Master in Biomedical Research

2021-2022

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.

“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, 2022, UPF

Project Title: Antiprions: structural mutants against neurodegenerative diseases

Project supervisor:

Name: Martí Aldea
Mail: mambmc@ibmb.csic.es
Group name: Spatial control of cell cycle entry
Institution: Institut de Biologia Molecular de Barcelona, CSIC
Webpage of the group: www.ibmb.csic.es/groups/spatial-control-of-cell-cycle-entry

Main grant associated with this project:
Principal investigator: Martí Aldea
Agency: MICINN
Reference/ years: PID2019-109638GB-I00, 2020-2023

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

Prions and amyloid prion-like aggregates have been directly implicated in more than 20 human diseases, among them neurodegenerative pathologies such as Alzheimer's, Parkinson's, and Huntington's diseases. Prion proteins are self-propagating and transmissible protein isoforms that accumulate as large structure-driven aggregates, and it is generally accepted that prion accumulation in the human brain is a direct cause of neuronal degeneration. However, appropriate therapeutic approaches and effective treatments are largely lacking, and efforts to prevent or decrease the rate of prion aggregation with peptides have produced very limited results. Here we hypothesize that, similarly to the opposing twins Prometheus and Epimetheus, antiprions could originate from prion domains as quasi-twin structures that (1) still bind with high efficiency to prion aggregates but (2) do not transmit the pathological fold to newly recruited monomers, thus preventing prion aggregate growth. Giving support to this hypothesis, prion misfolding and aggregation takes place in successive steps of conformational change. However, the structural details of these transitions are largely unknown, making impossible the post hoc design of mutants based on predicted structural properties. For this reason, our proposal is grounded in a non-biased approach, and plans to use human prion sequences (Aβ42 and αSyn) as initials seeds to perform (1) an unprecedented, extensive and highly sensitive random-mutagenesis based screen designed to generate and test more than ten million independent mutant peptides as antiprion factors, and (2) a comprehensive functional survey of the isolated antiprion peptides by their ability to counteract aggregation of human prions and their concomitant pathological effects in neurons.

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

Main grant associated with this project:
Principal investigator: Jose Aramburu and Cristina López-Rodríguez
Agency: Plan Estatal I+D+i 2018 European Union FEDER; Fundació la Marató de TV3
Reference/ years: RTI2018-095902-B-I00 (2019-22); FMTV3: 20161930 (2018-21)

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 influence 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 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. 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, 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:

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, 2022, UPF

Project Title: Cell cycle control: elaborating an integrative map of DNA synthesis regulators and tumour progression.

Project supervisor (principal investigator of the laboratory)
Name: José Ayté
Mail: 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: 2019-2021

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

We are ultimately interested in deciphering the mechanisms that control cell cycle progression. Inactivation of the Retinoblastoma protein (RB) leads to unregulated cell cycle progression promoting cell growth, genomic instability and aneuploidy, hallmarks of tumor progression. RB activity is achieved through binding the E2F family of transcription factors. It is well known that a tumor process is very complex, accumulating secondary mutations that eliminate the brakes to the cell cycle. Even though many regulators of the RB-E2F are known, an integrative view of all the regulatory events controlling the G1/S transition is required to anticipate putative interventions able to block proliferative processes.

The candidate will characterize the regulation of the yeast MBF complex (functional homolog of human RB-E2F). The regulated activity of this complex is also essential for the G1/S transition since cells with hyperactive MBF have genomic instability. The candidate will perform 2 whole-genomic screens searching for global regulators of MBF. We have developed a reporter strain in the laboratory that measures MBF activity in vivo as an YFP/RFP output, either on FACS or on an automated fluorescence microscope platform. This reporter strain will be introduced in a commercial yeast KO deletion library. These screenings will allow the creation of a complete map with all the MBF regulators and, by extrapolation, will establish the nodes that regulate the RB pathway.

Required student background: A high motivation towards a scientific career in projects related to basic research, which is the research that is carried out in our group, is a must. Also, a solid background in Genetics, Cell Biology and Molecular Biology is a requirement to carry out this project. Since the project includes bar-code sequencing of pools of KO strains, previous experience with ultra-sequencing will be appreciated. Similarly, previous work with yeast and/or cell cycle will be a plus.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Epigenetic regulation of chromatin structure and function

Project supervisor (principal investigator of the laboratory)
Name: Ferran Azorín
Mail: ferran.azorin@irbbarcelona.org
Group name: Chromatin structure and function
Institution: IRB Barcelona and IBMB, CSIC
Webpage of the group: https://www.irbbarcelona.org/en/research/chromatin-structure-and-function

Main grant associated with this project:
Principal investigator: Ferran Azorín
Agency: Agencia Española de Investigación. Ministerio de Ciencia, Innovación y Universidades
Reference/ years: PGC2018-094538-B-I00 / 3 years

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

Genomic functions are regulated epigenetically. Changes in chromatin structure have a fundamental contribution to the regulation of genomic processes, from gene expression to chromosome segregation and the maintenance of genome integrity and stability. Consequently, epigenetic alterations are frequently linked to disease onset and progression, such as in cancer and some neurological disorders. Our work aims to a better understanding of the epigenetic factors and mechanisms that regulate chromatin structure and function. In recent years, we focused our studies to the analysis of linker histones H1 as epigenetic regulators, as well as to the identification and functional characterization of new centromeric components.

Linker histones H1 functions. We have unveiled the essential role of somatic dH1 in the maintenance of genome stability and we have determined the pattern of post-translational modifications (PTMs) of dH1. We have also identified a novel germline specific linker histone, dBigH1, and uncovered its crucial functions in germ stem cell (GSC) lineage differentiation and early embryo development. Currently, we are analyzing the contribution of linker histones H1s to the tridimensional (3D) organization of the genome and the mechanisms that coordinately regulate their expression in health and in cancer.

Centromere assembly and function. We have determined the essential role of proteolysis in the assembly of centromeric chromatin. We have also identified novel centromere associated proteins that participate in the regulation of mitosis progression. Currently, we are addressing the molecular mechanisms that coordinate chromosome segregation and nuclear envelope (NE) breakdown and reassembly.

Some recent publications

M. Torras-Llort et al. (2020) **Commun Biol**, 3, 454 (doi: 10.1038/s42003-020-01182-y).
P. Climent-Cantó et al. (2020) **Nucleic Acids Res**, 48, 4147-4160.
O. Moreno-Moreno et al. (2019) **Nucleic Acids Res**, 47, 3395-3406.
A. Carbonell et al. (2017) **Cell Rep**, 21, 3178-3189.
A. Bayona-Feliu et al. (2017) **Nature Commun**, 18, 283 (doi: 10.1038/s41467-017-00338-5).
R. Kessler et al. (2015) **Nature Commun**. 6:7049 (doi: 10.1038/ncomms8049).
S. Pérez-Montero et al. (2013) **Dev Cell**, 26, 578-590.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Preventing metastasis initiation by targeting the tumor stroma

Project supervisor (principal investigator of the laboratory)

Name: Josep Baulida
Mail: jbaulida@imim.es
Group name: Mechanisms of Tumorigenesis and Tumor Progression
Institution: IMIM
Webpage of the group: **Molecular mechanisms that regulate pro-metastatic tumoural stroma.**

Main grant associated with this project:
Principal investigator: Josep Baulida & Antonio García de Herreros
Agency: Agencia Estatal de Investigación
Reference/ years: 2020-2023

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

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

CAFs are common fibroblasts embedded in the connective tissue surrounding the tumor mass which have been activated by occasional signalling generated by tumor cells.

We have demonstrated that a subpopulation of Snail1-expressing CAFs promote the remodelling of the connective tissue properties generating a pro-metastatic tumor micro-environment characterized by elevated rigidity and aligned extracellular fibers, such as fibronectin and collagen fibers.

The project proposal aims to better understand how these CAFs facilities cancer malignance and how their activity can be inhibited.

We propose a molecular approach to unveil new pharmacological targetable molecules acting on the harmful activity of CAFs.

Cell cultures including generation of in vivo-like extracellular matrices from cultured fibroblast, molecular-biochemical techniques and genetically modified mouse models for cancer will be used.

Project Title: MUSCLE REGENERATIVE POTENTIAL IN MODELS OF SARCOPENIA AND CACHEXIA: FROM THE MOLECULE TO THE PATIENT

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

Dr Esther Barreiro, MD, PhD
Staff physician, IMIM-Hospital del Mar
Visiting professor, Universitat Pompeu Fabra
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Summary of project summary or current research lines (less than 300 words).

Our research is based on the use of patients from clinical settings, animal models of disease, and in vitro primary cultures. We use all kinds of biochemical and molecular biology techniques (RT-PCR, immunoblotting, immunohistochemistry, 2-D electrophoresis, proteomics analysis, ELISA, activity assays, mitochondrial respiration, flow cytometry, etc.) in order to explore the target mechanisms of our research. In the last five years, we have also started a new avenue of research focusing on the underlying biology that accounts for the greater susceptibility of patients bearing chronic respiratory diseases (e.g. COPD) to develop lung tumors. The most relevant achievements of our research have been the following: the demonstration that oxidative and nitrosative stress, ubiquitin-proteasome system, NF-kB and FoxO signaling, alterations of epigenetic regulation, and loss of muscle-specific proteins are important players in chronic obstructive pulmonary disease (COPD)- and lung cancer-associated cachexia, whereas muscle inflammation does not participate in such a process. Moreover, we have also demonstrated that increased oxidative stress, inflammatory cytokines and disruption of epigenetic regulation are involved in the greater susceptibility of patients with COPD to develop lung cancer. In the last decade, my research group has published extensively (180 publications including 16 book chapters) in the field of the underlying biology of skeletal muscle dysfunction and loss in chronic respiratory conditions including lung cancer and acute diseases (sepsis). Recently, we have demonstrated the potential role of muscle regenerative potential in sarcopenia and models of disuse induced muscle atrophy. Ongoing research in my group will pursuit the identification of novel therapeutic strategies targeted to alleviate muscle mass loss and cachexia in patients with chronic disorders including lung cancer.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Insulin and embryo development in insects

Project supervisor (principal investigator of the laboratory)
Name: Xavier BELLES
Mail: xavier.belles@ibe.upf-csic.es
Group name: Evolution of insect metamorphosis
Institution: Institute of Evolutionary Biology (CSIC-Universitat Pompeu Fabra)
Webpage of the group: https://www.biologiaevolutiva.org/xbelles/

Main grant associated with this project:
Principal investigator: Jose Luis MAESTRO and Xavier BELLES
Agency: Plan Estatal de Investigación (Spain)
Reference/ years: PID2019-104483GB-I00 (2020-2022)

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

The year 2018 witnessed the surprising discovery of a third insulin receptor (InR3) in the insect lineage Blattodea (cockroaches and termites). Until then, insects were considered to have two InRs (InR1 and InR2), as products of a gene duplication occurred in the Insecta last common ancestor. The project aims to find out what is the function of InR3, using the cockroach *Blattella germanica* as model. Our preliminary studies indicate that InR3 is preferentially expressed in the early days of embryogenesis. Therefore, we assume that InR3 will play a role in the formation of the germ band. In the context of the present project, we will test this conjecture through maternal RNA interference, thus depleting the InR3 transcripts from the first day of the embryo, and studying the phenotype.

Our research group studies the origin and evolution of insect metamorphosis. As the mode of metamorphosis (direct or indirect) is determined by the type of embryogenesis, we are also interested in the mechanisms that regulate embryo development.

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

Project supervisors Elena Casacuberta, Iñaki Ruiz-Trillo

Institut de Biologia Evolutiva (CSIC-Universitat Pompeu Fabra)

elena.casacuberta@ibe.upf-csic.es, inaki.ruiz@ibe.upf-csic.es

Summary:

Have you ever wondered how animals evolved from their unicellular ancestors? Have you ever wondered how are the protists that are most closely related to animals? Any idea how researchers develop new methodologies to convert an organism into a model organism?

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 soon to come 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 (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, 2022, UPF

Project Title: Dynamic immunogenicity of breast cancer stem cells during tumor initiation and metastasis

Project supervisor (principal investigator of the laboratory)
Name: Toni Celià-Terrassa
Mail: acelia@imim.es
Group name: Cancer Stem Cells & Metastasis Immunity Lab
Institution: Hospital del Mar Medical Research Institute
Webpage of the group: https://celiaterrassalab.com/

Main grant associated with this project: AECC LAB 2019
Principal investigator: Toni Celià-Terrassa
Agency: AECC
Reference/ years: AECC LAB 2019 01/12/2019 - 01/12/2022

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

This project focuses on understanding the tumor immune interplay during the different steps of the metastatic cascade, in particular during the metastatic colonization in distant organs depending on the phenotypic states of the metastatic cells, such as epithelial to mesenchymal transition and stemness.

Lab Research lines:

- Breast cancer stem cells and interplay with the stromal microenvironment
- Immunotherapy resistance in Triple-negative breast cancer (TNBC)
- Epithelial-to-mesenchymal transition (EMT) and mesenchymal-to-epithelial transition (MET) dynamics in the metastatic niche

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Genome editing by CRISPR to model cancer in *Caenorhabditis elegans*

Project supervisor (principal investigator of the laboratory)
Name: **Julián Cerón Madrigal**
Mail: jceron@idibell.cat
Group name: Modeling human diseases in *C. elegans*
Institution: Bellvitge Biomedical Research Institute (IDIBELL)

Webpage of the group: www.ceronlab.com and www.idibell.cat
Twitter: @ceronlab

Main grant associated with this project:
Principal investigator: Julián Cerón Madrigal
Agency: Asociación española contra el cáncer
Reference/ years: IDEAS20078 / 2020-2022

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

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 on 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 using distinct Cas9 systems to increase efficiency and the capacity of inserting long DNA fragments in the genome site of interest (*Vicencio et al, 2019*). Thus, a Master research project in our lab would include training in molecular biology, CRISPR and genetics. The student will participate in the project of modelling cancer in *C. elegans* by using mutations producing tumor-like structures.

