robles, S. K. Lemmon, M. I. Geli "Calmodulin dissociation regulates Myo5 recruitment and function at endocytic sites" ***EMBO J.*** *(2010) 29: 2899-914.*

F. Z. Idrissi, H. Grötsch, I. M. Fernández-Golbano, C. Presciatto-Baschong, H. Riezman and M. I. Geli (2008) " Distinct acto/myosin-I structures associate with endocytic profiles at the plasma membrane" ***J. Cell Biol.*** *180: 1219-32.*

B. Schmelzl, and M. I. Geli (2002) "An efficient genetic screen in mammalian cultured cells" ***EMBO Rep.*** *3, 683-87.*

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Evaluation of pantranscriptome RNA-Seq mapping tools.

Project supervisor (principal investigator of the laboratory/group)
Name: Roderic Guigó
eMail: roderic.guigo@crg.eu
Group name: Guigó Lab (Computational Biology of RNA Processing)
Institution: Centre for Genomic Regulation
Webpage of the group: https://www.crg.eu/roderic_guigo

Main grant associated with this project:
Principal investigator: Roderic Guigó
Agency: CRG
Reference/ years: Internal budget

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

RNA sequencing (RNA-Seq) has revolutionized the field of transcriptomics by providing a high-throughput and accurate method to measure gene expression levels and to identify novel transcripts. Fast and accurate alignment of RNA-Seq data is a critical step for many downstream analyses. However, due to the non-contiguous transcript structure, ever-increasing read lengths, and constantly increasing throughput of the sequencing technologies, aligning RNA-Seq data accurately is still a challenging and still unsolved problem. Current RNA-Seq aligners suffer from high mapping error rates, low mapping speed, and mapping biases. Pangenomics is emerging as a powerful computational paradigm in bioinformatics. In this project, we propose to evaluate pantranscriptome RNA-Seq mapping tools, which use a population-level transcriptomic reference to mitigate reference bias and facilitate analyses that were challenging with previous reference-based methods.

In this project, we will evaluate the performance of different transcriptome RNA-Seq mapping tools by using simulated and real RNA-Seq datasets. We will compare the accuracy, speed, and mapping biases of pantranscriptome RNA-Seq mapping tools with existing reference-based RNA-Seq aligners such as VG toolkit (RPVG), STAR, HISAT2, and TopHat2. We will also assess the effect of using a population-level transcriptomic reference on downstream analyses such as gene expression quantification and differential gene expression analysis. We will use performance metrics such as mapping accuracy, sensitivity, specificity, precision, recall, F1-score, mapping speed, and memory usage to compare different tools.

In summary, this project pursues the following main objectives:

- Evaluate the performance of different pantranscriptome RNA-Seq mapping tools.
- Compare the accuracy, speed, and mapping biases of pantranscriptome RNA-Seq mapping tools with existing reference-based RNA-Seq aligners.
- Assess the effect of using a population-level transcriptomic reference on downstream analyses and the limitations of current state-of-the-art tools.
- Develop a suitable analysis pipeline for the RNA-Seq mapping and anlaysis of real datasets.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Pipeline for genome annotation across the eukaryotic phylogeny.

Project supervisor (principal investigator of the laboratory/group)
Name: Roderic Guigó
eMail: roderic.guigo@crg.eu
Group name: Guigó Lab (Computational Biology of RNA Processing)
Institution: Centre for Genomic Regulation
Webpage of the group: https://www.crg.eu/roderic_guigo

Main grant associated with this project:
Principal investigator: Roderic Guigó
Agency: CRG
Reference/ years: Internal budget

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Understanding Earth's biodiversity and responsibly administrating its resources is among the top scientific and social challenges of this century. The Earth BioGenome Project (EBP) aims to sequence, catalog and characterize the genomes of all of Earth's eukaryotic biodiversity over a period of 10 years (https://www.pnas.org/content/115/17/4325). The outcomes of the EBP will inform a broad range of major issues facing humankind, such as the impact of climate change on biodiversity, the conservation of endangered species and ecosystems, and the preservation and enhancement of ecosystem services. It will contribute to our understanding of biology, ecology and evolution, and will facilitate advances in agriculture, medicine and in the industries based on life: it will, among others, help to discover new medicinal resources for human health, enhance control of pandemics, to identify new genetic variants for improving agriculture, and to discover novel biomaterials and new energy sources, among others.

The value of the genome sequence depends largely on the precise identification genes. The aim of the research project is to develop a gene annotation pipeline that produces high quality gene annotations that can be efficiently scaled to more than one million species. Our group has a long-standing interest in gene annotation. Roderic Guigo developed one of the first computational methods to predict genes in genomic sequences, which has been widely used to annotate genomes during the past years. On the other hand, we are part of GENCODE, which aims to produce the reference annotation of the human genome. Within GENCODE we have developed experimental protocols to efficiently produced full-lengh RNA sequences.

Within the framework of this program, there are three possible specific projects
1. Methods for genome annotation based on long read RNAseq (experimental/computational)

2. Methods for selenoprotein prediction and annotation (bioinformatics)

3. Prediction of long non coding RNAs using Machine learning approaches (ie. structured decoding from learning embedding (strongly computational)

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:

Immunological and non-immunological mechanisms involved in the etiopathogenesis of chronic urticaria

Project supervisor

Name: Ramon Gimeno
eMail: ramon.gimeno@upf.edu
Group name: Immunity and Infection
Institution: IMIM-Hospital del Mar
Webpage of the group:

Main grant associated with this project:

Principal investigator: Ramon Gimeno / Ana María Gimenez-Arnau
Agency: ISCIII
Reference/ years: REF PI22/00108 2023-2025

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Our laboratory has a deep interest in investigating how immune cells react to environmental stimuli. We study the mechanisms that are set in motion during development to facilitate the acquisition of effector competencies. We are also interested in deciphering the impact of therapeutic inhibition of these effector molecules (mainly, but not exclusively, cytokines) on immune responses to both natural infection and vaccination. Finally, and from a clinical point of view, we are developing different approaches (cellular and epigenetic studies) to stratify patients suffering from inflammatory diseases with the ultimate goal of optimizing their treatment. Our current efforts in this direction are aimed at distinguishing the relative contribution of immunological and non-immunological mechanisms involved in the etiopathogenesis of chronic urticaria. Flow cytometry, cell culture and different epigenetic approaches will be used regularly along the project.

Call for project proposals, master in Biomedical Research practicum, 2024, UPF

Project Title: ***Molecular analysis of proteins of biomedical interest***.

Project supervisor (besides the name, title and position, please include the relevant contact information: e-mail, phone postal address, and webpage).

F. Xavier Gomis-Rüth
Proteolysis Laboratory
Department of Structural Biology
Barcelona Science Parc, Helix Building
C/ Baldiri Reixac,15-21
08028 Barcelona
Tel. 934020186 / Fax. 934034979 / e-mail. xgrcri@ibmb.csic.es /
https://www.ibmb.csic.es/proteolysis

Main grant associated with this project: PID19-107725RG-00I
Principal investigator: F. Xavier Gomis-Rüth
Agency: State Research Agency (AEI), Ministry of Science and Innovation
Reference/ years: 2020-2023

Summary of project summary or current research lines (less than 300 words).

The research group is centered on the study of proteins involved in host-microbiome interactions, including microbial virulence factors and antibiotic resistance determinants, as well as potential therapeutic targets. Such molecules include proteins of mammals, protozoans and prokaryotes, as well as their interacting partners. The student would participate in the cloning, overexpression and purification of such protein targets under the supervision of an experienced member of the lab. In addition, or alternatively, she/he could participate in the biochemical, biophysical, functional, and structural characterization. The candidate should have strong marks and a very hard-working capacity, dedication and lab skills. This work could be continued within the frame of a Ph.D. thesis.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: A novel molecular recorder to investigate the basis of stem cell ageing

Project supervisor (principal investigator of the laboratory/group)
Name: Irene Hernando Herraez
eMail: irene.herraez@babraham.ac.uk / ihernandoherraez@gmail.com

Group name: Epigenetic regulation and single cell dynamics
Institution: IBMB (located at PCB)
Webpage of the group: Under construction

Main grant associated with this project:
Principal investigator: Irene Hernando Herraez
Agency: Agencia Estatal de Investigación
Reference/ years: Pending/ 2023-2026

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

The cells in our body divide constantly throughout life. As they divide, the transmission of epigenetic and transcriptional states establishes a form of cellular memory, where daughter cells retain very similar properties to their ancestors. This allows distinct gene expression patterns to persist in different cell types despite a common genotype. But why does this form of cellular memory change over time? Ageing is an extraordinary complex process and our understanding is still very limited. My main interest is understanding how the accumulation of errors in the epigenome can lead to the degradation of cell identity, ultimately contributing to age-related dysfunction and disease such as cancer.