Recent publications:

Mimicking of splicing-related retinitis pigmentosa mutations in C. elegans allow drug screens and identification of disease modifiers. Kukhtar D, Rubio-Peña K, Serrat X, Cerón J. *Human Molecular Genetics* 2020 Jan 10. pii: ddz315. 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, Kukhtar D, Cornes E, Esteve-Codina A, Benlloch H, Cecere G, Cerón J. *PLoS Genetics.* 2019 Oct 21;15(10):e1008464. doi: 10.1371/journal.pgen.1008464

Efficient Generation of Endogenous Fluorescent Reporters by Nested CRISPR in Caenorhabditis elegans. Vicencio J, Martínez-Fernández C, Serrat X, Cerón J. *Genetics.* 2019 Apr;211(4):1143-1154. doi: 10.1534/genetics.119.301965

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Regulation of gut B cell responses

Project supervisor
Name: Andrea Cerutti
Mail: acerutti@imim.es
Group name: B Cell Biology
Institution: FIMIM
Webpage of the group: https://www.imim.es/programesrecerca/rct/bcellbiology.html

Main grant associated with this project:
Principal investigator: Andrea Cerutti
Agency: Ministerio de Ciencia, Innovación y Universidades, Agencia de Investigación
Reference/ years: RTI2018-093894-B-I00, 3 yrs

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

We dissect the geography, phenotype, clonal architecture, microbiota reactivity and antibody profile of B cells and plasma cells from distinct segments of intestinal and respiratory tracts. We are particularly interested in intestinal IgA class-switched and respiratory IgD class-switched B cells and plasma cells, but B cells and plasma cells selectively expressing IgM or IgG are also studied. Histologically normal or diseased surgical specimens, including samples from patients with inflammatory bowel disorder (IBD), are dissected through state-of-the-art approaches. The analysis of tissue-based B cells and tissue-derived antibodies is paired with that of circulating B cells and antibodies. The group involves a second independent investigator, Giuliana Magri, PhD. Dr. Magri is dissecting systemic B cell and antibody responses elicited by SARS-CoV-2 during COVID-19 in addition to studying intestinal B cell and antibody responses from IBD patients.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Integrating Protein Biochemistry and Machine Learning to Study Cancer Signaling and Overcome Drug Resistance

Project supervisor (principal investigator of the laboratory)

Name: Pau Creixell

Mail: pau.creixell@cruk.cam.ac.uk

Group name: Cancer Signaling and Therapeutics

Institution: University of Cambridge – Cancer Research UK Cambridge Institute

Webpage of the group: https://www.cruk.cam.ac.uk/research-groups/creixell-group

Main grant associated with this project:

Principal investigator:

Agency:

Reference/ years:

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

Our lab integrates machine learning and high-throughput biochemistry to study how proteins selectively recognize their substrates, how this process is perturbed in cancer and how it can be hijacked to find highly selective and mutant-specific drugs to overcome drug resistance.

Targeted therapies have significantly improved outcomes for patients and shifted the clinical and biological goal towards targeting evolutionary trajectories and overcoming resistance. To overcome these challenges, it is critical to repurpose existing cancer drugs and design news ones with higher selectivity, lower toxicity and less prone to resistance. In our lab we combine and develop technology ranging from peptide display, deep sequencing, machine learning, drug design and functional protein biochemistry with the long-term goal to make an impact in our understanding and treatment of cancer and drug resistance.

Our previous studies have taught general principles in cellular signaling specificity, which we are now using to investigate unexplored cancer signaling, molecular recognition and epistasis, novel therapeutics and predict and overcome drug resistance.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: From super resolution nanoscopy of cell fate to tissue regeneration

Project supervisor (principal investigator of the laboratory)
Name: Maria Pia Cosma
Mail: pia.cosma@crg.es
Group name: Reprogramming and Regeneration Laboratory
Institution: CRG
Webpage of the group: http://www.crg.eu/en/maria_pia_cosma
http://piacosmalab.com/

Main grant associated with this project:
Principal investigator: Maria Pia Cosma
Agency: EU
Reference/ years: FET-Open 2021-2024

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

Main interests of Cosma's group are to dissect mechanisms and factors controlling somatic cell reprogramming and tissue regeneration in mammals. We showed that activation of the Wnt/ß-catenin signalling pathway enhances reprogramming of somatic cells after their fusion with embryonic stem cells. We are dissecting gene networks and reprogramming factors controlled by the activation of Wnt/ß-catenin pathway. Furthermore, by using super resolution microscopy we are investigating on the remodelling and looping of the chromatin fiber during the reprograming process. The activation of Wnt pathway controls regeneration in response to damage in lower and higher vertebrates. We found that the Wnt/ß-catenin signalling is also key to control cell-fusion-mediated regeneration in mammals. We recently showed that in vivo reprogramming of neurons and hepatocytes after fusion with hematopoietic stem and progenitor cells is a mechanism for tissue regeneration.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Identification of brain RNA alterations in the amyotrophic lateral sclerosis/frontotemporal dementia continuum to decipher novel biomarkers

Project supervisor (principal investigator of the laboratory)
Name: Oriol Dols Icardo
Mail: odols@santpau.cat
Group name: Genetics of Neurodegenerative Diseases Unit
Institution: Sant Pau Biomedical Research Institute
Webpage of the group: https://santpaumemoryunit.com/

Main grant associated with this project:
Principal investigator: Jordi Clarimon Echavarria and Oriol Dols Icardo
Agency: Instituto de Salud Carlos III
Reference/ years: PI18/00326/ 2019-2021

Principal investigator: Oriol Dols Icardo
Agency: The Association for Frontotemporal Degeneration
Reference/ years: AFTD/2020-2022

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

Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) share clinical, genetic and neuropathological features and are considered part of the same disease continuum (ALS/FTD). The diagnosis of ALS and/or FTD relies on the assessment of a neurologist, as no accurate biomarker to diagnose ALS or FTD has been described. Alterations in the RNA metabolism represent one of the main pathological hallmarks in the ALS/FTD spectrum and might be used to decipher novel biomarkers.

Our research is focused on the identification of transcriptome-wide changes in the human brain of ALS and FTD patients using high throughput sequencing approaches (total and small RNA sequencing together with bioinformatics tools) and wet lab validation techniques. In addition, we apply immunohistochemistry in the same human brain areas to investigate neuropathological insults and correlate them with RNA perturbations. Ultimately, we aim to identify novel biomarkers in the blood and cerebrospinal fluid of ALS and FTD patients to unravel novel diagnostic biomarkers.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Understanding stress adaptation

Project supervisor
Name: Eulàlia de Nadal
Mail: eulalia.nadal@irbbarcelona.org; eulalia.nadal@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: Eulàlia de Nadal
Agency: Spanish Government
Reference/ years: BFU2017-85152-P / 2017-20

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

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, 2022, UPF

Project Title: Land animal evolution: genomic landmarks on the path to terrestrial life.

Project supervisor (principal investigator of the laboratory)

Name: Rosa Fernández

Mail: rosa.fernandez@ibe.upf-csic.es

Group name: Metazoa Phylogenomics Lab

Institution: Institut de Biologia Evolutiva (CSIC-UPF)

Webpage of the group: www.metazomics.com

Main grant associated with this project: Principal investigator: Rosa Fernández Agency: European Research Council, ERC Starting Grant Reference/ years: 948281 (SEA2LAND), 2021-2026

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

All animals share a common origin: a marine one. **To conquer land from marine environments, animals changed radically the way they breathe, reproduce, move or smell.** And they did it multiple times in the history of Earth, with terrestrial animals massively outnumbering aquatic ones. Understanding terrestrialization is therefore key to comprehending animal biodiversity and biological adaptation. Despite the relevance of such an episode, the genetic underpinnings orchestrating terrestrialization in animals are largely unexplored. The project will test the hypothesis that animals are equipped with a highly plastic 'terrestrialization genetic toolkit' that allowed their adaptation to the extreme environmental conditions in terrestrial ecosystems. We will focus on two pivotal questions: **which genes facilitated life on land and how do they differ between aquatic and terrestrial animals?** and **how did animals reshape their genomes to adapt to dry land?** Moreover, we will study a case example of a critical process common to all terrestrial animals -protection against UV light- to illuminate **what molecular and biochemical changes allowed terrestrial animals to repair their DNA after UV light damage.** This project will deliver fundamental insights into a core question in evolutionary biology: **what shaped the land animal genetic toolkit.** Furthermore, it will provide insights into the evolution of key proteins relevant to human health and industry.

Title: Flow Cytometry, the basis for the molecular study of exosomes.

Project supervisor (principal investigator of the laboratory)
Name: Oscar Fornas
Mail: Oscar.fornas@upf.edu
Group name: Flow Cytometry Unit
Institution: Universitat Pompeu Fabra
Webpage of the group: https://www.upf.edu/web/sct-flow-cytometry

Main grant associated with this project: Internal budget of the unit.

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

Flow Cytometry Unit is a facility that supports more than 350 users from more than 120 research groups from PRBB and externals. We provide technical support to users on daily experiments, from simplest to the most complex flow cytometry applications. Furthermore, we develop new flow cytometry applications. In that direction, during last five years we have been focused to identify and isolate nanoparticles by flow cytometry, such as single-virus isolation for single-virus genomics or flow karyotyping for chromosome sequencing (see below recent publications). Now, we are interested in developing new strategies to study Extracellular Vesicles (EV). EV are basically ranged from 50 to 400 nm. Its small size difficult its identification and study. The study of its content reveals its functions. Among others, cell communication, metastasis induction and regeneration of damaged tissues as the most relevant ones. This is the reason why the biomedical scientific community is interested in their identification and isolation. Strategies and methodologies have been described during the past two decades to identify and isolate exosomas, but most cases haven't demonstrated its reliability.

Our project aims to develop completely new strategy to avoid unwanted steps related with specific low reliability of previous described methods to identify smallest EV. Our preliminary results show our resolution limit around 40 or 50 nm, which is really promising. Finally, the aim of the proposal concerns to the study of exosome content with the final aim is develop a tool for its usage on diagnosis and/or prognosis. Our proposed method, will be based on the direct exosome fluorescence-staining method, contained into cell culture supernatant or human blood plasma. Confocal and super-resolution fluorescence microscopy and electron microscopy will be used as a final imaging "gold standard" to validate our new approach.

Once confirmed, exosomes cargo will be characterized by molecular techniques (RNA sequencing and mass spectrometry) for a final aim of the project to identify biomarkers associated to specific diseases.
Finally, the project has high expectations to finalize with a publication.

Recent publications related with the project:

- Benmarching of single-virus genomics: a new tool for uncovering the virosphere. Garcia-Heredia I, Bhattacharjee AS, Òscar Fornas, Gomez ML, Martínez JM, Martínez-García M. Environ Microbiol. 2020 Dec28. doi: 10,1111/1462-2920.15375.
- Flow Sorting Enrichment and Nanopore Sequencing of Chromosome 1 From a Chinese Individual. Lukas F. K. Kuderna, Manuel Solis-Moruno, Laura Batlle-Masó, Eva Julià, Esther Lizano, Roger Anglada, Erika Ramírez, Àlex Bote, Marc Tormo, Tomàs Marqués-Bonet, Òscar Fornas, Ferran Casals. Front Genet. 2019; 10:1315.
- Ecogenomics of the SAR11 clade. Jose M. Haro-Moreno, Francisco Rodrigeuz-Valera, Riccardo Roselli, Francisco Martinez-Hernandez, Juan J. Roda-Garcia, Monica Lluesma Gomez, Òscar Fornas, Manuel Martinez-Garcia, Mario López-Pérez. Environ Microbiol. 2020 May; 22(5): 1748-1763
- Selective single molecule sequencing and assembly of a human Y chromosome of African origin.Kuderna LFK, Lizano E, Julià E, Gomez-Garrido J, Serres-Armero A, Kuhlwilm M, Alandes RA, Alvarez-Estape M, Juan

D, Simon H, Alioto T, Gut M, Gut I, Schierup MH, Fornas O, Marques-Bonet T. Nat Commun. 2019 Jan 2;10(1):4.

- Single-cell genomics uncover Pelagibacter as the putative host of the extremely abundant uncultured 37-F6 viral population in the ocean. Martinez-Hernandez F, Fornas Ò, Lluesma Gomez M, Garcia-Heredia I, Maestre-Carballa L, López-Pérez M, Haro-Moreno JM, Rodriguez-Valera F, Martinez-Garcia M. ISME J. 2019 Jan;13(1):232-236.
- Deciphering the Human Virome with Single-Virus Genomics and Metagenomics. de la Cruz Peña MJ, Martinez-Hernandez F, Garcia-Heredia I, Lluesma Gomez M, Fornas Ò, Martinez-Garcia M. Viruses. 2018 Mar 6;10(3). pii: E113.
- Single-virus genomics reveals hidden cosmopolitan and abundant viruses. Martinez-Hernandez F, Fornas O, Lluesma Gomez M, Bolduc B, de la Cruz Peña MJ, Martínez JM, Anton J, Gasol JM, Rosselli R, Rodriguez-Valera F, Sullivan MB, Acinas SG, Martinez-Garcia M. Nat Commun. 2017 Jun 23;8:15892.

Project Title: Tumor microenvironment and cancer invasion during epithelial tumorigenesis

Project supervisor: **Antonio García de Herreros**, 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). 1/06/2020-31/05/2023.

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

Our group has a long staining 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 also required for the acquisition of resistance to apoptosis or cancer stem properties. We have analyzed molecular targets of Snail1 involved in these two properties; for a recent article, see, Mazzolini et al, Nucl Acid Res, 46, 146-158, 2018). In the last years we have studied how Snail1 expression is controlled, focusing in the transcriptional control by Wnt ligands (Villarroel et al, Cell Mol Life Sci 77, 919-935, 2020) and also in the role of ubiquitin ligases and deubiquitinases in the modulation of the protein half-life. We have recently characterized a new deubiquitinase, Usp27X that antagonizes the action of Snail1 E3 ligases and stabilizes Snail1 during EMT (Lambies et al, Cancer Res 79, 33-46, 2019).

Although we are also interested in determining how Snail1 is upregulated in tumor cells by anti-neoplasic drugs, the most recent work of the group has been focused on the relevance of Snail1 expression in the tumor microenvironment. We have described that Snail1 expression is detected in few cases in the epithelial component of the tumors, whereas is often observed in the stroma, more specifically in activated fibroblasts. Snail1 is necessary for the activation of cancer-associated fibroblasts (CAFs) by TGFβ or other cytokines derived from the tumor cells. We have investigated currently characterizing the effect of Snail1 expression in fibroblasts on the coadjuvant effect of these cells on tumoral cell invasion and implantation. Our results indicate that the invasive capability of tumoral cells towards growth factors or nutrients is markedly enhanced in the presence of CAFs, supporting the well-known effect of the microenvironment cells on tumor development. Snail1 expression in fibroblasts is required for this supportive effect (Lorena-Castellón et al, Cancer Res, 76, 6205-6217, 2016, Mestre-Farrera et al Cancer Res, 81, 438-451, 2021). The molecular basis of these effects is being investigated, both in in vitro assays (in cell culture) and in tumor animal models. Our group is also analyzing the role of Snail1 on other cells of the tumor microenvironment, such as endothelial cells where it is required for tumor angiogenesis (Cabrerizo et al, submitted). We also plan to assess the role of other cancer microenvironment cells, such as adipocytes, in the activation of CAFs and in the invasive properties of tumor cells. Finally, we are also interested in the characterization of new drugs interfering with Snail1 expression and therefore enhancing the action of chemotherapeutic drugs on tumor cells.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Molecular mechanisms involved in synaptic plasticity

Project supervisor (principal investigator of the laboratory)
Name: Carme Gallego
Mail: cggbmc@ibmb.csic.es
Group name: Control of local mRNA expression
Institution: Institut de Biologia Molecular de Barcelona (IBMB-CSIC)
Webpage of the group: Lab web page

Main grant associated with this project:
Principal investigator: Carme Gallego
Agency: MINECO BFU2017-83375-R
Reference/ years: 2018-2021

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

Molecular mechanisms of neuronal plasticity: the role of KIS kinase:

KIS is a protein kinase that associates with stathmin, a modulator of the tubulin cytoskeleton. KIS is found in RNA granules and stimulates translation of AMPA receptor subunits and PSD-95. Furthermore, KIS enhances β-actin polymerization in dendritic spines accordingly the absence of KIS produces morphological defects in synaptic spines. All these data suggest that KIS is a particularly attractive protein for the study of dendritic plasticity. Search for the synaptic inputs that activate KIS and identify endogenous targets will allow us to better understand the molecular mechanisms of synaptic plasticity.

Synaptic plasticity and neurological disorders: the brain elongation factor eEF1A2 isoform:

Synthesis of many synaptic proteins is under local control, and recent evidence suggests that modulation of the elongation steps of translation may be the key regulatory process underlying synaptic plasticity. Notably, the essential elongation factor eEF1A that binds the aminoacyl-tRNA to drive the first steps of translation elongation displays two very similar forms in vertebrates, eEF1A1 and eEF1A2. While the first is expressed throughout life in almost all tissues, the second form is specific to brain and skeletal muscle, pointing to specific roles of eEF1A2 in tissues where cellular plasticity is most relevant. The recent discovery that missense de novo mutations in eEF1A2 have causal effects in autism and epilepsy underline the relevance of this elongation factor in cognitive functions.

Functional relevance of intron retention mechanism in dendrites:

We are interested in investigating the possibility of local splicing in synapses and the underlying molecular mechanisms. Published data and our own results show dendritic localization of several spliceosome related proteins. We hypothesize that dendritic splicing could be an important mechanism for increasing the molecular complexity and functional capacity of the synapse.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Nanotools for super resolution microscopy of the machinery controlling cell growth

Project supervisor (principal investigator of the laboratory)

Oriol Gallego
PI at the Live-cell structural biology group
Department of Experimental and health Sciences, UPF
PRBB Building
Dr. Aiguader 88, Barcelona

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Email: oriol.gallego@upf.edu
Web: www.gallegolab.org

Main grant associated with this project:
Principal investigator: Oriol Gallego
Agency: Human Frontiers Science Program
Reference/ years: RGP0017, 2020-2022

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

Understanding the molecular mechanisms that drive life (and those that lead to death) requires structural characterization of the protein machinery sustaining the biology of the cell, both in a healthy and in a pathological situation. However, the degree of knowledge acquired to improve human health will be determined not only by the precision of the experimental measurements but also by their proximity to a physiological context. This project aims to develop intracellular nanotools to undertake future investigations relevant for biomedicine and to implement structural biology in living cells.

Our group develops advanced methods of fluorescence microscopy that allow the study of macromolecular complexes directly in living cells. For instance, these methods can quantify protein-protein interactions and reconstruct the 3D architecture of protein complexes. We apply this new technology to study the molecular basis that control cell growth. The aim of the project is to develop new genetically-encoded nanotools to boost the power of quantitative fluorescence microscopy. In collaboration with the group of Alex De Marco, at the Monash University (Australia), we will also asses the implementation of these new nanotools in cryo-electron microscopy. During the progression of the project the student will acquire a strong expertise in gene editing tools, advanced light microscopy, image analysis and proteomics. Depending on the student's skills and interest, the project could also involve *in silico* integration of acquired data to model 3D structures of large protein complexes controlling exocytosis.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Use of Next Generation Sequencing (NGS) as a unique genomic technique to use to improve diagnosis, prognosis and treatment of T-cell Acute Lymphoblastic Leukemia patients

Project supervisor (principal investigator of the laboratory)
Eulàlia Genescà-PhD
ALL Research Group,
Josep Carreras Leukaemia Research Institute (IJC)
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egenesca@carrerasresearch.org
http://www.carrerasresearch.org/ca/acute-lymphoblastic-leukemia-all-_3726

Main grant associated with this project:
Principal investigator: Eulàlia Genescà
Agency: ISCIII-FIS

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

ALL is characterized by a multistep oncogenic process leading to maturation arrest and malignant transformation of lymphoid hematopoietic precursors. T-ALL is the less common and the most complex and heterogeneous at the genetic level. Genetics plays a key role in the development of T-ALL and also has prognostic value. However, until now in the diagnosis only cytogenetic data have been considered. Nowadays, genomics allows obtaining a large amount of genetic data that can help to improve the stratification of these patients and design new specific therapeutic alternatives. However, we are still far from applying it routinely in the diagnosis of patients. To do this we must simplify the analysis of genomic data and apply the minimum number of possible genomic techniques, obtaining the maximum information, in order to reduce the cost involved in the extensive use of these techniques. Here we propose to design, analyze and validate a customized NGS panel to detect structural alterations, point mutations and *indels* in order to stratify patients with T-ALL according to the potential treatment to apply. We also want to use the panel as a predictive tool for relapse. In this way, we believe that we will accelerate the implementation of genomics at the healthcare level, a fact that will undoubtedly help improve the survival of patients with this neoplasm.

Goals

The main goal of this project is to test and validate a NGS panel that will allow us to integrate all the necessary genomic information in a single technique to improve the stratification of patients with T-ALL and predict their relapse.

For that we will do the following steps:

1.1. Design of a sequencing panel
1.2. Application of the panel in the T-ALL Spanish cohort (panel test)
1.3. Check the usefulness of the panel for each of the initially defined uses:
- **1.3.1**. Improve the diagnosis of ETP-ALL
- **1.3.2.** Detection of CNA and rearrangements and refinement of the prognostic value of the alterations included in the panel.
- **1.3.3**. Use the panel as a predictive tool for relapse

Methods include NGS sequencing, mRNAseq, Statistical analysis, Engraftment of T-ALL leukemias in NSG mice

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Natural and vaccine-induced responses to SARS-CoV-2

Project supervisor (principal investigator of the laboratory)
Name: RAMON GIMENO
Mail: rgimeno@imim.es
Group name: Immunity & Infection
Institution: IMIM
Webpage of the group:
https://www.imim.cat/programesrecerca/rct/en_receptorscellularsnkiinfecci_.html

Main grant associated with this project:
Principal investigator: Ramon Gimeno
Agency: ISCIII
Reference/ years: 2020-

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

During the course of the present SARS-CoV-2 pandemic, the laboratory has shifted part of its activity to the study of memory immune responses to the virus. Using flow cytometry, ELISPOT, and other cellular approaches, we aim to assess the quality and persistence of these responses. We will also use our previous experience in immunomonitoring to analyze the response to the vaccine in groups of patients and volunteers. In addition, through transcriptomic analysis, we will investigate how the innate system could contribute to achieve better immunization results.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: ***Molecular analysis of proteins of biomedical or biotechnological 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 Lab
Department of Structural Biology
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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, 2022, UPF

Project Title:

Project supervisor (principal investigator of the laboratory)
Name: Josefa González
Mail: josefa.gonzalez@ibe.upf-csic.es
Group name: Evolutionary and functional genomics
Institution: Institute of Evolutionary Biology (CSIC-UPF)
Webpage of the group: www.gonzalezlab.eu

Main grant associated with this project:
Principal investigator: Josefa González
Agency: ERC, MINECO/AEI, EU
Reference/ years: H2020-ERC-2014-CoG-647900, BFU2017-82937-P

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

The lab generates its own genome-wide datasets, including long-reads genome sequencing (nanopore and PacBio), genome assemblies, RNA-seq, ChIP-seq, ATAC-seq and HiC. We combine the lab-generated data with other available datasets, in public databases or through collaborations with other labs, to investigate the genomic basis of adaptation. We integrate genome-wide analyses with experimental validation using different methodologies such as enhancer assays, CRISPR, qRT-PCR.

We currently focus on three main research lines:

1. The genomic basis of environmental adaptation.

What is the role of epigenetic changes in environmental adaptation? What is the role of structural variants in adaptive evolution? What is the temporal and the spatial scale of adaptation?

3. Urban adaptation in Anopheles mosquitoes.

Identifying genetic signatures of adaptation to urban environments in Anopheles mosquitoes. Which genes and pathways are more relevant for urban adaptation? How can this information be used for implementing vector control strategies?

3. Genomics of invasive species

What is the role of non-coding sequences in the invasion capacity of species?

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title:

Project supervisor (principal investigator of the laboratory)

Name: Alena Gros

Mail: agros@vhio.net

Group name: Tumor Immunology and Immunotherapy

Institution: Vall d'Hebron Institute of Oncology

Webpage of the group: https://www.vhio.net/principal-investigators/alena-gros/

Main grant associated with this project:

Principal investigator: Alena Gros

Agency: Grant for Oncology and Innovation

Reference/ years: 2017-2021

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

Dr. Alena Gros is a young investigator who is driven to understand and exploit the naturally occurring T cell response to treat cancer. Initially trained as a Biologist, she obtained a PhD in Genetics and did a 7- year postdoctoral fellowship at the NCI working with Steven A. Rosenberg. She has been directly involved in several clinical studies where patients received neoantigen-enriched or 4-1BB+ selected lymphocytes. Her most cited contribution to the field is the identification of PD-1 as a biomarker of tumor-reactive lymphocytes residing in the tumor (JCI 2014), and the use of this marker to develop noninvasive personalized T cell therapies from peripheral blood (Nature Med 2016, JCI 2019). She is author of 39 articles and inventor in 5 patents, 3 of them related to the development of personalized T-cell therapies. In 2016, she received a Miguel Servet I Fellowship award and was recruited to VHIO, where she initiated her independent career leading the Tumor Immunology and Immunotherapy Group.

Our team is international and multidisciplinary, including two postdoctoral fellows, four PhD students, two master's students and two technicians. Our group's research is devoted to understanding the immune response to cancer and developing more effective personalized T-cell therapies. Together with Dr. Elena Garralda, the leader of the phase I clinical unit at VHIO, and the Blood and Tissue Bank, we have filed an IND and a clinical trial and received 1M € funding to conduct a Phase I clinical trial to treat patients with solid cancers of epithelial origin with neoantigen-reactive TILs.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Gene-editing technology-based therapeutics

Project supervisor (principal investigator of the laboratory)
Name: Marc Güell
Mail: marc.guell@upf.edu
Group name: Translational Synthetic Biology
Institution: UPF
Webpage of the group: https://www.upf.edu/en/web/synbio

Main grant associated with this project:
Principal investigator: Marc Güell
Agency: European Union
Reference/ years: 825825 - UPGRADE

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

Our laboratory is focused on applied synthetic biology for therapeutic purposes. We have two lines of research, one in technology development for gene therapy, and one in skin microbiome engineering.