In this project by developing a novel cellular barcoding approach, you will investigate the fundamental basis of cellular heterogeny during muscle stem cell ageing. You will not only investigate one of the greatest mysteries in biology, but also gain transferable valuable skills in cutting edge techniques including CRISPR barcoding and single-cell multiomics.

Call for project proposals, master in Biomedical Research practicum, 2023, UPF

Project Title: Mitochondrial metabolism, reactive oxygen species and aging

Project supervisor:

Elena Hidalgo / Montse Vega
elena.hidalgo@upf.edu
Oxidative Stress and Cell Cycle Group
Universitat Pompeu Fabra
www.upf.edu/osccg

Main grant associated with this project:

Principal investigator: Elena Hidalgo
Agency: MICINN (Spain)
Reference/ years: 2022-2025

Brief summary of the project or current research lines of the group

Our group is interested in studying the components and molecular mechanisms controlling cellular fitness, in particular during aging. Thus, the master project proposal will be related to:

(i) study cellular processes linked to healthy aging;
(ii) selection of fission yeast strains with altered lifespan;
(iii) characterization of the selected mutants, especially regarding mitochondrial homeostasis and ROS production.

We use the fission yeast ***Schizosaccharomyces pombe*** as a model system. To obtain more information about the laboratory and about our research interests, please consult our group's web page (www.upf.edu/osccg). Some recent publications include:

Salat-Canela et al. 2023. TiCB 33:124.
Vega et al. 2022. BMC Biol. 20:160.
Salat-Canela et al. 2021. Cell Rep. 37: 109951.
Corral-Ramos et al. 2021. Autophagy 23:1-16.
Boronat et al. 2020. iScience 23:101725
Cabrera et al. 2020. Cell Rep. 30:2430-2443
Carmona et al. 2019. Nat. Commun. 10:4526.
García-Santamarina et al. 2014. Nature Protocols 9:1131.
Calvo, I.A. et al. 2013. Cell Reports 5:1413.
Zuin, A. et al. 2010. EMBO J. 29:981.

Call for project proposals, master in Biomedical Research practicum, 2024, Universitat Pompeu Fabra

Project Title: Imaging stem cell dynamics in live embryos: molecular signature of self-protection

Project supervisor (principal investigator of the laboratory/group)
Name: Esteban Hoijman
eMail: ehoijman@idibell.cat
Group name: Embryonic Cell Bioimaging
Institution: Program of Regenerative Medicine, IDIBELL
Webpage of the group: www.embryobioimaging.com

Main grant associated with this project:
Principal investigator: Esteban Hoijman
Agency: Spanish Ministry of Science and Innovation
Reference/ years: 2021-2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos)

Early human embryos usually contain defective cells, considered a main cause of developmental failures. In our group we study how early embryos deal with these cells by activating self-healing responses. We recently discovered a phagocytic program able to detect and remove defective stem cells (Nature 2021, www.nature.com/articles/s41586-021-03200-3). Using quantitative imaging of live zebrafish and mammalian embryos, we study single cells dynamics during tissue repair. In this project we want to elucidate the molecular signature of this protective program of the embryo, with the long-term aim of improving the survival of human embryos.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Decoding relapse in leukemia to identify new therapeutic targets and prognosis biomarkers.

Project supervisor
- Name: Biola M. Javierre
- eMail: bmjavierre@carrerasresearch.org
- Group name: 3D Chromatin Organization Group
- Institution: Josep Carreras Leukaemia Research Institute (IJC)
- Webpage of the group:
https://www.JavierreLab.com
https://www.carrerasresearch.org/es/organizaci%C3%B3n-3d-de-la-cromatina_78766;
@BiolaMJavierre; @JavierreLab

Main grant associated with this project:
- Associated Grant 1:
Principal investigator: Biola M. Javierre
Agency: European Hematology Association (EHA)
Reference/ years: EHA4823998 (2021-2024)

- Associated Grant 2:
Principal investigator: Biola M. Javierre
Agency: Fundación Científica de la Asociación Española Contra el Cáncer
Reference/ years: LABAE21981JAVI (2022-2025)

Brief summary of the project or current research lines of the group:

Relapse is a major challenge in B-cell acute lymphoblastic leukemia (B-ALL) since 50% of the adult patients relapse and 90% of those do not overcome the disease. While the causes of relapse are not completely understood, there is evidence suggesting that noncoding mutations and the tumor microenvironment might play important roles in disease persistence. Are these factors key to understand relapse? Can these factors be used to better predict patient outcome and design new therapies?
In this project we will use a multi-omics approach to decipher the cellular and molecular basis of relapse in B-other ALL, a B-ALL heterogeneous subtype characterized by high rate of unexpected relapse and mortality. We will first use single-cell multi-omics to characterized the cell types in the tumor microenvironment and the subpopulations of leukemic cells at diagnosis, remission and relapse. The comparison of relapsed versus non-relapsed patients will allow us to discover new biomarkers to better predict relapse. This data, in combination with gene regulatory data of healthy B cell differentiation recently generated by us, will pinpoint regulatory elements (e.g., enhancers) and their target genes that, when mutated or epimutated, promote malignant transformation and/or relapse. Finally, focused on these regulatory elements and using EC-seq, a new method that we are developing, we will perform the first comprehensive screening of noncoding germline and somatic mutations and epimutations underlying B-ALL. It will allow us to disclose new transcriptional alterations in genes and pathways potentially implicated in malignant transformation and relapse, which could be novel therapeutic targets and biomarkers.
In summary, this interdisciplinary project will provide unprecedented insights into our understanding of B-ALL and relapse. Besides, it will allow to predict which patients will unexpectedly relapse and propose new therapeutic strategies to ultimately avoid relapse and mortality.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: **Role of human histone H1 variants in cell proliferation, gene expression and cancer progression**

Project supervisor (principal investigator of the laboratory)
Name: Albert Jordan
Mail: ajvbmc@ibmb.csic.es
Group name: Chromatin regulation of human and viral gene expression
Institution: Institut de Biologia Molecular Barcelona IBMB-CSIC, Dept. Molecular Genomics

Webpage of the group: https://www.ibmb.csic.es/en/department-of-structural-and-molecular-biology/chromatin-regulation-of-human-and-viral-gene-expression/#lab-presentation

Main grant associated with this project:
Principal investigator: Albert Jordan
Agency: Ministerio de Ciencia e Innovación – Plan Nacional BFU
Reference/ years: PID2020-112783GB-C21 (2021-24)

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

We focus our research on the control of gene expression in human cells by chromatin organization, components and modifications. The degree of compaction of chromatin affecting a gene promoter dictates accessibility to transcription factors and RNA polymerase, and many chromatin modifying enzyme families act to overcome difficulties imposed by chromatin. DNA repeats and satellites immersed in heterochromatin are also regulated by these factors.

We investigate the role and specificity of histone H1 variants in chromatin organization and gene expression control. By RNA interference of the different human H1 variants we have found that they have different involvement in cellular processes such as cell cycle progression and gene expression. We have also described a differential role of H1 variants in pluripotency and differentiation. Currently, we are investigating the occupancy of H1 variants genome-wide by ChIP-seq (NGS) and the consequences of altering H1 levels on chromatin organization (ATAC-seq, DNA methylation, chromosome conformation-HiC, etc), with an extensive use of Genomics and Bioinformatics. Additionally, we are performing proteomics of H1 variant specific protein complexes in chromatin and nucleoplasm.

More recently we have found that depletion of multiple H1 variants in breast cancer cells induces the interferon response as a consequence of derepression of ERVs and satellites. We will investigate whether this also occurs in melanoma cells and this could help immunotherapy to fight cancer cells.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:
Bacterial cellulose an emerging polymer with exciting applications

Project supervisor (principal investigator of the laboratory/group)
Name: Anna Laromaine Sagué
eMail: alaromaine@icmab.es
Group name:Group of Nanoparticles and nanocomposites
Institution: ICMAB-CSIC, campus UAB
Webpage of the group: nn.icmab.es

Main grant associated with this project:
Principal investigator: Anna Roig
Agency: National
Reference/ years: PID2021-122645OB-I00/ 3 years

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Bacterial nanocellulose (BNC) is produced by bacteria strains like K. xylinus. BNC is obtained as highly pure cellulose and its properties such as high water holding capacity and porosity, tunable morphology, mechanical strength, and biocompatibility make it a unique material. As a result, BNC has attracted interest in the paper and food industry, biotechnology, photonics, and optoelectronics.
The group of Nanoparticles and Nanocomposites we have experience in the biosynthesis of bacterial cellulose, and its modifications with a variety of compounds, ranging from nanoparticles to polymers.
We look for a candidate who is eager to learn from biosynthesis and modification of BC, and its characterization and exploit the potential of the BC and BC composites to identify them as innovative applications.
Student will work with a highly interdisciplinary and international team, and would learn techniques from chemistry-physics and biology.
Group of Nanoparticles and Nanocomposites
https://nn.icmab.es @NNgroupICMAB