Advanced cell and gene therapies are gaining important impact in medicine. There are currently more than 2,500 on-going gene therapy trials on multiple diseases (cancer, genetic disease, infectious disease, etc…)[1] . However, multiple concerns have been raised on the safety of current technologies which prevent a wider deployment. Uncontrolled on-target[2], pro-cancer pathway activation[3], controversy on off-target[4], and lack of efficacy[5] still represent a major concern.

We are offering a master position in developing a new family of gene editing technologies that combines efficacy from viral vectors and precision of modern systems such as CRISPR/cas9. We will combine our system in a single unit called UNI-LARGE, to encapsulate tissue delivery and genome engineering.

Currently, we are deploying our technology to tackle congenital muscle dystrophies. We have initially focused in MDC1A (merosin-deficient congenital muscular dystrophy), which is a devastating disease caused my mutations in LAMA2 gene. However, we are planning to use our technology as a platform in further indications such as CAR-T therapy for cancer and others.

1- http://www.abedia.com/wiley/indications.php
2- Kosicki et al, Nat Biotech 2018
3- Haapaniemi et al, Nat Medicine 2018
4- Editorial comment: https://www.nature.com/articles/nmeth.4664
5- Mollanoori et al, Biotechnology letters 2018

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Efficient gene annotation across the entire phylogenetic spectrum

Project supervisor (principal investigator of the laboratory)
Name: Roderic Guigo
Mail: Roderic.guigo@crg.cat
Group name:
Institution: Center for Genomic Regulation, UPF
Webpage of the group: https://www.crg.eu/en/programmes-groups/guigo-lab

Main grant associated with this project:
Principal investigator: Roderic Guigo
Agency: Internal funding
Reference/ years:

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

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 (http://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 precised 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 (geneid, Guigó et al, 1992), 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.

Our pipeline will be based on identifying the genes that can be precisely predicted computationally in a given species, subtract them from RNA samples, and produced high quality RNA sequences for the genes that are more difficult to annotate.

The master student will work specifically on the identification of selenoprotein genes.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Natural and vaccine-induced responses to SARS-CoV-2

Project supervisor (principal investigator of the laboratory)
Name: INMACULADA HERNANDEZ-MUÑOZ
Mail: mhernandez@imim.es
Group name:
Institution: IMIM
Webpage of the group:

Main grant associated with this project:
Principal investigator: Inmaculada Hernández-Muñoz
Agency:
Reference/ years:

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

Cutaneous squamous cell carcinoma (cSCC) is a highly prevalent malignant tumor that occasionally spreads to lymph nodes and / or distal regions. A subset of high-risk cSCC (HRcSCC) shows a 15%-38% of local or metastatic spread. The mechanisms responsible for the metastasis of the cSCC are not fully understood, and there is a lack of prognostic biomarkers that allow to identify HRcSCC and their potential therapeutic targets. The project aims to characterize the impact of the conditions media from cSCC cultures on the differentiation of myeloid and endothelial cells, both of them important participants of the metastasic process. The final goal of the project is to find biomarkers with clinical relevance that could predict cSCC metastasic progression.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Oxidative stress, protein aggregation and aging

Project supervisor:

Elena Hidalgo
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: 2019-2022

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

Our group is interested in studying the components and molecular mechanisms controlling cellular fitness, both after stress conditions and during aging. Thus, our projects are related to:

(i) study cellular adaptation responses to oxidative stress;
(ii) study of the control protein aggregation.

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:

Boronat et al. 2020. iScience 23:101725
Cabrera et al. 2020. Cell Rep. 30:2430-2443
Carmona et al. 2019. Nat. Commun. 10:4526.
Boronat et al. 2017. PLoS Genet. 13:e1006858.
Encinar del Dedo et al 2015. PLoS Genet. 11:e1005106.
García-Santamarina et al. 2014. Nature Protocols 9:1131.
Calvo, I.A. et al. 2013. Cell Reports 5:1413.
Calvo, I.A. et al. 2012. Nucleic Acids Res. 40:4816.
Zuin, A. et al. 2010. EMBO J. 29:981.

Two of our current goals are (i) to characterize the thermo-sensitive proteome of *S. pombe,* that is, the collection of unstable proteins which may contribute to cell aging; and (ii) to study the participation of mitochondrial metabolism in redox signaling and in longevity, by measuring ROS production and activation of redox cascades.

Call for project proposals, master in Biomedical Research practicum, 2021, UPF

Project Title: Deciphering novel molecular targets for therapies aimed at childhood acute lymphoblastic leukemia

Project supervisor (principal investigator of the laboratory)
Name: Biola M. Javierre
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Group name: 3D Chromatin Organization
Institution: Josep Carreras Leukaemia Research Institute
Webpage of the group: http://www.carrerasresearch.org https://www.javierrelab.com/

Main grant associated with this project: Dissecting the role of non-coding genome in B-precursor Acute Lymphoblastic Leukaemia under the THREE-DIMENTIONAL genome architecture point of view [ALL-3D]
Principal investigator: Biola M. Javierre
Agency: European Haematology Association
Reference/ years: 2019-2022

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

ABSTRACT OF THE PROJECT:

20% of children with acute lymphoblastic leukemia (ALL), the most common pediatric cancer in developed societies, die within 5-years of diagnosis, highlighting the need to novel molecular targets for improving therapeutic strategies. Most of single nucleotide polymorphisms that confer susceptibility, as well as ALL-associated mutations and epimutations, lie in non-coding regions, frequently at regulatory regions, and could exert their functions by altering the regulation of the target genes that physically contact. Unfortunately, most of genes controlled by each regulatory element are unknown. Motivated by these findings, we are determined to significantly improve pediatric ALL clinical outcome by revealing novel genes associated with the development of this hematological disorder, which could be new therapeutic targets. For this aim, we propose to describe the three-dimensional genome architecture of hematopoietic stem cells and common progenitors, and to integrate this insight with ALL-associated genetic susceptibility, mutational and epimutational data. This project is based on the development of a new experimental and computational methodology to genome-wide detect the regulatory regions of the genome for all genes in rare cell types. In summary, this interdisciplinary project will provide unprecedented knowledge into our understanding of human hematopoiesis with a tremendous impact at regenerative medicine and blood malignancies.

BIG PICTURE OF THE GROUP:

Every cell in our body has about 2 meters of linear DNA containing the genes that shape our being. This DNA, which is the same in every cell, is not-randomly packed into the nucleus of a few microns diameter, and the manner in which it is wrapped plays a fundamental role in regulating genome function. In some cases it does this by putting regulatory elements, such as enhancer, and target gene promoters into physical contact. In fact, this can partially explain how cells encoding the same genetic information are phenotypically and functionally different. It has been estimated that the genome harbors around one million regulatory elements, some of these are cell-type specific, but the vast majority of interactions between these elements and the corresponding regulated gene are uncharted, constituting a major missing link in understanding genome control.

Chromatin interactions are crucial for cellular health due to their main role in genome expression regulation and errors in these interactions give rise to the development of a broad range of diseases including blood cancer. The investigation of these altered 3D structures can help us to improve our knowledge of the tumour process, providing new opportunities for the development of novel treatment approaches and diagnostic strategies.

Additionally, genetic studies have identified thousands of single nucleotide polymorphisms and mutations associated with blood cancer, but most of them expand non-coding regions, which makes them difficult to interpret. Interestingly these non-coding genetic variants cluster on DNA hypersensitivity sites, which are the hallmark of a regulatory element, pointing to a potential role for these genetic variants in the deregulation of target genes. By studying the physical interactions between gene promoter and regulatory elements we are able to connect blood cancer genetic alterations to putative target genes, prioritizing new disease-candidate genes and pathways, and revealing insights into genomic regulatory mechanisms underlying cancer. The interpretation of non-coding variation will also help us to improve the prediction of patient outcome as well as allowing us to design better and more personalized treatments.

The main research goals of our lab are:

- Defining the cell type-specific 3D chromatin organization in human hematopoietic cells
- Identifying the altered DNA topology in blood cancer
- Prioritizing new candidate genes and pathways related to blood cancer

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Unrevealing mechanism for p53-mediated tumour suppression

Project supervisor (principal investigator of the laboratory)
Name: Ana janic
Mail: ana.janic@upf.edu
Group name: Cancer Biology
Institution: Department of Experimental and Health Sciences
Webpage of the group: https://www.upf.edu/web/cancer-biology/

Main grant associated with this project:
Principal investigator: Ana Janic
Agency: Retos- Plan Estatal
Reference/ years: 2019-2021

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

The tumour suppressor gene p53 is mutated in half of the human cancers, and there is still extensive morbidity and mortality associated with cancers bearing p53 mutations. Given the difficulties in developing strategies for targeting wild-type or mutant p53, further understanding of its basic biology is required for successful clinical translation. Recent studies, including ours, have challenged the previously understood model of how the p53 gene is involved in tumour suppression. We found that several p53 activated target genes implicated in DNA repair have critical functions in suppressing blood cancer development. Based on this observation, we hypothesise that coordination of DNA damage repair is the most critical mechanism by which p53 suppresses tumour development. In line with this hypothesis our laboratories current research focuses on answering following questions i) how p53 controls a DNA repair–coordinated program to protect tumorigenesis; ii) how tissue specificity controls which p53-regulated DNA repair effectors are crucial for tumour suppression and iii) how we could use p53-dependent DNA repair signalling therapeutically to kill tumour cells.

Selected publications:

Best et al., CDDis 2020

Janic et al., Nat Medicine 2018

Valente et al., Oncogene 2016

Valente et al., Cell Reports 2013

More info about our research at https://www.upf.edu/web/cancer-biology

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Transcriptional regulation in *Drosophila* development

Project supervisor (principal investigator of the laboratory)
Name: Gerardo Jiménez
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Group name: Gene expression and signaling
Institution: Institut de Biologia Molecular de Barcelona (CSIC), ICREA
Webpage of the group:
http://www.ibmb.csic.es/groups/gene-expression-and-signaling

Main grant associated with this project:
Principal investigator: Gerardo Jiménez
Agency: Ministerio de Ciencia e Innovación
Reference/ years: BFU2017-87244-P (2018-2020)

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

Precise control of gene expression is at the heart of virtually all biological processes and is therefore critically involved in human disease. During gene regulation, DNA-binding transcription factors act in concert with other transcriptional and epigenetic co-regulators to activate or repress gene expression, and the activities of all these proteins is often modulated by cell signaling pathways. Our group is currently studying two paradigms of transcriptional control. First, we are investigating how the Ras-MAPK signaling pathway –the most frequently mutated pathway in human cancer– directs changes in gene expression during development and differentiation. We are addressing this question by focusing on Capicua (Cic), an evolutionarily conserved transcriptional repressor that acts downstream of MAPK signaling and functions as a tumor suppressor in humans. We are studying Cic function from different perspectives, including its basic mechanism of action, its interaction with MAPK signaling and other signaling pathways, and the functional significance of its two conserved isoforms, Short and Long. Second, we are interested in the Atrophin (Atro) transcriptional corepressor, so named because of its involvement in dentatorubral-pallidoluysian atrophy (DRPLA), a neurodegenerative disease. Although Atro proteins are known to regulate many repressor processes, their mechanism of action remains poorly understood, and we are studying it using genetic, molecular and genome-engineering (e.g. CRISPR-Cas9) approaches. For both projects, we are mainly using the fruit fly *Drosophila* (where both Cic and Atro were initially discovered or functionally characterized), but we also turn to mammalian systems and have ongoing collaborations with expert national and international groups.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

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-molecular-genomics-dmg/chromatin-regulation-of-human-and-viral-gene-expression/

Main grant associated with this project:
Principal investigator: Albert Jordan
Agency: Ministerio de Ciencia e Innovación – Plan Nacional BFU
Reference/ years: BFU2017 (2018-21)

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

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-LADs, 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 induce 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, 2022, UPF

Project Title: Single-cell RNA-seq characterization of Juvenile Idiopathic Arthritis

Project supervisor (principal investigator of the laboratory)
Name: Antonio Julià Cano
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Group name: Rheumatology Research Group
Institution: Vall d'Hebron Research Institute (VHIR)
Webpage of the group: http://es.vhir.org/portal1/grup-equip.asp?t=reumatologia&s=recerca&contentid=216875 ; www.urr.cat

Main grant associated with this project:
Principal investigator: Sara Marsal
Agency: AES, PI19
Reference/ years: PI19/00225 (2020-2022).

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

Background: single-cell analysis technologies are revolutionizing our understanding of chronic autoimmune diseases. Juvenile Idiopathic Arthritis (JIA) is the most frequent chronic rheumatic disease during childhood, and is a leading cause of disability in the short and long term. JIA encompasses different clinical entities, where oligoarticular JIA (oJIA) is the most prevalent. However, despite involving more than 50% of the patients, oJIA has been much less studied in comparison to other less prevalent forms like polyarticular JIA (pJIA) or systemic JIA. Objective: to identify the pathogenic cell subtypes associated with oJIA. Methods: samples of inflammatory synovial fluid and blood from patients with oJIA will be obtained, as well as from healthy control infants. Using single cell RNA-seq technology (10xGenomics), the different cell subpopulations will be determined in both tissues. With advanced analytical methods we'll identify the pathogenic subset/s that are specific for oJIA.

References:

"Defining inflammatory cell states in rheumatoid arthritis joint synovial tissues by integrating single-cell transcriptomics and mass cytometry.". *Nature Immunology* 2019.

Massoni-Badosa, Ramon, et al. "Sampling time-dependent artifacts in single-cell genomics studies." *Genome biology* 21 (2020): 1-16.

Prakken, Berent, Salvatore Albani, and Alberto Martini. "Juvenile idiopathic arthritis." *The Lancet* 377.9783 (2011): 2138-2149.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: New anticancer therapies based on modulation of the MAP kinase ERK5. Role of ER stress and autophagy

Project supervisor (principal investigator of the laboratory)
Name: Jose M Lizcano
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Group name: Protein Kinases in Cancer Research
Institution: Universitat Autònoma de Barcelona
Webpage of the group: https://inc.uab.cat/en/investigadors/info/jose-miguel-lizcano-de-vega

Main grant associated with this project:
Principal investigator: Jose M Lizcano (OCID: 0000-0002-3154-5383)
Agency: Ministerio de Ciencia e Innovación. Proyectos I+D+I Retos de la Sociedad
Reference/ years: Ref. PID2019-107561RB-I00 2020-23

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

Our laboratory is interested in dissecting new cellular signaling pathways that control cancer cell proliferation and differentiation. We collaborate with academics and Biopharma Companies to perform preclinical development of new anticancer drugs. Among others, we are interested in deciphering the role of the new MAP kinase ERK5 (a MAP kinase) in cancer proliferation and survival. We are also involved in generating small compounds that target ERK5 (inhibitors and degraders/PRTOACs), to be tested as a new targeted therapy to tackle cancer.

We are also interested in modulation of autophagy and endoplasmic reticulum (ER) stress as new strategies to treat cancer. Recently, and in collaboration with Harvard Medical School, we have developed the first specific ERK5 inhibitor (ERKi) (manuscript submitted). This molecule impairs cancer cell survival and proliferation, and inhibits tumor growth *in vivo* (mice engrafted with human tumor cells). Mechanistic studies show that this ERK5i greatly potentiates the cytotoxicity of chemotherapy agents (taxols or platins), both in cells and in animal models. Of interest for this project, preliminary results suggest that activation of ER stress (and the UPR) and of autophagy by ERKi might play a crucial role in sensitizing tumors to chemotherapy.

Therefore, the aim of this project is to investigate the role of ER stress and autophagy in the antitumoral action of the ERK5i. To do so, the student will be trained in the use all sort of biochemical techniques, such as cancer cell cultures, transfection and viral infection of cells, cell viability and proliferation assays, immunoblot, confocal microscopy, RT-PCR and molecular cloning, immunohistochemical analysis of tumors, among others. The student will also participate in our weekly laboratory meetings, as well as in departamental sessions.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Biochemical alterations in Lesch-Nyhan disease, a metabolic illness with severe neurological manifestations

Project supervisor (principal investigator of the laboratory)
Name: José Manuel López
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Group name: Stress protein kinases
Institution: Universitat Autònoma de Barcelona (UAB)
Webpage of the group: https://inc.uab.cat/es/investigadors/info/jose-manuel-lopez-blanco#

Main grant associated with this project:
Principal investigator: José Manuel López
Agency: Fundació La Marató de TV3
Reference/ years: 2021-2023

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

Lesch-Nyhan disease is an illness with severe neurological manifestations, including dystonia, spasticity, cognitive deficit, and self-injurious behavior. The illness is caused by a deficiency in the purine savage enzyme hypoxanthine-guanine phosphoribosyltransferase (HGprt). How a simple alteration in the purine metabolism produces dramatic effects in human behaviour is still a mystery. HGprt deficiency is associated with a relatively selective dysfunction of brain dopamine systems. Different hypotheses have been suggested, some of them claiming for purine abnormalities and/or the accumulation of a toxic metabolite in the brain. We propose that ATP depletion and ZMP accumulation can induce cellular alterations accounting for brain dysfunction. We are investigating the cellular changes induced by HGprt deficiency and how to revert these alterations. In this project we will use fibroblasts, lymphocytes, and iPSC cells obtained from patients and controls.

Recent Publications:

López JM, Outtrim EL, Fu R, Sutcliffe DJ, Torres RJ, Jinnah HA. Physiological levels of folic acid reveal purine alterations in Lesch-Nyhan disease. *Proc Natl Acad Sci U S A.* 117: 12071-12079, 2020.

Yue J, López JM. Understanding MAPK Signaling Pathways in Apoptosis. *Int J Mol Sci.* 21: 2346, 2020.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title:
HARNESSING INFLAMMATORY PATHWAYS IN ANTITUMOR IMMUNE INTERVENTION

Project supervisor (principal investigator of the laboratory)
Name: Cristina Lopez-Rodriguez
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Group name: GENIMMUNE
Institution: Universitat Pompeu Fabra, department of Experimental and Health Sciences
Webpage of the group: https://www.upf.edu/web/genimmune
https://www.upf.edu/web/biomed/entry/-/-/23934/adscripcion/cristina-lopez-rodriguez

Main grant associated with this project:
Principal investigator: Cristina Lopez-Rodriguez and Jose Aramburu
Agency: Plan Estatal I+D+i 2018 European Union FEDER, Worldwide Cancer Research United Kingdom
Reference/ years: RTI2018-095902-B-I00 (2019-2022), WWCR UK: 20-0144 (2020-2023)

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

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:

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, 2022, UPF

Project Title: Insulin Receptor pathway and development in insects

Project supervisor (principal investigator of the laboratory)
Name: José Luis Maestro
Mail: joseluis.maestro@ibe.upf-csic.es
Group name: Nutritional signals in insects
Institution: Institute of Evolutionary Biology (CSIC-UPF)
Webpage of the group: http://www.biologiaevolutiva.org/jmaestro/

Main grant associated with this project:
Principal investigator: José Luis Maestro and Xavier Bellés
Agency: Plan Nacional, Ministerio de Ciencia e Innovación
Reference/ years: PID2019-104483GB-I00 (junio 2020 – mayo 2023)

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

In our group we are studying the function of the insulin pathway in insects and its relationship with different processes, including reproduction, metamorphosis and embryogenesis. Insects have two insulin receptors (InR1 and InR2), produced by an old duplication of an ancestral gene. However, it has been recently discovered that in the lineage that gave rise to cockroaches, termites and stick insects, there was a duplication of an ancestral receptor that gave rise to InR1 and InR3. The objective of our project is to study the functions of the three InRs, InR1, InR2 and InR3. The model used is the cockroach, *Blattella germanica*, a very common domestic pest with which our group have been working for decades and of which a great deal of information (including transcriptomes generated in the group or the sequenced genome produced also with our contribution), and tools (we have found that it is very sensitive to the RNAi, which is extremely useful for functional genomics studies), are available.

For the project offered for the practices of this master, we propose to analyze at the molecular level the phenotype that depletion of InR1 levels produces at the metamorphic molt. At a morphological level, we have already identified that the silencing of InR1 at the time of molting to adult causes high mortality and, in individuals that can molt, the molt is abnormal, with problems in the ecdysis that produce limbs and wings badly extended or not extended at all. The project will analyze which genes and signaling pathways are involved in the production of this phenotype.

Among other methodologies, we will perform RNAi for specifically depleting InR1 expression and we will analyze the expression of different genes belonging to the ecdysis and the molting hormone (ecdysone) signaling pathways.

The project will help to determine the outcome of the InRs that appeared after the duplication, which could be: non-functionalization, subfunctionalization or neofunctionalization.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Computational genomics of proteins containing the special amino acid selenocysteine

Project supervisor (principal investigator of the laboratory)

Name:	**Marco Mariotti**
Mail:	marco.mariotti.mm@gmail.com
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:	RYC2019-027746-I 2021/2026

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

Our lab employs comparative genomics to study the mechanisms of gene expression and protein synthesis. We focus in particular on “recoding” events, 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, where it provides enhanced biochemical properties, typically for improved redox catalysis.

Due to recoding, the genes encoding for selenocysteine-containing proteins (“selenoproteins”) are often missed or wrongly annotated in genomes, since gene annotation programs only consider the canonical role of UGA as stop. Indeed, selenoprotein genes in human have various well-known essential functions, but a large part of the tree of life remains unexplored in this sense.

The student may choose to participate in various tasks, altogether constituting a wide-ranging hands-on training on computational biology:

- Development of automated approaches to recognize and correctly annotate selenoprotein genes in nucleotide sequences. In practice, the student will combine and improve programs for gene prediction and RNA motif finding. This is particularly important in context of new species being sequenced at unprecedented speed.
- Evolutionary analysis of selenoprotein evolution. The student will apply tools from phylogenetics and sequence analysis to selenoprotein genes from diverse organisms, tracing how the selenocysteine utilization pathways changed throughout lineages.
- Analysis of selenoprotein function and regulation in disease. In practice, the student will make use of large public datasets of human or mouse data to analyse patterns of selenoprotein expression across tissues and disease conditions.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: GROWTH OF THE CNS AND ASSOCIATED PRIMARY MICROCEPHALIES

Project supervisor (principal investigator of the laboratory)
Name: Elisa Martí
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Group name: Development of the Spinal Cord in health and disease
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Webpage of the group: https://www.ibmb.csic.es/en/department-of-developmental-biology-ddb/development-of-spinal-cord-in-health-and-disease/
Main grant associated with this project:
Principal investigator: Elisa Martí
Agency: Ministerio de Ciencia
Reference/ years: **PID2019-104134GB-I00 (2020-2023)**

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

GROWTH OF THE CNS AND ASSOCIATED PRIMARY MICROCEPHALIES

Our aim is to study the control of cell numbers and organ size at birth, as a model to study primary microcephalies. Tight control of the balance between self-expanding symmetric and self-renewing asymmetric neural progenitor divisions is crucial to control the number of cells in the developing nervous system and brain size at birth, and thus to prevent primary microcephalies.
We demonstrated that Sonic hedgehog (Shh) and BMP signalling are required for the expansion of the pool of progenitors by maintaining symmetric divisions. By combining high resolution imaging, and data from transcriptomics and functional genetics, we aim to describe the mechanisms downstream growth factor activities that regulate neural stem cell maintenance.

Relevant recent papers form the lab
1._ 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.
2.- Murielle Saade, Jose Blanco-Ameijeiras, Elena Gonzalez-Gobartt, and Elisa Martí (2018) A centrosomal view of CNS growth. **Development** 145: dev170613 doi: 10.1242/dev.170613
3.- Murielle Saade, Elena Gonzalez-Gobartt, Rene Escalona, Susana Usieto and Elisa Martí (2017) Shh-mediated centrosomal recruitment of PKA promotes symmetric proliferative neuroepithelial cell division. **Nature Cell Biology** 19, 493–503 (2017) doi:10.1038/ncb3512
4.- Murielle Saade, Irene Gutierrez, Gwenvael Le Dreau, M Angeles Rabadán, David G. Miguez, Javier Buceta and Elisa Martí (2013) Sonic hedgehog signaling switches the mode of division in the developing nervous system. **Cell Reports** 4(3):492-503. doi: 10.1016/j.celrep.2013.06.038.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Association of genetic variants of inflammation, thrombosis and ACE2 receptor with the development of severe/fatal forms of COVID-19

Project supervisor (principal investigator of the laboratory)
Name: Jaume Marrugat & Irene Roman
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Group name: REGICOR
Institution: Hospital del Mar Medical Research Institute (IMIM)
Webpage of the group: https://regicor.cat/en/

Main grant associated with this project: CARdiovascular GENetic risk score for Risk Stratification of patients positive for SARS-CoV-2 (COvid 19) virus (CARGENCORS)
Principal investigator: Jaume Marrugat
Agency: CRUE
Reference/ years: 26/06/2020-31/10/2021

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

Summary of the CARGENCORS project

CARGENCORS aims at improving risk stratification of COVID-19 patients by identifying genetic variants associated with severe/fatal forms of COVID-19. CARGENCORS is a case-control study recruiting 3000 COVID-19 patients, who suffered a mild/moderate or a severe/fatal form of COVID-19, at hospitals and primary care centres of Catalonia. Clinical data and blood samples are obtained from the patients. Clinical data includes demographics, medical history, glucose and lipid profile and follow-up information. DNA will be extracted from blood samples and 67 genetic variants will be genotyped. The primary objective is to analyze the association of a coronary artery disease genetic risk score (GRS) with the development of severe/fatal forms of COVID-19. Secondary objectives are: to examine the association of the GRS with mortality in COVID-19 patients, to evaluate the association of the GRS with the presence of hyperinflammatory response in severe COVID-19 patients, and to determine the association of genetic variants of inflammation, thrombosis and ACE2 receptor with the development of severe/fatal forms of COVID-19.

Summary of the master project

The master project will be one of the secondary objectives of the CARGENCORS project: to determine the association of genetic variants of inflammation, thrombosis and ACE2 receptor with the development of severe/fatal forms of COVID-19. To undertake this project the master student will participate in patient recruitment, clinical data gathering processes, DNA extraction and genotyping. The student will also participate in the data analysis with R.