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:
Evaluation of development effects on C. elegans upon exposure to novel drugs

Project supervisor (principal investigator of the laboratory/group)
Name: Anna Laromaine Sagué
eMail: alaromaine@icmab.es
Group name:Group of Nanoparticles and nanocomposites
Institution: ICMAB-CSIC, campus UAB
Webpage of the group: nn.icmab.es

Main grant associated with this project:
Principal investigator: Anna Laromaine
Agency:EU
Reference/ years: NEXTGEM / 3 years

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

We use the 1 mm-long nematode Caenorhabditis elegans as an animal model to test the toxicity of the materials and drugs. Between 60-80% of the C. elegans genome has human homologous genes, and most of the metabolic pathways are also conserved. Transparency, short life cycle, and minimal maintenance and growth requirements stand out among all the advantages of using this worm. The use of simple non-mammalian model organisms minimizes the cost associated with in vivo experiments in the early stages of discovery and yields highly informative results such as survival rate, growth effects, reproduction toxicity, and changes in metabolism. Moreover, we can study how the materials are transformed by characterizing them after passing through the organism. Polymers synthesized by living organisms, biopolymers, are used for drug and food complementation without any evidence of being toxic, but their size at the nanoscale can affect the toxicity and their properties. Additionally, it has been observed that the oral administration of biopolymers produced changes in the motility, absorption, and metabolism of the intestine, key for treating gastrointestinal diseases. In this work, we want to evaluate how drugs affect the reproduction rate of the animals and if some formulations cross the membrane of the egg affecting their development.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:
HARNESSING INFLAMMATORY PATHWAYS IN ANTITUMOR IMMUNE INTERVENTION

Project supervisor (principal investigator of the laboratory)
Name: Cristina Lopez-Rodriguez
Mail: cristina.lopez-rodriguez@upf.edu; jose.aramburu@upf.edu
Group name: GENIMMUNE
Institution: Universitat Pompeu Fabra, Department of Medicine and Life Sciences
Webpage of the group: https://www.upf.edu/web/genimmune
https://www.upf.edu/web/cristina-lopez-rodriguez

Main grant associated with this project:
Principal investigator: Cristina Lopez-Rodriguez and Jose Aramburu
Agency: Plan Estatal I+D+i (Ministerio de Ciencia e Innovación, FEDER, EU); Worldwide Cancer Research United Kigdon
Reference/ years: PID2021-128721OB-I00 (2022-2025) WWCR UK: 20-0144 (2020-2023, extended)

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Alterations in immune functions not only impair our organism defenses to pathogens but also underlie diseases such as cancer, neurodegenerative, cardiovascular and metabolic disorders. We focus our work on transcription regulators that control innate and adaptive immunity in different scenarios, such as inflammation, transplant rejection, tumor progression and viral infection. By uncovering circuits that tune different immune cell functions, our work can guide innovative approaches that improve antitumor immunotherapy and anti-pathogen defense.

We offer a master position in a project based on our recent identification of a unique transcription mechanism that, while promoting other inflammatory responses, limits type I interferon (IFN-I) expression to control antiviral responses and preserve hematopoietic stem cell (HSC) function (Huerga Encabo et al. 2020 J Exp Med). Natural IFN-I-repressive mechanisms are necessary since an excess of IFN-I can compromise key systems such as the regeneration of hematopoietic stem cells and certain antimicrobial defenses. On the other hand, IFN-I can induce cancer cell senescence and antitumor immunity, so enhancing these responses could be applied to improve anticancer immunotherapy.

In this project, we will apply our experience with tumor mouse models, gene-edited mice, and cutting-edge molecular and cellular biology techniques, to identify new mechanisms that can push the boundaries of IFN-I and other inflammatory responses, to boost antitumor immunity by enhancing tumor detection by immune cells and also by promoting cancer cell senescence.

Leading recent publications of the group:

Lunazzi et al., 2021 Journal of Immunology
Huerga Encabo et al., 2020 Journal of Experimental Medicine
Aramburu and López-Rodríguez, 2019 Frontiers in Immunology
Buxadé et al., 2018 Journal of Experimental Medicine
Tellechea et al., 2018 Journal of Immunology
Aramburu et al., 2014 Science Signaling
Berga-Bolaños et al., 2013 Proc Natl Acad Sci USA

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: **Microtubule organization and its role in tissue formation during neurodevelopment**

Project supervisor (principal investigator of the laboratory/group)
Name: Jens Luders
eMail: jens.luders@irbbarcelona.org
Group name: Microtubule organization in cell proliferation and differentiation
Institution: IRB Barcelona
Webpage of the group:

https://www.irbbarcelona.org/en/research/microtubule-organization-cell-proliferation-and-differentiation#jens-luders
http://microtubul.es

Main grant associated with this project:
Principal investigator: Jens Luders
Agency: MICINN
Reference/ years: PID2021-127603NB-I00 2022-2025

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

The master thesis will be performed within the project described below:

Microtubules mediate various essential cellular processes such as intracellular transport or segregation of chromosomes during cell division. To carry out these functions they need to be organized as ordered arrays. While many studies focus on studying the microtubule network during mitosis, it is the interphase microtubule network that directly impacts on cell shape and interaction with neighboring cells, and thus tissue formation and integrity. However, the mechanisms underlying interphase microtubule organization in different cell types remain poorly understood.
In this project we ask how highly polarized neural progenitors of the neuroepithelium organize their microtubule network. This question is not only relevant to normal brain development, but also in the context of various neurodevelopmental disorders caused by defects in the microtubule cytoskeleton. We hypothesize that microtubule organization in neural progenitors involves both centrosomal and non-centrosomal mechanisms. To address this, we will (i) characterize candidate factors for generating interphase microtubules, and (ii) probe the roles of these factors in highly polarized neural progenitors including their contribution to cell and tissue integrity. For this we will employ genome CRISPR/Cas9-based editing and advanced microscopic imaging of polarized progenitors in fixed and live neuroepithelium-like neural rosettes obtained by differentiation of human induced pluripotent stem cells (hiPSCs) in vitro.
This pioneering project will explore fundamental questions at the interface of cell biology and development, namely how non-mitotic microtubule arrays are established and how they contribute to tissue formation and integrity.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Study of the molecular changes in the nervous system in animal models of chronic pain

Project supervisor (principal investigator of the laboratory/group)

Name: Rafael Maldonado (Principal Investigator)
Beltrán Álvarez Pérez
eMail: rafael.maldonado@upf.edu
beltran.alvarez@upf.edu
Group name: Laboratory of Neuropharmacology (NeuroPhar)
Institution: Department of Medicine and Life Sciences
Webpage of the group: https://www.upf.edu/es/web/neurophar

Main grant associated with this project:

Principal investigator: Rafael Maldonado
Agency: European Comission
Reference/ years: 848099, 2020-2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Chronic pain is a clinical entity that causes great suffering and impairment. The great variability, the difficulty to correctly diagnose the type of pain and the absence of an effective treatment, turns chronic pain into a huge health concern. To study the behavioural and molecular changes that cause this condition, animal models are great research tools and have been used to better characterize different illnesses. In the NeuroPhar research group, different animal models of pain are used to further describe different pain conditions (endometriosis, fibromyalgia, chronic peripheral and central pain, etc.) and to investigate new pharmacological and therapeutical targets. Nowadays, we are focusing on the characterization of the function of different receptors and molecules in these pathologies. For this reason, this master's project will be focused on the behavioural characterization of animal models of pain, and the molecular work with different nervous system samples from mice models, the characterization of the molecular profile of these samples, and the explanation of how these molecular changes correlate with the actual behavioural observed effects.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Neurobiological mechanisms involved in the development of food addiction

Project supervisor (principal investigator of the laboratory/group)
Name: Rafael Maldonado and Elena Martín
eMail: elena.martin@upf.edu
Group name: NeuroPharm
Institution: UPF
Webpage of the group: Web: http://www.upf.edu/neurophar/

Main grant associated with this project:
Principal investigator: Rafael Maldonado
Agency: La Caixa
Reference/ years: 2022-2025

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Food addiction is linked to obesity and eating disorders and is characterized by losing behavioral control and compulsive food intake. Here, we will use a sophisticated food addiction mouse model. In this model, we measure 3 addiction criteria for diagnosing the disease and 4 phenotypic traits suggested as predisposing factors related to vulnerability to addiction. Also, it is possible to evaluate the extended food addiction mouse model with mice genetically modified. We target the endocannabinoid system with specific mutations in the CB1 receptor. Notably, the novelty of this protocol is the adaptation of this food addiction model to a short protocol to evaluate genetic manipulations targeting specific brain circuitries by using a chemogenetic approach that could promote the rapid development of this addictive behavior. These adaptations lead to a short food addiction mouse protocol, in which mice follow the same behavioral procedure of the early period in the long food addiction protocol with some variations due to the surgical viral vector injection. There is no paradigm in mice allowing us to study the combination of such a robust behavioral approach that allows uncovering the neurobiology of food addiction at the brain circuit level . We can study using this protocol if modifying the excitability of a specific brain network confers resilience or vulnerability to developing food addiction. Understanding these neurobiological mechanisms is expected to help find novel and efficient interventions to battle food addiction.