Current research lines of the group (detailed information can be found on the REGICOR website)

- Classic and emerging cardiovascular risk factors:
    - analysis of the prevalence of classical and biochemical risk factors of cardiovascular disease

    - association between cardiovascular disease events and biochemical, environmental, imaging and molecular biomarkers
- Cardiovascular risk functions:
    - development and validation of cardiovascular risk functions
    - analysis of cardiovascular risk function improvement with biochemical, imaging and molecular biomarkers
- Cardiovascular genetics:
    - identification of genetic variants associated with cardiovascular disease events and risk factors
    - analysis of cardiovascular risk function improvement with genetic variants
    - evaluation of the impact of epigenetic variants on the incidence of cardiovascular disease events and risk factors
- Register of acute myocardial infarction:
    - estimation of myocardial infarction incidence, mortality and survival rates
    - study of patient management, prognosis and treatment effectiveness
- COVID-19:
    - association of genetic variants of coronary artery disease, inflammation, thrombosis and ACE2 receptor with the development of severe/fatal forms of COVID-19

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: **Uncovering the Metabolic component of Intellectual Disability: role of the histone demethylase PHF8 maintaining neural progenitor expansion**

Project supervisor (principal investigator of the laboratory)
Name: Marian Martínez Balbás
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Group name: Signalling to chromatin
Institution: IBMB-CSIC
Webpage of the group: https://www.ibmb.csic.es/en/department-of-molecular-genomics-dmg/molecular-signaling-and-chromatin/

Main grant associated with this project:
Principal investigator: Marian Martinez Balbás
Agency: Ministerio de Ciencia y tecnología
Reference/ years: PGC2018-096082-B-I00 Chromatin activity and homeostasis in neural stem cells: characterization of the role histone demethylases PHF2 and JMJD3. 01/01/2019 - 31/12/2021

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

In the lab we are interested in understand the contribution of epigentic mechanisms to neurogenesis and how their alteration leads to disease.

In the past years a high number of genes have been identified that link intellectual to disrupted epigenetic mechanisms, one of this is the histone demethylase PHF8/2 whose mutations have been found in patients with X-linked intellectual disability and cleft lip/palate. A critical process during neurogenesis is the generation of proper number of neural progenitors that will give raise the total number of cells in the nervous system. Increasing evidence suggests that metabolites can regulate progenitors proliferation, self renewal and differentiation. However, it remains unknown the epigenetic factors that rewire endogenous metabolic programmes in neural progenitors cells.

Recently, results from our laboratory have led us to hypothesize that PHF8/2 might be crucial to maintain the endogenous metabolic programmes that allows progenitor proliferation, and doing so, generation of the proper number of neurons. Thus, PHF8 mutations associated to intellectual disability could lead to deficient metabolic control in neural progenitors and neurons. To investigate this hypothesis we will use genome wide assays, biochemical and functional experiments to address our main objectives:

1. To determine the metabolic alterations associated to the PHF8's lack of function.
2.- To analyse the molecular mechanisms underlying the metabolic changes.
3.- To investigate the functional consequences of these metabolic changes in proliferation, self renewal, morphology, differentiation and synapsis.
4.- To determine the contribution of PHF8 XLID-linked mutations to maintain the endogenous metabolic programmes.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Exploration of the predictive and functional value of exo-proteins in the context of therapy-induced senescence in Prostate Cancer

Project supervisor (principal investigator of the laboratory)
Name: PI of the lab is Joaquín Mateo, but the student's supervisors will be **Nicolás Herranz**, a Miguel Servet senior investigator and **Irene Casanova,** a senior postdoctoral researcher and a La Caixa Junior Leader fellow.

Mail: nherranz@vhio.net, icasanova@vhio.net
Group name: Prostate Cancer Translational Research lab
Institution: Vall d'Hebron Institute of Oncology (VHIO)
Webpage of the group: https://www.vhio.net/en/prostate-cancer-translational-research-group/

Main grant associated with this project:

1) Principal investigator: Nicolás Herranz

Agency: Proyectos de Investigacion en Salud" FIS Program by the Spanish Ministry of Science and Innovation. "Exploiting therapy-induced senescence in a synthetic lethal approach to treat advanced Prostate Cancer". Reference/ years: 2021-2024. 125.000€

2) Principal investigator: Irene Casanova Salas

Agency: Obra Social La Caixa. "Integrated analysis of blood circulating tumor signatures to monitor genomic evolution and therapy responses in advanced Prostate Cancer". Reference/ years: 2020-2023. 300.000€

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

A position for a Master student is available at the Vall d'Hebron Institute of Oncology's (VHIO) Prostate Cancer Translational Research Group headed by Joaquín Mateo MD PhD. We are a young research group with a highly motivating environment that focuses on studying and testing hypothesis-based targeted therapies in prostate cancer. We are especially committed to applying the potential clinical value of our findings to clinical trials.

The successful candidate will form an integral part of the scientific team and will work in a novel research line co-led by Dr. Nicolás Herranz and Dr. Irene Casanova that aims to:

1) Identify novel biomarkers of therapy-induced senescence in Prostate Cancer via proteomic profiling of circulating exosomes.

2) Characterize the expression and functional relevance of exosomal immunosuppressive ligands in Prostate Cancer patients following therapy.

In order to develop this project, the student will work with prostate cancer models such as patient-derived xenografts (PDXs) and 2D/3D cell cultures; and with patients' solid and liquid biopsies. This project aims to further define the role of therapy-induced senescence as a tumour-adaptation mechanism following treatment and may open previously unexplored possibilities and tools to develop new therapeutic strategies and response/resistance biomarkers that may improve clinical outcome for patients.

We are looking for a highly motivated and team-oriented student with good communication skills and great interest in Cancer translational Research. Ideally, candidates should be strongly oriented to do a PhD.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: **NK CELL AND TGF-β CROSSTALK IN COLORECTAL CANCER: FROM BIOMARKERS TO IMMUNOTHERAPY**

Project supervisor (principal investigator of the laboratory)
Name: Aura Muntasell Castellví
Mail: Aura.Muntasell@uab.cat; amuntasell@imim.es
Group name: Immunity and Infection
Institution: IMIM
Webpage of the group:
https://www.imim.cat/programesrecerca/rct/en_receptorscellularsnkiinfecci_.html

Main grant associated with this project:
Principal investigator: Aura Muntasell
Agency: Ministerio de Ciencia, Innovación y Universidades, Instituto de Salud Carlos III
Reference/ years: 2020-2023

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

Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide. Natural Killer (NK) cells are cytotoxic innate lymphocytes participating in cancer surveillance. Recent data have evidenced the importance of NK cells as orchestrators of effective anti-tumor immunity and the role of TGF-β in inhibiting NK cell effector function. Our current research integrates both players in complementary studies devoted to: i) the identification of NK cell- and TGF-β-related biomarkers of response to treatment in CRC patients and iii) the development of TGF-β resistant NK cells as novel tools for CRC treatment.

Our experimental approach takes advantage of state-of-the-art technologies applied to basic studies in human experimental models in combination with observational studies exploring the value of NK cells as biomarkers of response to treatment in primary and metastatic CRC patients, developed through established collaborations involving Medical Oncologist, Surgeons and Pathologists from Hospital del Mar.

Call for project proposals, master in Biomedical Research practicum, 2021, UPF

Project Title: Neuronal calcium intracellular signalling in Alzheimer's disease

Project supervisor (principal investigator of the laboratory)
Name: Francisco José Muñoz López
Mail: paco.munoz@upf.edu
Group name: Ageing Brain Research Group
Institution: UPF
Webpage of the group:

Main grant associated with this project:
Principal investigator: Francisco José Muñoz López
Agency: SAF- Ministerio de Ciencia, Innovación
Reference/ years: SAF 2017-83372-R

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

Alzheimer's disease (AD) is the most common cause of dementia affecting more than 47 million people worldwide, being a major public health problem with a high economic impact. Due to the progressive increase in life expectancy, it has been proposed that its prevalence will triple in the next 30 years.

EA is characterized by the accumulation of amyloid ß-peptide (Aß) which aggregates into ß-sheets forming neurotoxic oligomers and fibers. The fibers accumulate in the senile plaques of the cerebral parenchyma while the oligomers initiate the damage producing synaptotoxicity that will eventually produce neuronal death. Therefore the production and toxicity of Aß aggregates are determinants in the onset and progression of AD.

There are many experimental evidences that calcium dysregulation is related to the pathophysiology of the disease affecting to synaptic transmission, neuronal death and even increasing Aß production. Our group has recently screened 5,154 mutants of S. cerevisiae that overexpress Aβ, identifying a large number of genes involved in amyloid pathology. Of these we have selected 9 genes that regulate homeostasis and calcium signaling that have not been related to AD at the present time.

HYPOTHESIS: Based on previous studies by our group and other laboratories, we propose the study of the importance of calcium regulation in the pathophysiology of AD by characterizing new genes, not previously related to AD, that play key role in Aß neurotoxicity and production.

OBJECTIVES:

1. Characterization of the new molecular mechanisms mediated by calcium that affect Aß-induced toxicity. The mammalian orthologs of yeast genes that affect Aβ-induced toxicity will be studied in human neuroblastoma cells (SH-SY5Y) and in primary cultures of mouse hippocampal neurons to study their pathophysiological role in neurons. In this study we will focus on the SURF4 protein because of its possible direct relationship with the Ca2 + Store-Operated (SOC).

2. Study of the effect of calcium signaling on Aß production. Characterization of the role of SPCA1 in the production of amyloid through the study of intracellular trafficking of APP, beta- and gamma-secretases and Aß itself.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Study of immunothrombosis and lipotoxicity processes as mechanisms of pathogenesis in Chagas disease.

Project supervisor (principal investigator of the laboratory)
Name: Julio Alonso Padilla
Mail: julio.a.padilla@isglobal.org
Group name: Trypanosoma cruzi Biology Lab
Institution: Barcelona Institute for Global Health (ISGlobal)
Webpage of the group: https://www.isglobal.org/en/-/chagas https://www.isglobal.org/our-team/-/profiles/11902

Main grant associated with this project:
Principal investigator: Joaquim Gascón
Agency: Instituto de Salud Carlos III
Reference/ years: 2019 - 2022

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

Chagas disease is caused by the parasite *Trypanosoma cruzi*. It affects ~7 million people worldwide, over 65,000 of them in Spain. Its main clinical sign is cardiac damage. Despite there are two drugs to treat the infection, benznidazole and nifurtimox, both have variable efficacy at the cost of severe toxicity. Thus, the discovery of better chemotherapeutic options is urgent. However, this is hampered by the poor understanding of the disease pathogenesis mechanisms. Herein we propose to unveil these mechanisms departing from two previous research lines: (i) chronic *T. cruzi* infection causes alterations of hemostasis levels that induce a pro-thrombotic state; and (ii) the parasite stage that multiplies in mammalian cells, the amastigotes, is highly dependent on the metabolism of fatty acids as energy source. In relation to them, our hypotheses are that: (1) the parasite systemic intermittent presence leads to dysregulated immunothrombosis processes that stand as a cardiovascular risk factor; and (2) cardiac cells infection by the parasite generates a metabolic unbalance, which in similarity to what has been observed in type II diabetes cardiomyopathy, will lead to the accumulation of fatty acids by-products in them, inducing lipotoxicity and driving to tissue inflammation and fibrosis. In order to undermine Chagas disease pathophysiology we will study the parasite interactions with the distinct components of the blood, as well as with human endothelial and cardiac cells.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: **Single-Cell Spatial Resolution in intrahepatic cholangiocarcinoma (iCCA)**

Project supervisor (principal investigator of the laboratory)
Name: Sandra Peiró Sales
Mail: speiro@vhio.net
Group name: Chromatin Dynamics in Cancer Group
Institution: Vall d'Hebron Oncology Institute (VHIO)
Webpage of the group:

Main grant associated with this project:
Principal investigator:
Agency:
Reference/ years:

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

Project

Brief description: Cholangiocarcinomas (CCAs) are the second-most common hepatobiliary malignancy, accounting for 10%–20% of primary liver cancers. CCA remains an incurable cancer type, with an overall 5-year survival rate of less than 10%. CCA is frequently diagnosed in advanced stages, and the therapeutic options are limited. Developing efficient treatments has been hindered by our lack of understanding of the biology of CCA.

While the current cutting-edge technical and computational analyses have revolutionized investigation of complex organs and tissues, several challenges still need to be addressed, including how to acquire spatial and temporal information for the tumor cells as related to the tumor microenvironment and during the course of the treatment.

Specific objectives: The overarching goals of this project are to: 1) perform an in-depth architectural characterization of iCCA tumors, and 2) identify potential therapeutic targets. We will use cutting-edge techniques to address these questions, including high-throughput single-cell technologies, spatial transcriptomics, advanced MRI, CRISPR screens, and in vivo approaches. Further, we will provide tools to analyze the spatial and temporal information that is needed for identifying tumor-specific processes.

Value for scientific field and society: Our analysis will provide spatio-temporal, transcriptional, and epigenetic information for patients under standard-of-care treatment, and give a deeper understanding of the iCCA etiology, responses and resistance. We will develop numerous tools (including single-cell and high-dimensional spatial datasets, iCCA cell lines, and PDX models) that will be available for researchers, and will publish our results in open-source, high impact journals. Importantly, our results should help to expand possible treatments for iCCA and eventual lead to effective treatment and/or early detection options for iCCA patients.