References

Domingo-Rodriguez, L., Ruiz de Azua, I., Dominguez, E., Senabre, E., Serra, I., Kummer, S., Navandar, M., Baddenhausen, S., Hofmann, C., Andero, R., Gerber, S., Navarrete, M., Dierssen, M., Lutz, B., Martín-García, E., & Maldonado, R. (2020). A specific prelimbic-nucleus accumbens pathway controls resilience versus vulnerability to food addiction. *Nature Communications*, *11*(1), 1–16. https://doi.org/10.1038/s41467-020-14458-y

Martín-García, E., Domingo-Rodriguez, L., & Maldonado, R. (2020). An Operant Conditioning Model Combined with a Chemogenetic Approach to Study the Neurobiology of Food Addiction in Mice. *Bio-Protocol*, *10*(19), 1–23. https://doi.org/10.21769/bioprotoc.3777

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Characterization of non-genetic mechanisms of drug resistance

Project supervisor (principal investigator of the laboratory/group)
Name: Dr Oskar Marin-Bejar
eMail: marinoskar@gmail.com
Group name: Transcriptional regulation in cancer and non-genetic mechanism of drug resistance
Institution: Institut Germans Trias I Pujol
Webpage of the group: https://www.germanstrias.org/en/research/cancer/

Main grant associated with this project:
Principal investigator: Oskar Marin Bejar
Agency: MINECO
Reference/ years: 3

Brief summary of the project or current research lines of the group:

It has been described that about 40% of resistant melanoma isolated from patients treated with MAPK inhibitors could not be accounted for by any validated mutational mechanism (Hugo et al., 2015). **How prevalent non-genetic resistance is in patients and whether it can be targeted to prevent disease relapse are key unanswered questions**. Therefore, in my previous work (Marin-Bejar et al, 2021), I elucidated this aspect using melanoma patient samples and patient-derived xenograft (PDX) mouse models to study the evolution of non-genetic acquired resistance. However, the **mechanism of how the persister cells switch from a pseudo-quiescent to a proliferative state** remains still unknown. In contrast with genetic resistance, not only the clonal evolution of one cell, which acquires genetic advantage, is the responsible of drug resistance. But several persister cells will become drug evaders through transcriptional adaptation. Moreover, the possibility of a cancer cell harboring **intrinsic "epigenetic" plasticity** that permits random activation of alternate gene-regulatory networks needs to be elucidated, this adaptation capacity will give advantage for the **acquisition of specific phenotypic properties in the presence of drug pressure** (Flavahan et al., 2017).

The aim of the project is to model drug resistance *in vitro* to study persister cell fate.

Some cancer cells can enter a reversible drug-tolerant persister state in response to treatment. Those cells comprise a rare, transiently resistant and proliferative persister population; to study them specifically, melanoma cells will be infected with a high complexity expressed barcode lentiviral library for simultaneous tracing of each cell's clonal origin, trajectories, proliferative rate and transcriptional states.

The methodologies use for the achievement of this goal are the following:

- Cell culture of melanoma primary cells.
- Lentivirus production to introduce a sophisticated barcoding system, **Watermelon**, to trace the persister cells.
- Fluorescence-activated Cell Sorting (FACS) to isolate the Watermelon-cells.
- Cell viability assay to establish the BRAF/MEKi IC90 of melanoma cells.
- The cell growth will be monitored using an automated cell tracker to acquire and analyse images of living cells.
- Transcriptomic profiling of persister and drug evader cells.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Bioinformatics of selenocysteine, the 21st amino acid

Project supervisor (principal investigator of the laboratory/group)

Name:	Marco Mariotti
eMail:	marco.mariotti@ub.edu
Group name:	Comparative Genomics and Recoding lab
Institution:	Universitat de Barcelona
Webpage of the group:	https://www.mariottigenomicslab.com/

Main grant associated with this project:

Principal investigator:	Marco Mariotti
Agency:	Spanish Ministry of Science, Innovation and Universities
Reference/ years:	Proyectos de I+D+I PID2020-115122GA-I00 2021/2024

Brief summary of the project or current research lines of the group:

Our lab studies the mechanisms of gene expression and protein synthesis. We focus in particular on "recoding" events, i.e. programmed exceptions to the genetic code. A remarkable example of recoding is selenocysteine: this special amino acid is present in human and many other species, but it is not among the canonical 20 residues of the genetic code. Instead, it is encoded by the UGA codon, which is normally a stop, but it is recoded to selenocysteine through a highly regulated "readthrough" mechanism occurring only in specific mRNAs. Selenocysteine is found in the catalytic site of specialized enzymes known as selenoproteins. Here, it provides enhanced biochemical properties, typically for improved redox catalysis.

Human selenoprotein genes have several known essential functions, most notably in redox homeostasis. Due to the functions of selenoproteins, selenium is an essential trace element for human and other vertebrates. Intriguingly, many cancer types heavily rely on selenoprotein function, which is being explored as liability for therapy.

From a comparative genomics perspective, the genes encoding for selenoproteins are often missed or wrongly annotated in genomes, since gene annotation programs only consider the canonical role of UGA as stop.

We have several active projects on selenoproteins which the student may contribute to, such as:

- Analysis of selenoprotein function and regulation in cancer, investigating patterns of gene expression of selenoproteins and other related proteins across cancer types and cell lines

- Development of automated approaches to recognize and correctly annotate selenoprotein genes in nucleotide sequences.

- Evolutionary analysis of selenoprotein evolution, tracing how the selenocysteine utilization pathways changed throughout lineages.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Building Human Spinal Cord Organoids to study human-specific developmental features and Neuro_Developmental Disorders.

Project supervisor (principal investigator of the laboratory/group)
Name: Elisa Martí
eMail: emgbmc@ibmb.csic.es
Group name: Development of the Spinal Cord in health and disease
Institution: Instituto de Biología Molecular de Barcelona (IBMB-CSIC)
Webpage of the group: https://www.ibmb.csic.es/en/department-of-cells-andtissues/development-of-spinal-cord-in-health-and-disease/

Main grant associated with this project:
Principal investigator: Elisa Martí
Agency: MCINN
Reference/ years: PID2019-104134GB-I00

Brief summary of the project or current research lines of the group
Human neural development occurs mainly in embryonic and foetal stages therefore, studies on how the human brain is built during development have been limited due to the little access to these tissues. Today, neural organoids derived from human pluripotent stem cells not only recapitulate major developmental processes during morphogenesis and neurogenesis, but also exhibit human-specific features, thus providing an unprecedented opportunity to study human neurodevelopment in health and disease. Our team has recently developed human Spinal Cord Organoids, with specific features of anterior and posterior spinal cord regions. Currently, we are exploiting these technological developments to understand (1) the collective tissue dynamics required for building the secondary neural tube and the possible accidents in the process of de novo lumen formation that might result in Spina Bifida Oculta, (2) the cellular events related to centrosome biology that control the balance between the specialized modes of divisions that neural progenitor cells undergo, and how malfunction of the centrosome might result in primary Microcephaly, and (3) the signalling events and cell responses generating cell diversity in the early developing human Spinal Cord.

Relevant recent papers form the lab
1.- Elena Gonzalez-Gobartt, José Blanco-Ameijeiras, Susana Usieto, Guillaume Allio, Bertrand Bénazéraf and Elisa Martí (2021) Cell intercalation driven by SMAD3 underlies secondary neural tube formation Developmental Cell 56, 1147–1163 April 19, 2021 10.1016/j.devcel.2021.03.023 https://pubmed.ncbi.nlm.nih.gov/33878300/
2._ Murielle Saade, Diego S Ferrero, José Blanco-Ameijeiras, Elena Gonzalez-Gobartt, Victor M Ruiz-Arroyo, Elena Martínez-Sáez, Santiago Ramón y Cajal, Nuria Verdaguer and Elisa Martí (2020) Multimerization of Zika Virus-NS5 causes a ciliopathy and forces premature neurogenesis. Cell Stem Cell 2020 Oct 27;S1934-5909(20)30496-3. doi: 10.1016/j.stem.2020.10.002. https://pubmed.ncbi.nlm.nih.gov/33147489/
3.- Murielle Saade, Elena Gonzalez-Gobartt, Rene Escalona, Susana Usieto and Elisa Martí (2017) Shhmediated centrosomal recruitment of PKA promotes symmetric proliferative neuroepithelial cell division. Nature Cell Biology 19, 493–503 (2017) doi:10.1038/ncb3512 http://www.nature.com/ncb/journal/v19/n5/abs/ncb3512.html

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Coordination of the remodelling of the peripheral nervous system and musculature during metamorphosis in *Drosophila*

Project supervisor

Name: Enrique Martin-Blanco
eMail: embbmc@ibmb.csic.es
Group name: Signalling events controlling cell migration during morphogenesis
Institution: Instituto de Biologia Molecular de Barcelona
Webpage of the group: https://www.ibmb.csic.es/en/department-of-cells-and-tissues/signalling-events-controlling-cell-migration-during-morphogenesis/

Main grant associated with this project:

Principal investigator: Enrique Martin-Blanco
Agency: Ministerio de Ciencia e Innovacion
Reference/ years: PID2020-116273GB-I00 / 01/09/2021-31/08/2024

Brief summary of the project or current research lines of the group

Our laboratory studies the processes controlling morphogenesis employing Drosophila, with a special emphasis on the biomechanics of coordinated events. The current interest of the lab is centred in two main issues: the mechanisms ruling the coordination of the morphogenesis of nerves, muscles and epidermis for rebuilding the fly abdomen during metamorphosis; and the mechanical control of the development and morphogenesis of the embryonic Central Nervous System (CNS). These analyses demand quantitative parametric studies of cellular and physiological functions not achievable without a combination of imaging, experimental genetics, cell behavior analysis, nanotechnology and mathematical modelling.

Coordination at the structural and functional level between nerves and muscles during development and adult life is a phenomenon highly conserved during evolution. Yet, very little is known on how nerves and muscles coordinate their morphogenesis and which are the mechanisms implementing their crosstalk. *Drosophila melanogaster* undergoes metamorphosis, a process in which tissues and cells rearrange to fulfil adult physiological and behavioral requirements. In this project, we will focus on the coordination of the remodelling of the peripheral motoneural system and the replacement of the musculature at this time, aiming to discover factors playing key roles in this process.

1) Screening of specific motoneurons clusters for their presence on the innervation of newborn and larval dorsal abdominal muscles.
2) identifying and characterizing axonal-related molecules that may play an important role in neural remodelling (test the role of specific adhesion-related molecules)
3) Determine if the epithelial landscape directs or influences neuronal remodelling and adult muscular pattern during metamorphosis.
4) Analysis of the instructive role of the developing dorsal adult muscles on the remodelling of the neural pattern.
5) Characterization of the EGFR signalling cascade role in the coordination of muscular and neural development.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:

Uncovering the epigenetic component of Intellectual Disability: role of the PHF2/8 histone demethylase maintaining neural progenitor expansion

Project supervisor (principal investigator of the laboratory/group)
Name: Marian Martínez-Balbás
eMail: mmbbmc@ibmb.csic.es
Group name: Molecular signaling and chromatin
Institution: CSIC
Webpage of the group: https://www.ibmb.csic.es/en/department-of-structural-and-molecular-biology/molecular-signaling-and-chromatin/

Main grant associated with this project:
Principal investigator:
Agency: Ministerio de Ciencia e Innovación
Reference/ years: PID2021-125862NB-I00

Brief summary of the project or current research lines of the group :

Recently a high number of genes have been identified that link intellectual disability to disrupted epigenetic mechanisms, one of this is the histone demethylase PHF2/8 whose mutations have been found in patients with X-linked intellectual disability (XLID) and cleft lip/palate and autism. These conditions are neurodevelopmental diseases. During neural development, a critical process is generating the right number of neural progenitors that will give raise the total number of cells in the nervous system. Increasing evidence suggests that metabolites can regulate progenitor proliferation, self-renewal and differentiation. However, it remains unknown the epigenetic factors that rewire endogenous metabolic programs in neural progenitor cells.

Recent results from our laboratory suggest that PHF2/8 is involved in the regulation of metabolic pathways that are crucial to maintain progenitor proliferation, and doing so, generation of the proper number of neurons. Thus, PHF2/8 mutations could cause epigenetic alterations that lead to deficient metabolic control in neural progenitors and neurons. We are investigating this hypothesis.

To do that we are using next generation sequence experiments, biochemical and functional assays. Moreover, we are modeling human neurogenesis in vitro using brain organoids to study the contribution of PHF2/8 mutations to XLID. The proposed training plan will be included in this project.

In general, the student will learn to handle neural stem cells and to perform transcriptomic and functional experiments with them. In particular, the student will address the following objectives, using the techniques described below:

1.- To determine the metabolic alterations associated to the PHF8's lack of function.

2.- To analyse the molecular mechanisms underlying the metabolic changes. The student will identify the genes responsible for the metabolic changes using the RNA.seq and ATAC.seq previously performed in the laboratory. Once identified, he/she will analyze the chromatin landscape by ChIP analysis of the epigenetic modifications and transcription factors.

3.- To investigate the functional consequences of these metabolic changes in proliferation, self-renewal and morphology by immunostaining assays using specific markers.

4.- Finally, the student will contribute to set up the conditions to growth the stem cells control and mutated in PHF8/2 into brain organoids.

Call for project proposals, master in Biomedical Research practicum, 2023, Universitat Pompeu Fabra

Project Title: The metabolic origin of cellular senescence

Project supervisor (principal investigator of the laboratory/group)
Name: Mate Maus
eMail: matemaus@vhio.net
Group name: Aging and Cancer group
Institution: Vall d´Hebron Institute of Oncology (VHIO)
Webpage of the group: https://vhio.net/pf/ageing-and-cancer-group/

Main grant associated with this project:
Principal investigator: Mate Maus, PhD
Agency: Startup Funding to the Lab
Reference/ years: 5 years

Brief summary of the project or current research lines of the group

Aging is the best predictor of cancer. This connection had been partly attributed to the age-associated accumulation of senescent cells, and to their secretion of cytokines that can promote tumorigenesis in neighbouring cells. Senescent cells originate from proliferating cells that encountered irreparable DNA-damage, and as a result halted their cell cycle. Understanding what drives the protumorigenic activity of senescent cells could expose new targets to combat cancer in the elderly.

We have recently found that senescent cells activate a program of mysterious nature, that causes them to accumulate large amounts of iron. Shockingly, we found that removing this iron from senescent cells was completely able to switch off their secretome. This Master work will aim to understand the mechanisms and oncological relevance of senescence associated iron accumulation.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Revolutionizing Multiple Myeloma Treatment: Internship Opportunity in Machine Learning and Single-Cell Analysis.

Project supervisor (principal investigator of the laboratory/group)
Name: Elisabetta Mereu
eMail: emereu@carrerasresearch.org
Group name: Cellular Systems Genomics
Institution: Josep Carreras Leukemia Research Institute
Webpage of the group: Cellular Systems Genomics Lab, Mereu's lab.

Main grant associated with this project:
Principal investigator: Elisabetta Mereu
Agency: Spanish Ministry for Science and Innovation
Reference/ years: 2023-2026

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

The Cellular Systems Genomics Group at the Josep Carreras Leukemia Research Institute is led by Dr. Elisabetta Mereu, and focuses on the cellular and molecular characterization of complex tissues in both healthy and diseased states. The group is particularly interested in studying the role of inflammation in cancers and age-related dysfunctions. We adopt a multidisciplinary approach, utilizing single-cell multiomics, image-based spatial analysis, and machine learning tools to advance the clinical management of patients and identify new targets for non-invasive diagnosis, monitoring, and treatment. We are composed of 4 PhD students and 2 research assistants with diverse backgrounds and have access to human samples through a network of local clinicians.

Join us in the fight against Multiple Myeloma! As an intern in our group, you will have the opportunity to contribute to a comprehensive research program aimed at improving patient outcomes and revolutionizing MM treatment. Our focus is on identifying patients at high risk for relapse and tailoring their treatment accordingly. By generating a longitudinal single-cell map of T cell states in MM patients, we will gain a deeper understanding of the immune response to MM and its relation to disease progression. Additionally, you will be involved in developing a cutting-edge Machine Learning tool, IMPACT, that predicts the evolution of the disease over time using temporal and simultaneous profiling of single-cell RNA-seq and TCR-seq data. This research has the potential to lead to a more personalized approach to MM treatment and improve patient outcomes. If you are passionate about using cutting-edge technology to make a difference in the lives of others, this is the opportunity for you! Apply now and join our team in the quest for a cure.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Apaf-1 role in angioimmunoblastic T cell lymphoma appearance. Study of the molecular origin of the disease.

Project supervisor (principal investigator of the laboratory/group)
Name: Laura Mondragón Martínez
eMail: lmondragon@carrerasresearch.org
Group name: T cell lymphoma group
Institution: Josep Carreras Leukaemia Research Institute
Webpage of the group: https://www.carrerasresearch.org/en/t-cell-lymphoma_177482

Main grant associated with this project:
Principal investigator: Laura Mondragón Martínez
Agency: Agencia estatal de investigación - «Proyectos I+D+i» 2019 - Modalidades «Retos Investigación» y «Generación de Conocimiento»
Reference/ years: PID2019-104508RJ-I00 - IMPLICACION DE LA PROTEINA APAF-1 EN EL DESARROLLO DE LINFOMAS DE TIPO T. VALIDACION DE NUEVAS TERAPIAS BASADAS EN EL USO DE NANOMEDICINAS. 01/09/2021-31/08/2024.