Current research lines

The group has multidisciplinary experts in molecular biology and genome-wide studies:

- Genomic approaches: RNA-seq, ATAC-seq, ChIP-seq
- Ex vivo and in vivo culture of primary human tumor cells
- Establishment of patient-derived xenographs from cholangiocarcinoma (CCA) and NUT-midline carcinoma (NMC) patients
- CCA and NMC cell lines genetically-engineered with CRISPR/Cas9. These cells are currently used in our laboratory for negative and positive genome-wide screening upon drug treatments.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: How do dendrites grow to support visual motion detection in the fly eye?

Project supervisor (principal investigator of the laboratory)
Name: Filipe Pinto Teixeira
Mail: filipe.pinto-teixeira@univ-tlse3.fr
Group name: Neural Circuit Development Lab
Institution: CBI/CNRS- Toulouse, France
Webpage of the group: https://www.pintoteixeiralab.com

Main grant associated with this project:
Principal investigator: Filipe Pinto Teixeira
Agency: Fondation Bettencourt/Atip-AVENIR-CNRS/INSERM
Reference/ years: 2020-2023 (extended to 2025 upon positive evaluation)

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

We use the fruit fly *Drosophila melanogaste*r visual system as a model to understand the genetic, molecular and cellular mechanisms that regulate wiring specificity, from development to circuit function.

In the fly, as in the human eye, dedicated sets of neurons extract the direction of image motion from specific points in the visual word. Such local motion detectors are known as T4/T5 neurons in the fly. Some T4/T5 neurons are sensitive to a stimulus presented to the eye moving from left to right, others top to bottom, and so forth. To compute motion, each neuron must compute information from neighboring points in the visual space. T4/T5 neurons achieve this by extending their dendrites across small regions of the fly optic lobe to receive signals from various presynaptic partners that relay information from neighbouring points in the visual space. As such, the size of each T4/T5 dendrite is poised to establish the neuron's acuity and local motion resolution.

We have used scRNAseq to profile developing T4/T5 neurons. This offered us candidate genes involved in establishing the size of each T4/T5 dendritic arbor. Departing from this dataset you will use sophisticated genetics and advanced live imaging approaches, to study how dendrite size is regulated to achieve wiring specificity and establish visual motion detection in the fly.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Maternal-zygotic transition. Role of parental piRNAs

Project supervisor (principal investigator of the laboratory)
Name: Maria-Dolors Piulachs
Mail: mdolors.piulachs@ibe.upf-csic.es
Group name:Insect Reproduction lab
Institution: Institute of Evolutionary Biology (IBE; CSIC-UPF)
Webpage of the group: https://www.biologiaevolutiva.org/mdpiulachs/

Main grant associated with this project: Ayudas extraordinarias para la preparación de proyectos 2019. (2020-2021) Codigo: 2019AEP028.
Principal investigator: M.Dolors Piulachs.
Agency: CSIC
Reference/ years: 2019AEP028/2020-2021

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

The piRNAs are small non-coding RNAs that were first described in male germ cells of *Drosophila melanogaster*. The first function associated with the piRNAs was the repression of transposable elements (TE) expression. But, since that time, more piRNA functions have been discovered. They are not only repressors of TEs but also act as regulators of the expression of some mRNAs. Besides, they not only act in germ cells but also exert their function in somatic cells.

Insects and their reproductive processes are a good model to study piRNA functions. In our laboratory, we use the cockroach *Blattella germanica* as a model to study insect reproduction. In previous studies, we compared libraries of small RNAs from unfertilized eggs with libraries from zygotes, and a small number of highly expressed piRNAs with a parental origin emerged.

We propose to study these piRNAs differentially expressed, by depleting each of them (or suppressing them in the best of cases), as well as increasing their concentration. Since we hypothesize that piRNAs regulate the expression of mRNAs, we will predict mRNA target candidates for each piRNA, using the transcriptomes available in the laboratory. Later, these predictions will be validated by measuring the expression of the mRNA target candidate after depleting or increasing the concentration of the piRNA under study.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Modulation of gut microbiota as a therapeutic approach to improve cognitive phenotypes of Ts65Dn mice and decelerate the onset of neurodegenerative processes.

Project supervisor (principal investigator of the laboratory)
Name: Nieves Pizarro
Mail: npizarro@imim.es
Group name: Integrative Pharmacology and Systems Neuroscience
Institution: IMIM
Webpage of the group: https://www.imim.es/programesrecerca/neurociencies/grfh/es_index.html?t=membres&g=32

Main grant associated with this project:
Principal investigator: Nieves Pizarro
Agency: Jérôme Lejeune Foundation
Reference/ years: 2 years

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

Down syndrome (DS) is the genetic disorder responsible for the most common intellectual disability, characterized by a trisomy in chromosome 21. Medical advances have successfully increased DS life expectancy but, as a consequence, age-related neurodegenerative diseases such as Alzheimer disease, have emerged in this population, becoming a health and social concern.

There are growing evidences indicating that targeting gut microbiota (GM) may be a suitable therapeutic approach to modulate inherent risk factors of cognitive impairment in DS population at all stages of their lives, and also to decelerate cognitive decline related to neurodegenerative processes. In animal models, the most feasible approaches to modulate GM include the use of probiotics and prebiotics, and fecal transplantation.

This project proposes a thorough study of the GM role in the cognitive function of Ts65Dn mice at all stages of their lives, and also in the onset and progression of cognitive decline observed at old ages. The modulation of the gut microbiota will be done by performing a long-term administration of a probiotic and prebiotic (synbiotic) combination. There will be analyzed the microbiota composition (metagenomics) and functionally (metabolomics) of 1) animals that will receive the synbiotic since young adulthood (8-10 weeks) and until old ages (37-39 weeks), 2) animals that will receive the synbiotic since the moment of their pregnancy (by administering it to the breeding couples) and until old ages; and 3) control animals that will receive tap water during the whole experimental schedule. Phenotype and gender factors will also be considered.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: **Gene Regulation in Stem Cells, Cell Differentiation & Cancer**

Antonio Postigo
ICREA Professor
Group of Gene Regulation in Cell
Differentiation & Cancer
Institute of Biomedical Research IDIBAPS
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IDIBAPS -- https://bit.ly/3arJph3

Summary of project summary or current research lines

The Gene Regulation Lab is looking for a motivated MSc student to work in the area of "Gene Regulation of Stem Cells, Cell Differentiation, and Cancer". ZEB1 and ZEB2 play key roles in both homeostasis and in different pathologies. The MSc student will have the opportunity to work in one of the several projects currently ongoing in the lab. Available projects include the study of the mechanisms regulating gene expression in stemness (normal and cancer stem cells), cellular plasticity and differentiation, inflammation, tissue regeneration, and tumor initiation and progression. The project make use a wide array of in vitro and in vivo approaches including unique transgenic mouse models and high throughput techniques (RNAseq, ChIPseq, metabolomics).

See the links above https://bit.ly/3arJph3 , https://bit.ly/39BA46g and https://bit.ly/2TIeWox for additional details

Requirements: Bachelor in Biology, Biotechnology or in any other biomedical-related discipline. Candidates with a strong academic record (higher than 8.7/10), previous lab experience and interested in pursuing later a PhD will receive special consideration in the selection process.

Recent Publications by the Group (as corresponding author): ***Science Advances.*** In press (Impact Factor: 13.2); ***Nature Commun*** 10:1364 (Impact Factor 12.3); ***Nature Commun***. 9:2424 (IF 12.2); ***Nature Commun***. 4:2650 (IF 12.2); ***Nature Commun***. 5:5660 (IF 12.2); ***Gut*** 68:2129 (IF: 19.8); ***Gut*** 66:666 (IF 19.8); ***Nucleic Acids Res*** 46:10697 (IF: 11.6), ***EMBO J*** 36:3336 (IF 11.2); ***Clin Cancer Res*** 19:1071 (IF 10.2), ***PNAS*** 108:19204 (IF 9.8).

Information. To obtain more information and to set up a visit to the laboratory, please send CV and the names and contact details of 2-3 persons familiar with the candidate's academic and/or research performance to **idibaps.postigo4@gmail.com** indicating "**Master UPF** " in the subject of the email.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title:

Elucidating the balance between cell proliferation and differentiation within the embryonic brain

Project supervisor

Cristina Pujades, PhD
Full Professor
Department of Experimental and Health Sciences
Universitat Pompeu Fabra
PRBB, Dr Aiguader 88
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https://www.upf.edu/web/pujadeslab

Main grant associated with this project:

Unveiling the coordination between progenitor dynamics and tissue morphogenesis during neural development: towards a 4D-perspective
MICIU, 2019-21 PGC2018-095663-B-I00

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

The development of the brain is a highly regulated process that requires a precise balance between proliferation and differentiation, in order to generate the correct number and types of cells to maintain its cognitive, sensory and motor functions. The knowledge of how the brain acquires its final functional structure and size entails the study of clonal dynamics, this is, the biological behaviour of all the cells issued from a common progenitor. This assessment includes parameters such as proliferation rate and neuronal output of progenitors, cell division pattern, overall migration and final location of differentiating cells, and spatiotemporal changes in proliferation and differentiation.

The candidate will be involved in a project that aims at understanding how the brain balances cell proliferation vs. differentiation in order to produce an organ of a specified robust size and composition. We will focus on the embryonic brainstem -the hindbrain-, which is responsible of life-sustaining functions and is extremely conserved in vertebrates. During brain development, cell differentiation results in an extraordinary displacement of neurons from their birth site due to complex morphogenetic movements, and extensive migration during development. To understand the impact of this displacement in the whole hindbrain, we will life-monitor using 4D-imaging the growth of the hindbrain and of specific progenitor populations combining multicolor lineage tracing and Machine Learning tools for its automatic analyses.

In the laboratory we use the zebrafish embryo as a model system because it allows us to combine cutting-edge complementary approaches such as: CRISPR-Cas9 genome editing, high-resolution 4D-imaging paired with cell tracking tools for cell lineage reconstruction, transcriptional profiling, and regulatory landscapes.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: In vivo maturation of human PSC-derived cardiomyocytes within mouse heart chimeras.

Project supervisor (principal investigator of the laboratory)
Name: Angel Raya
Mail: araya@idibell.cat
Group name: Stem Cell Potency
Institution: Bellvitge Biomedical Research Institute (IDIBELL)/P-CMR[C]
Webpage of the group: https://p-cmrc.cat/research/raya-group/

Main grant associated with this project:
Principal investigator: Angel Raya
Agency: MINECO
Reference/ years: RTI2018-095377-B-100/2019-2021

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

Thanks to continuous funding from MINECO/Plan Nacional for previous projects, we have developed cardiac engineering strategies to generate human myocardial constructs derived from pluripotent stem cells (PMID: 31231023, Patent Application number: EP18382391). However, although such constructs showed a high degree of functional maturation at the tissue level, cardiomyocytes at the cellular level still showed clear signs of immaturity. The relative immaturity of human pluripotent stem cell derivatives is currently one of the main hurdles in the field of regenerative medicine. In this project, we plan to hijack the normal development (embryonic, fetal, and postnatal) of the mouse heart to provide the necessary clues that guide terminal cardiomyocyte differentiation. Whereas similar strategies have been widely available for many years for other organs or tissues, in the case of the heart only recently has neonatal transplantation into rat hearts been accomplished, with conflicting results. Our laboratory has accumulated considerable expertise in the manipulation of neonatal mouse hearts for our research on regeneration (e.g. PMID: 29732402), which we will exploit to implement the neonatal transplantation technology. Human pluripotent stem cell derivatives (including, but not restricted to cardiomyocytes) will be generated using advanced 2D and 3D cell culture systems. The persistence and fate of human cells after intramyocardial microinjection into the mouse heart will be evaluated using cutting-edge in vivo microscopy techniques (e.g. PMID: 31160803, PMID: 28659386, PMID: 30167169). The implementation of this project will require close collaboration (including short stays) with top national and international laboratories.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Revealing the unknown biology of the most abundant marine microbial eukaryotes

Project supervisor (principal investigator of the laboratory)
Name: Daniel J. Richter
Mail: daniel.richter@ibe.upf-csic.es
Group name: Biology and Ecology of Abundant Protists
Institution: Institut de Biologia Evolutiva (UPF-CSIC)
Webpage of the group: https://www.beaplab.org

Main grant associated with this project:
Principal investigator: Daniel J. Richter
Agency: European Research Council (ERC), EU Horizon 2020 Research and Innovation Programme
Reference/ years: Grant agreement no. 949745 / 5 years (starting 1 September, 2021)

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

Our goal is to isolate, culture and subsequently characterize the cell biology, behavior and ecosystem relevance of the most abundant unknown protists on earth. Protists are single-celled and colonial microbial eukaryotes which, due to their size (generally between a few micrometers and a few hundred micrometers) are a critical part of the food webs in all of earth's principal ecosystems. In addition, protists form the backbone of the eukaryotic tree of life, meaning that studies of protists inform our understanding of the evolution of eukaryotic cell biology, gene content and species diversity. Our work currently consists of four related projects:

1. Biology of Globally Abundant Protists: we aim to isolate and culture the most abundant, and as yet unknown, protists on earth. Once in culture, we will characterize their cell biology, ultrastructure, life history, behavior and interspecies interactions using time-lapse and fluorescence microscopy techniques, accompanied by single-cell sequencing. In this process, we hope to establish these protists as new model systems whose biology and ecosystem relevance can be studied intensively in the lab.