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Our research group has two main lines of research which are: a) the study of the molecular mechanisms leading to a type of T cell lymphoma, the angioimmunoblastic T cell lymphoma (AITL) and b) the development of therapeutic strategies based on nanoparticles and blocking antibodies that could help to eliminate this disease.

To pursue our objectives we make use of several animal models lacking Apaf-1 expression that mimic AITL. We follow two different strategies: a) we regularly develop thymocytes maturation studies to find possible defects that could predispose cells to tumour appearance since birth and, b) we develop several in vivo immune response activation studies in adult Apaf-1 deficient mice to determine possible imbalance in T cell activation and shut down of the immune response. Our final objective is to determine the molecular origin of AITL and to provide new therapeutic targets for its treatment and cure.

Once the therapeutic targets are established, we validate them making use of blocking antibodies or, when possible, make use of nanoparticles containing molecules able to modulate the activity of these therapeutic targets for therapeutic gain. In vivo validation of the therapeutic strategies is developed by means of NSG mice injected either with mice tumour cells or human patients' samples (PDXs).

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Study of the role of mechanoreceptors in amyloid toxicity in Alzheimer's disease

Project supervisor (principal investigator of the laboratory/group)
Name: Francisco J. Muñoz López
eMail: paco.munoz@upf.edu
Group name: Aging Brain and Neurodegeneration
Institution: MELIS-Universitat Pompeu Fabra
Webpage of the group: https://www.upf.edu/web/lmp/aging-and-neurodegeneration

Main grant associated with this project:
Principal investigator: Francisco J. Muñoz
Agency: Spanish Science and Innovation Ministry
Reference/ years: AEI/PID2020-117691RB-I00/AEI/10.13039/501100011033

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):
Alzheimer's disease (AD) is due to the extracellular aggregation of the amyloid ß-peptide (Aß) into oligomers and fibrils, which are synaptotoxic leading finally to cell death. There is not specific treatments that can cure, prevent of retard the disease.
The hypothesis proposes that oligomeric Aß (oAß) directly or indirectly (by oxidative stress) affect to the physiological function of mechanoreceptors that will have deleterious effects in the growth and maintenance of the synaptic spines, and a rise in intracellular calcium.
The objectives is the characterization of the effect of the oAß binding and/or the oxidative stress induced by oAß on TRPM7 and Piezo1 functions in the synaptic spines. The mechanical forces that drives dendrite growth are related to mechanoreception. In particular, spine growth and the maintenance of the functional shape of the spines are under the control of mechanoreceptors that regulates actin cytoskeleton. Therefore, we will study the effect of oAß on these receptors and how it will affect to synaptic plasticity and the existing spines, and we will also address the study of their role in the dysregulation of intracellular calcium.

The biological materials will be cell lines, neuronal primary cultures from mice and hiPSCs. Results will be validated in brain samples from APPswe/PSEN1dE9 transgenic mice and AD patients and no demented individuals.

The methodology includes molecular biology of proteins and mRNA, gene overexpression and silencing, siRNAs, confocal microscopy, spectrofluorometry, calcium image, path-clamp, flow cytometry and in silico studies.

The expected results of our project are the identification of new molecules involved in Aß pathophysiology that would be considered as therapeutic targets for the treatment of AD.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Molecular mechanisms of signal integration in tumorigenesis

Project supervisor (principal investigator of the laboratory/group)
Name: Angel R. Nebreda
eMail: angel.nebreda@irbbarcelona.org
Group name: Signaling and Cell Cycle
Institution: IRB Barcelona
Webpage of the group: http://www.irbbarcelona.org/en/research/signalling-and-cell-cycle-laboratory

Main grant associated with this project:
Principal investigator: Angel R. Nebreda
Agency: MINISTERIO DE CIENCIA E INNOVACIÓN
Reference/ years: PID2019-109521RB-I00 (2020-2023), PID2022-136646OB-I00 (Solicitado)

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

We are investigating molecular mechanisms of tumorigenesis, especially regarding how kinases in general, and p38 MAPK in particular, regulate tumor development, metastasis generation, and the response to cancer therapies. We use a combination of biochemical approaches and studies in cancer cell lines, together with genetically modified mice, which allow the inactivation of this pathway in a tissue-specific manner. We are very interested in the identification of therapeutic opportunities based on the modulation of p38 MAPK or other kinases, either alone or in combination with other therapeutic agents.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Genetics of histone methyltransferase expression in C. elegans

Project supervisor (principal investigator of the laboratory/group)
Name: Marcos Francisco Perez Browne
eMail: mpbbmc@ibmb.csic.es
Group name: Epigenetics and Metabolism
Institution: CSIC Barcelona Molecular Biology Institute (CSIC-IBMB)
Webpage of the group: *under construction*

Main grant associated with this project:
Principal investigator: Marcos Francisco Perez Browne
Agency: Mineco
Reference/ years: Ramon y Cajal RYC2021-034496-I (5 years)

+ Plan nacional pending evaluation

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Covalent modifications of chromatin such as DNA or histone methylation, often referred to as epigenetics, are understood to have a critical role in encoding information to direct gene expression programs in eukaryotic cells.

A different and revolutionary perspective recognises that chromatin is so abundant in the cell that these epigenetic processes can also be understood as metabolic processes, which are regulated by metabolism and affect metabolism in turn by consuming large quantities of intermediate metabolites.

The roundworm Caenorhabditis elegans is a popular model organism which has been at the forefront of major discoveries in genetics, epigenetics and development for decades. In C. elegans, many histone methyltransferases (HMTs) with strongly differing roles in controlling transcription are nonetheless tightly co-regulated.

We will conduct genetic screens by RNA interference (RNAi) in C. elegans to understand how this regulation occurs, and in response to which metabolic or signalling pathways. The student will learn molecular biology techniques, such as DNA extraction and quantitative PCR, fluorescence microscopy and quantitative imaging analysis, in addition to C. elegans maintenance and genetics techniques.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Understanding stress adaptation

Project supervisor (principal investigator of the laboratory/group)
Name: Francesc Posas
Mail: francesc.posas@irbbarcelona.org; francesc.posas@upf.edu
Group name: Cell Signaling Group
Institution: IRB Barcelona
Webpage of the group: https://www.irbbarcelona.org/en/research/cell-signaling

Main grant associated with this project:
Principal investigator: Francesc Posas
Agency: Spanish Government
Reference/ years: ANALISIS DE LAS ACTIVIDADES REQUERIDAS PARA LA CORRECTA ADAPTACION Y SUPERVIVENCIA CELULAR AL ESTRES (PID2021-124723NB-C21). Ministerio de Ciencia, Innovación y Universidades. 2022-2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

We aim to unravel how cells detect and respond to environmental changes. We focus our studies on the characterisation of stress signal transduction pathways, especially those regulated by MAP kinases of the Hog1/p38 family, also known as the stress-activated MAP kinases (SAPKs). Proper adaptation to stress involves the modulation of several basic aspects of cell biology, among them the cell cycle and gene expression. Using *S. cerevisiae* budding yeast as a model organism, as well as higher eukaryotic cells, we are dissecting the molecular mechanisms underlying cell response to changes in the extracellular environment and characterising the adaptive responses required for cell survival. Based on our knowledge of signal transduction and using synthetic biology, we also seek to modify cell behaviour to reprogram cell response to specific inputs/stimuli.

Research lines:

- SAPK signalling: Using quantitative data in single cells and mathematical modelling, together with mutational analyses, we study the basic signalling properties of stress-responsive MAP pathways and how to alter them.

- SAPK targets: Using proteomics, biochemistry and genetics, our main goal is to identify new targets for SAPKs and thus widen our understanding of cellular adaptation to stress. This information is expected to facilitate the characterisation of the bases of adaptation in eukaryotes.

- Cell cycle control: SAPKs act in several phases of the cell cycle to allow prompt response to extracellular stimuli and the maintenance of cell integrity. We are uncovering the mechanisms by which Hog1 and p38 SAPKs regulate the cell cycle.

- Regulation of mRNA biogenesis: SAPKs control critical steps of mRNA biogenesis and are thus key regulators of stress-responsive gene expression. Our main aim is to determine the contribution of multiple factors to overall gene expression in response to stress. We are also using genome-wide CRISPR screening to identify essential genes for stress adaptation.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:
Recycling cell routines to regulate cell fate in the vertebrate hindbrain

Project supervisor (principal investigator of the laboratory/group)
Name: Cristina Pujades (co-supervisor Gonzalo Ortiz-Alvarez)
eMail: cristina.pujades@upf.edu
Group name: Neurodevelopmental Dynamics
Institution: MELIS-UPF
Webpage of the group: https://pujadeslab.upf.edu/

Main grant associated with this project:
Principal investigator: Cristina Pujades
Agency: MICIN/AEI
Reference/ years: PID2021-123261NB-I00, 2022–2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

During the early development of the hindbrain, the posterior and most evolutionary-conserved part of the brain, neural progenitor cells (NPCs) undergo symmetric proliferative divisions, generating two new NPCs, to increase the organ in size. Later, upon the onset of neurogenesis, new neurons are born through asymmetric and symmetric neurogenic divisions. The correct balance of these three cell modes of division gives the hindbrain its right size, composition and function.

Asymmetrical divisions, where one daughter cell becomes a NPC and the other a neuron, are particularly interesting because either the cell or the environment instruct distinct fates on spatially and temporally associated sister cells. The mechanisms by which this happens are yet not completely understood. Many studies suggest that the differential inheritance of proteins, DNA or cellular macrostructures can instruct these differences in cell fate. Interestingly, also cellular cargoes that are deleterious, such as poly-ubiquitinated proteins targeted for degradation, have been shown to be asymmetrically inherited during NPC divisions, in mammalian models.

Our aim is to elucidate whether poly-ubiquitinated proteins can be “recycled” by the cell as instructors of cell fate in the zebrafish hindbrain, and whether this depends on distinct NPC populations and/or time. For that, we will combine genomic edition, high-resolution 4D imaging, and gene expression and cell cycle dynamics analyses. The answers to these questions will provide much-needed knowledge about hindbrain morphogenesis mechanisms, which could be similar in other tissues.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title:

Project supervisor (principal investigator of the laboratory/group)
Name: Patricia Robledo
eMail: probledo@imim.es
Group name: Integrative Pharmacology and Systems Neurosciences
Institution: Instituto Hospital del Mar de Investigaciones Médicas (IMIM)
Web page of the group:
https://www.imim.cat/programesrecerca/neurociencies/grfh/probledo/

Main grant associated with this project:
Principal investigator: Patricia Robledo
Agency: Instituto de Salud Carlos III (FIS)
Reference/ years: 3

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Despite the efforts made in research, the biological processes underlying major depressive disorder (MDD) are still unknown, and there are no biomarkers that identify different subtypes of depression in women. Thus, the objective of this project is the identification of male foetal microchimerism (FM) in the olfactory neuroepithelium (ON) as a differential biomarker of subtypes of female depression. For this, a translational approach will be applied with studies in humans and animal models. First, Y chromosome levels in ON cells and blood will be identified and quantified by qPCR and digital PCR in women diagnosed with MDD and postpartum depression with male offspring, and in samples from control women. The levels of the Y chromosome in ON cells and in the blood will be associated with the severity of the depressive disorder, mother-child attachment, stress levels during pregnancy, and demographic, clinical, previous course, and disease evolution variables. In order to establish a correlation with the presence of male FM in the ON and in the brain, the levels of the Y chromosome will be quantified in the dorsolateral prefrontal cortex of women diagnosed with MDD who died by suicide and compared with those of control women. Finally, the Y chromosome will be identified and quantified in different brain structures of female mice with male offspring subjected to a stress protocol during pregnancy, and will be correlated with depressive-like and maternal attachment behaviour.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Novel multifunctional natural-polymer and nanoparticles hybrids for tissue regeneration

Project supervisor (principal investigator of the laboratory/group)
Name: Anna Roig
eMail: roig@icmab.es
Group name: Nanoparticles and Nanocomposites Group
Institution: Institut de Ciència de Materials de Barcelona del Consejo Superior de Investigaciones Científicas (ICMAB-CSIC)
Webpage of the group: nn.icmab.es

Main grant associated with this project:
Principal investigator: Anna Roig/Pablo Guardia
Agency: Ministerio de Ciencia e Innovación:
Reference/ years: PID2021-122645OB-I00 / Sept 2022 – August 2026

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Tissue engineering and regeneration medicine (TERM) are fast-evolving medical fields demanding the development of novel materials for our aging society. Therefore, natural polymers and nanocomposites with improved surfaces, response activities, and tuned properties are pushing the current state of the art. The objective of the M.Sc. project is to design natural hydrogels and NPs systems displaying a variety of shapes, topographies, and porosities encompassing features such as biocompatibility, bio integrability in different parts of the body (internally or externally), stimuli responsiveness or programmed biodegradation profiles while being mechanically compliant. The candidate will explore the synthesis of bacterial cellulose-natural polymer hybrids. The student will learn various techniques from physics, chemistry, and biology.

Related publications of this topic: 1. Roig-Sanchez S., Fernández-Sánchez C., Laromaine A., and Roig A. Bio and soft-imprinting lithography on bacterial cellulose films Materials Today Chemistry, 21, 100535, (2021). DOI: 10.1016/j.mtchem.2021.100535Mat. 2. Anton-Sales I., Roig-Sanchez, S., Sánchez-Guisado, M. J., Laromaine, A., and Roig, A. Bacterial nanocellulose and titania hybrids: cytocompatible and cryopreservable cell carriers. ACS Biomaterials Science and Engineering, 6 (9), 4893 - 4902, (2020). DOI: 10.1021/acsbiomaterials.0c00492 3. Roig-Sanchez S., Jungstedt E., Anton-Sales I., Malaspina D.C., Faraudo J., Berglund L.A., Laromaine A., and Roig A. Nanocellulose films with multiple functional nanoparticles in confined spatial distribution Nanoscale Horizons, 4 (3), pp. 634 - 641, (2019). DOI: 10.1039/c8nh00310f.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Encapsulation of mRNA in polymeric capsules

Project supervisor (principal investigator of the laboratory/group)
Name: Anna Roig
eMail: roig@icmab.es
Group name: Nanoparticles and Nanocomposites Group
Institution: Institut de Ciència de Materials de Barcelona del Consejo Superior de Investigaciones Científicas (ICMAB-CSIC)
Webpage of the group: nn.icmab.es

Main grant associated with this project:
Principal investigador: Anna Roig/Antonio Artigas (Parc Taulí)
Agency: XIX Concurso Nacional Ayudas Fundación Ramon Areces
Reference/ years: Although the project ended in Nov 2023, the collaboration ICMAB-Parc Taulí is continuing, and two Ph.D. thesis are working on the project

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

A worldwide health emergency concerns respiratory diseases, and despite recent advances, it is still challenging for many drugs to be distributed throughout the lungs, specifically to the lower respiratory tract. We have performed an in vivo study showing that the polymeric nanoparticles synthesized in our laboratory were retained in all lung lobules after 1 h of being intratracheally instilled and accumulated in lung macrophages after 24 h, making those nanocarriers suitable as a pulmonary immunomodulatory delivery system [1]. The M.Sc. candidate will work hand in hand with a Ph.D. student in the encapsulation of mRNA within the polymeric nanocarriers, studying the loading efficiency and the pharmacokinetics profile of this formulation. The candidate will also interact with the medical group to assess the biological and therapeutically profiles of the nanocarriers.

Reference: Fluorescent PLGA Nanocarriers for Pulmonary Administration: Influence of the Surface Charge, A. Areny-Balaguero, W. Mekseriwattana, M. Camprubí-Rimblas, A. Stephany, A. Roldan, A. Solé-Porta, A. Artigas*, D. Closa*, A. Roig*, Pharmaceutics 14(7), 1447, 2022

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: The PLK1/NEK9/NEK6/7 signaling axis in G2 and early mitosis

Project supervisor (principal investigator of the laboratory/group)
Name: Joan Roig Amorós
eMail: joan.roig@ibmb.csic.es
Group name: Cell Cycle and Signaling
Institution: Institut de Biologia Molecular de Barcelona IBMB-CSIC
Webpage of the group: https://www.ibmb.csic.es/en/department-of-cells-and-tissues/cell-cycle-and-signaling/

Main grant associated with this project:
Principal investigator: Joan Roig
Agency: Plan Nacional de I+D, Ministerio de Ciencia e Innovación, Spain
Reference/ years: PID2021-127045NB-I00, 2022-2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Our group is interested in understanding how G2 and early mitosis are controlled through phosphorylation. We focus our research on the roles of the signaling axis formed by the protein kinase PLK1 and its downstream partners NEK9, NEK6 and NEK7, three related NIMA-family kinases that are activated at the centrosomes and we have shown to be central for the control of centrosome separation and maturation during mitotic entry (Bertran *et al.* (2011) EMBO J. **30**: 2634-2647; Sdelci *et al.* (2012) Curr. Biol. **22**: 1516-1523; Eibes *et al.* (2018) Curr. Biol. **28**: 121-129.e4); Gallisà-Suñé, N. et al. (2021). *BioRxiv*. 2021.11.04.467245).