2. Global Gene Expression of Abundant Protists: we begin with hypotheses, based on our lab studies, regarding the potential ecological roles of the abundant protists we study. Armed with their gene catalogs from genome and transcriptome sequencing, we apply the bioinformatic methods we developed to investigate the patterns in their gene expression in global-scale metatranscriptomic sequencing databases. As examples, these hypotheses may relate to their ecological roles, in terms of species interactions, or their responses to changes in environmental conditions.

3. Eukaryotic Gene Family and Protein Domain Evolution: we develop new computational methods to study the genes and genomes of diverse eukaryotes in order to reconstruct the evolutionary history of gene families, protein domains and the biological processes they drive.

In addition, because only a tiny fraction of protist species are available in culture, we anticipate that the sequence resources we generate for newly isolated protists will be informative for studies of eukaryotic diversity and the evolution of gene content and function.

4. Resources for the Protist Research Community and Beyond: as we work, we design the output of our research projects to be reusable. We make our data, code and wet lab protocols available to the research community. We also lead or participate in projects to collect and organize eukaryotic sequence data and taxonomy, in order to standardize and streamline their use for all researchers.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: A nanomedicine in clinical oncology

Project supervisor (principal investigator of the laboratory)
Name: Pilar Rivera Gil
Mail: pilar.rivera@upf.edu
Group name: Integrative Biomedical Materials and Nanomedicine Lab
Institution: UPF-CEXS
Webpage of the group: https://www.upf.edu/web/nanomed

Main grant associated with this project:
Principal investigator: Pilar Rivera Gil
Agency: MICINN-AEI
Reference/ years: PID2019-106755RB-I00 / 2020-2023

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

Pancreatic cancer is a lethal disease which is expected to be the 3rd cancer death caused by 2025. 95% of the patients die within 5 years.

The reason for these dismal results is a failed diagnosis and an inefficient therapeutic strategy. NanoTarg therapeutic solution is to use an oncotarget present in tumor cells favouring tumor progression, to specifically direct a nanocapsule. Our previous results show specific targeting in xenografts (EESR approved, ongoing PCT). NanoTarg aims at nanoencapsulating and directing the therapeutic gold standard (paclitaxel) precisely to the tumour tissue and to promote its targeted release. NanoTarg will validate the therapeutic potential *ex vivo* using 3D organoids from murine models and from patients' pancreatic tumour cells, and *in vivo* using orthotopic xenografts. The oncotarget is present in other types of cancers and therefore, NanoTarg technology can be extrapolated to them. As an added value, NanoTarg introduces the concept of biomedical SERS for the detection of biomarkers, the clinical relevance of it and the challenges that might appear to this novel strategy for its implementation in clinical oncology. NanoTarg will synthesize a SERS-based sensor to correlate imbalances with enhanced proliferation, invasiveness and in general, with tumour progression.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Biomarkers of antidepressant response: early indicators and novel targets.

Project supervisor (principal investigator of the laboratory)
Name: Patricia Robledo
Mail: probledo@imim.es
Group name: Integrative Pharmacology and Systems Neuroscience
Institution: IMIM
Webpage of the group: https://www.imim.es/programesrecerca/neurociencies/grfh/es_index.html?t=membres&g=32

Main grant associated with this project:
Principal investigator: Patricia Robledo
Agency: ERANET-NEURON
Reference/ years: 3 years

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

Antidepressants (AD) are for now, the best treatment we have for major depression (MDD) a severe mental disorder. AD are one of the most commonly prescribed drugs in the western hemisphere, however their trial-and-error nature combined with unwanted side-effects, leave a lot to be desired. More than 60% of patients suffering from MDD fail to respond to the first AD they are prescribed. For those that respond, full response is only observed after several weeks of treatment, and, in case of failure it can take too long a time before alternative options are explored.

To be able to predict clinical response at an early-stage of AD treatment is an important aim for the clinician and the potential impact for patients suffering from MDD and for the health system is very high. However, up to date there are no early biomarkers that could help therapeutic decision while this is already true in cancer and other fields of medicine. In this proposal, we hypothesize that ELK1 gene expression variation but also variations of related genes and other regulators of cell machinery may occur earlier than clinical improvement and could be predictive of future clinical improvement. This is a significantly novel approach in biomarker discovery while past studies focused only on predictive biomarker measured before treatment onset.

First we aim to identify peripheral “early post-treatment biomarkers” in a novel multicenter human cohort of patients with MDE. Then, we want to validate “early post-treatment biomarkers” in animal models of depression, in the blood. Last, we want to explore the plausibility of our blood biomarkers by studying our biomarkers in the brain. We will focus our analysis on both long and small RNA, by using cutting-edge approaches. These results will constitute the necessary first step to develop new biomarkers predictive of AD response. Such biomarkers, would - reduce time to change medication and help avoid unnecessary side effects for patients, -inform therapeutic decisions - reduce stress for clinicians, and reduce personal and public health costs.

Specifically, our group will develop the following task: ***Animal models of individual variability of the response to AD treatment; longitudinal assessments (male and female mice; AD: fluoxetine, venlafaxine).***

Neurochemical evaluations will be performed using the *in vivo* intracerebral microdialysis technique in the prefrontal cortex and hippocampus of freely moving mice (responders and non-responders to chronic mild stress), focusing on measuring monoamines (DA, NE and 5-HT) that are the hallmark of action of all AD, and subsequent analysis by HPLC. Neurochemical evaluations will be collected at 4 time-points: (i) *Tb*: baseline (after stress but before AD treatment); (ii) *T1:* 72h *post* treatment *(iii) T2*: 1 week-post-treatment; (iii) *T3*: 4 weeks post treatment.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Monitoring senescence upon chemotherapy (MonSen)

Project supervisor(principal investigator of the laboratory)
Name: Verónica Rodilla
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Group name: Cancer Heterogeneity and Hierarchies
GroupInstitution: Josep Carreras Leukaemia Research Institute, IJC
Webpage of the group:under construction
Main grant associated with this project:
Principal investigator:Verónica Rodilla
Agency:ASEICA+queuntrail

Brief summary of the project or current research lines of the group (please do not include pictures or logos)
We are a newly-created group passionate for cellular hierarchies and tumour heterogeneity. Concretely, our main lines of research and specific goals are:
1.Illustrate cellular hierarchies within tumoursWe use a well-established hierarchical model to study multipotency in tumours. Our previous results studying clonal dynamics of cells within embryonic mammary buds revealed that embryonic multipotent mammary stem cells (MaSCs) differentiate into lineage-restricted unipotent precursors early in development (Lilja and Rodilla et al., 2018). Now, we separately monitor three mammary epithelial compartments to measure the presence ofmultipotency within breast tumours. Our hypothesis suggests that, similar to the findings observed in physiological mammary glands, breast tumours are indeed sustained by different subpopulations, which self-maintain independently. Moreover, we are interested in quantifying the metastatic capacity of each mammary epithelial cell type by performing lineage tracing experiments in breast cancer genetic mouse models to elucidate how the tumour cell of origin matters in this tumorigenic process.
2.Discover new cytotoxic agents for specific cellular subpopulationsHence, a therapy based on the combination of several drugs to target different cellular populations could eradicate the primary tumour avoiding relapse and metastasis. In collaboration, we are keen on screening for natural compounds that let selectively kill specific subsets of cells, which are responsible for tumour maintenance and/or intrinsically resistant to current therapies. Furthermore, we use 3D-organotypic cultures derived from murine and human tumours and CRISPR/Cas9 technology to identify genes involved in cellular survival and fate conversion. Definitely, our screening will allow us to draw a map of signalling pathways governing cellular plasticity and lineage commitment.
3. Target the tumour niche to avoid cancer spreading One of our main objectives is to generate in vivo tools that allow us to study new therapeutic targets that can avoid relapse in haematological cancer. Accumulating evidence have indicated that senescent cells could have a pro-tumorigenic role, since the specific inhibition of factors secreted by these cells resulted in a reduction of tumour growth in advanced stages of the disease and in a paracrine manner. Importantly, several chemotherapies and radiotherapies, which were designed to specifically target proliferating cells, can also induce senescence. In that direction, our lab works on different in vivo strategies, which includes murine and human models, to test a panel of drugs currently used as a standard of care for non-Hodgkin lymphoma (NHL) and explore the role of senescence in tumours cells as well as in their microenvironment.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: Roles of the Plk1/Nek9/Nek6/7 signaling axis in the control of the centriole cycle and chromosome segregation

Project supervisor (principal investigator of the laboratory)

Name: Joan Roig Amorós

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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-cell-biology-dcb/cell-cycle-and-signaling/

Main grant associated with this project:

Principal investigator: Joan Roig

Agency: Plan Nacional de I+D, Ministerio de Ciencia, Innovación y Universidades, Spain.

Reference/ years: PGC2018-096307-B-I00 (2019-2021)

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

Our group is interested in understanding how G2 and early mitosis are controlled, and we presently study how centrosomes and the microtubule cytoskeleton are regulated in order to organize the mitotic spindle and allow for proper chromosome segregation. We focus our research on the roles of the signaling axis formed by the protein kinase Plk1 and its downstream partners, the related Nek9, Nek6 and Nek7, three NIMA-family kinases that are activated at the centrosomes and we have shown in the past 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).

Failure to properly duplicate, separate or mature the centrosomes result in abnormal mitosis, aberrant chromosome segregation and aneuploidy -one of the major hallmarks of cancer cells. Using engineered animal models plus genetically modified cell lines produced through CRISPR-Cas9 technology and RNAi, the project will involve characterizing the consequences of Nek9/Nek6/7 malfunction at the cellular level, especially in relationship to the control of the centrosome cycle, chromosome segregation and the onset of aneuploidy. We will seek to relate our observations with clinical data with the aim of assessing the possible involvement of the kinases in the process of cell transformation and the apparition of cancer.

Project Title: Deciphering the role of HDAC11 in muscular dystrophies

Project supervisor

Mònica Suelves, PhD

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Summary of project summary or current research lines

Histone deacetylase 11 (HDAC11) is the latest member identified of the HDAC family, it is the unique member of the class IV HDAC subfamily and globally, its functions are poorly understood. HDAC11 is highly expressed in skeletal muscle tissue and very recently, our laboratory has shown that HDAC11 genetic deficiency in mice 1) promotes a glycolytic-to-oxidative muscle fiber switch, enhances mitochondrial content and increases lipid oxidation and globally, thus resulting in increased muscle performance (Hurtado et al, 2020); and 2) accelerates the regeneration process in response to muscle injury, by acting on SCs and macrophages, and enhancing SC differentiation Núñez-Álvarez et al, 2020). Because severe muscular dystrophies, including Duchenne muscular dystrophy (DMD) and myotonic dystrophy type 1 (DM1) course with cycles of degeneration, inflammation and regeneration, HDAC11 could be involved in their progression. Currently, in the laboratory we are performing experiments to better understand the contribution of HDAC11 in these chronic muscle pathologies and during aging.

The candidates should be very motivated students. Experience in cellular and molecular biology techniques and with mice handling will be well considered. We are interested in recruiting a PhD student, so the Master project can be continued with a PhD Thesis.

Contact to Mònica Suelves (msuelves@igtp.cat) sending a motivation letter, academic records and CV.

Call for project proposals, master in Biomedical Research practicum, 2022, UPF

Project Title: FUNDAMENTAL ELEMENTS OF THE SPLICING CODE

Project supervisor (principal investigator of the laboratory)
Name: Josep Vilardell
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Group name: Mechanisms of pre-mRNA splicing
Institution: Institute of Molecular Biology of Barcelona
Webpage of the group: http://www.ibmb.csic.es/groups/molecular-mechanisms-of-pre-mrna-splicing

Main grant associated with this project:
Principal investigator: Josep Vilardell
Agency: Spanish Ministry of Science and Innovation
Reference/ years: BFU2014-60550-P (Extended)

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

In a typical human gene, just about 1/10 of its transcribed DNA is devoted to exons, and the rest 90% to introns. What is exon and what is intron is a decision that is worked out by the spliceosome, likely to be the most complex machinery of our cells. Until we do not fully understand this process we will not be able to comprehend how genes and genomes function. We know that it can integrate many variables; and we know some of them, such as the type and location of pre-mRNA motifs that are recognized by the spliceosome as well as by regulatory factors. Other players, like chromatin structure or transcriptional activity, have an impact as well, yet it is not clear how.

We take advantage of the evolutionary conservation of the spliceosome to use budding yeast to study its fundamental properties. The yeast genome includes a few well-defined introns that we can decipher (something not possible yet for most genomes), and alternative splicing is rare. In light of this, it is accepted that the yeast spliceosome must be close to the “core” splicing machinery; defined as that devoted to remove constitutive (= non-changing, or unregulated) introns. Contrarily to what was to be expected, our data indicate that the yeast spliceosome remains capable of alternate modes of exon recognition, producing splicing outcomes thought to be exclusive of more complex systems that include a cohort of regulatory factors (human cells being a perfect example). Since a number of important diseases are caused by malfunctions in this process, it is imperative to reveal which, if any, is the contribution of the spliceosome itself. Our findings indicate that this now has become more feasible thanks to the usability of the yeast system. Moreover, we observe as well that the core spliceosome changes its activity depending on histone modifications, and we are investigating the mechanism at the root of this sensing.

Specific Research Areas:

- *Exon definition mechanisms by the core spliceosome*
- *Impact of histone modifications on RPL30 splicing regulation*
- *Substrate limitations of the yeast spliceosome*