Failure to properly duplicate, mature or separate the centrosomes result in abnormal mitosis, aberrant chromosome segregation and aneuploidy, a major cause of developmental defects and abortions and one of the hallmarks of cancer cells. Using engineered animal models and genetically modified cell lines produced through CRISPR-Cas9 technology plus RNAi, the project will involve characterizing novel functions of PLK1 and NEK9/NEK/7 in G2 and early M, and seek to understand how malfunction of these kinases may result in abnormal chromosome segregation and the onset of aneuploidy. We will relate our observations with clinical data with the aim of assessing the possible involvement of the studied kinases in the process of cell transformation and the apparition of cancer as well as the onset of developmental abnormalities.

We are additionally interested in understanding the roles of the NEKs in the organization and functioning of the primary cilia, a cellular structure also organized by the centrosome that has important signaling functions in development and organogenesis as well as during tissue maintenance. A project tackling this could also be considered.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: 1q21.1 Neurodevelopmental Disorders: In Search for the Biological Bases of the Disease (NeuroHuq21)

Project supervisor (principal investigator of the laboratory/group)
Name: Murielle Saade
eMail: msabmc@ibmb.csic.es
Group name: A new vision of centrosome-cilia in normal and pathological neural development
Institution: Instituto de Biología Molecular de Barcelona (IBMB-CSIC)
Webpage of the group: https://www.ibmb.csic.es/en/department-of-cells-and-tissues/a-newvision-of-centrosome-cilia-in-normal-and-pathological-neural-development/#lab-presentation

Main grant associated with this project:
Principal investigator: Murielle Saade
Agency: Jerome Lejeune Foundation
Reference/ years: GRT-2022A-2105

Brief summary of the project or current research lines of the group

Genetic dosage imbalances in the distal region of chromosome 1q21 lead to abnormalities in head size and mental pathologies. In a complex and unknown context of incomplete penetrance and heterogeneous expressivity, children born with deletions in 1q21.1 exhibit clinical features, including microcephaly and schizophrenia, while the 1q21.1 reciprocal duplications have been associated with macrocephaly and autism spectrum disorder. In fact, the 1q21 region contains a disproportionate number of genes that are 'human-specific' (HS) and that have arisen by evolutionary genetic mutations known as segmental duplications in the last million years. Recent discoveries have revealed an enrichment of 1q21 HS genes expression in neural precursor cells with a potential link with the centrosome/cilia axis. The centrosome is a non-membranous cellular organelle, involved in key functions during central nervous system (CNS) development, where it acts to regulate processes such as; cell division, cilia formation, and cell migration. While many mutations in centrosome/cilium-associated proteins lead to diseases, often predominantly affecting the brain, the basis for this specificity is in most cases not known. Combining the chick embryo neural tube as a basic in vivo experimental model of neurodevelopment with human derived 3D neural organoids in vitro model generated from healthy and patients induced pluripotent stem cells, we will 1/dissect the cellular mechanisms associated with selected 1q21 HS genes at the centrosome/cilium, 2/Interrogate the contribution of selected 1q21 HS genes in CNS growth and 3/understand the impact on cellular mechanisms behind the genetic aberration in this neurological disease. My previous seminal contributions and current work in the field of centrosome/cilia signaling in neural development, provide me with the unique scientific background and leadership capacities, to successfully study the biological bases underlying the key role of neural-specific centrosome/cilium proteins in the correct growth of human CNS development and acquisition of cognitive abilities. As an additional fundamental benefit, this work will provide a full landscape of the pathophysiological mechanisms of the poorly explored 1q21.1 syndrome.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Effects of circulating extracellular vesicles on pancreatic islets during obesity

Project supervisor (principal investigator of the laboratory/group)
Name: Joan-Marc Servitja Duque
eMail: servitja@recerca.clinic.cat
Group name: Pathogenesis and Prevention of Diabetes
Institution: Fundació de Recerca Clínic Barcelona-Institut d'Investigacions Biomèdiques August Pi i Sunyer (FRCB-IDIBAPS)
Webpage of the group: https://www.clinicbarcelona.org/en/idibaps/research-areas/liver-digestive-system-and-metabolism/pathogenesis-and-prevention-of-diabetes

Main grant associated with this project:
Principal investigator: Joan-Marc Servitja Duque
Agency: European Foundation for the Study of Diabetes (EFSD)
Reference/ years: EFSD/Boehringer Ingelheim European Research Programme (2 years, Jan 2023-Jan 2025)

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

One of the main lines of our group is to understand the mechanisms underlying the progression towards type 2 diabetes (T2D), which is crucial for the development of new therapeutics to treat this disease. Obesity-induced insulin resistance together with pancreatic beta-cell dysfunction lead to the onset of T2D. Compelling evidence indicates that extracellular vesicles (EVs) such as exosomes mediate crosstalk between distant organs by transferring small RNAs that exert major effects on glucose homeostasis and insulin resistance in the context of obesity. The objective of this project is to understand how circulating EVs and their small RNA cargo regulate the pancreatic islets at different stages of obesity. To achieve this goal, we will profile small RNAs (microRNAs, tRNAs and tRNA-derived small RNAs) contained in circulating EVs and evaluate how circulating EVs and specific small RNAs affect the pancreatic islets at different stages of obesity progression. This study will allow the student to acquire great experience on metabolism, organ crosstalk and molecular biology.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Genetic and molecular characterization of myeloid malignancies

Project supervisor (principal investigator of the laboratory/group)
Name: Francesc Solé
eMail: fsole@carrerasresearch.org
Group name: MDS group
Institution: Josep Carreras Lekaemia Research Institute (IJC)
Webpage of the group: https://www.carrerasresearch.org/ca/Myelodysplastic_Syndromes

Main grant associated with this project:
Principal investigator: Francesc Solé
Agency: Instituto de Salud Carlos III
Reference/ years: ISCIII PI 20/000531 (3 years)

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Myelodysplastic Syndrome (MDS) is an hematological malignancy characterized by ineffective hematopoiesis and increased risk of progression to Acute Myeloid Leukemia (AML). Risk factors such as chemotherapy and/or radiotherapy for primary tumor treatment compose a future risk of developing the so-called therapy related myeloid neoplasms (TRMN). However, only few genetic studies regarding the primary tumor etiology and the molecular pathways involved in secondary tumor progression has been described. Even more, although clonal hematopoiesis of indeterminate potential (CHIP) has been associated with the risk of developing TRMN, genetic predisposition might also explain the development of a secondary MDS (TRMN-like). Thus, a proposed series of TRMN patients will be studied at the germline level, but also the genetic-dependant key molecular drivers to compare at the genetic level with TRMN and MDS scenarios. We also propose to evaluate the prevalence of genetic predisposition to MDS (gMDS) in order to explore the pathogenic mechanisms that trigger different germline-dependant MDS scenarios.

Call for project proposals
Master in Biomedical Research practicum, 2024
Department of Medicine and life Sciences, Universitat Pompeu Fabra

Project Title: Investigating the role of disturbed timing in the microbiota – gut – brain axis in the development of Alzheimer's Disease

Project supervisor (principal investigator of the laboratory/group)
Name: Patrick-Simon Welz
eMail: pwelz@imim.es
Group name: Intercellular Communication in Cancer and Ageing
Institution: Institut Hospital del Mar d'Investigacions Mèdiques (IMIM)
Webpage of the group:
https://www.imim.es/programesrecerca/cancer/en_intercellular_communication.html

Main grant associated with this project:
Principal investigator: Patrick-Simon Welz
Agency: Fundación BBVA
Reference/ years: Becas Leonardo (Perdiendo el ritmo: comunicación circadiana huésped-microbiota en la enfermedad de Alzheimer)/ 2022-2024

Brief summary of the project or current research lines of the group (please do not include pictures or logos and do not exceed this page):

Alzheimer's Disease (AD), despite being known as a neurodegenerative disease, also alters systemic physiology. This is particularly true for signalling along the microbiota – gut – brain axis. For example, AD patients present with microbial dysbiosis and the altered intestinal microbiome seems to contribute to disease development. Additionally, intestinal inflammation is linked to the development of AD. Importantly, circadian rhythms, which are daily rhythmic processes on the behavioural level, such as the sleep-wake or feeding-fasting cycle, or on the molecular level, e.g. the activity of the immune system or the regulation of metabolic processes, are disturbed in AD. However, it has not been determined whether loss of circadian rhythmicity along the microbiota – gut – brain axis might impact on AD development.
In this project, we will analyse whether circadian rhythmicity is altered on the molecular level along the microbiota – gut – brain axis in a mouse model of AD, and we will determine how this might impact on disease development. Techniques that will be acquired throughout this project include mouse genetics and mouse colony administration, microbiome sequencing and analysis, histopathology and immunohistochemistry techniques, microscopy and imaging analysis, gene expression studies by qPCR, as well as metabolomics. It will also be possible to participate in behavioural studies with this AD mouse model, which will be conducted in collaboration with the laboratory of Dr. Arnau Busquets Garcia.