Master in Biomedical Research

2017-2018

List of potential laboratories

Other laboratories would also be accepted

(by alphabetical order using the last name of each principal investigator)
Note: a requisite for admission to the Master in Biomedical Research (BIOMED) is that the student has to be first accepted to do his/her research practicum in a research laboratory in Barcelona.

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

This document contains a few guidelines to help candidate students in finding a research group, and also a list of potential laboratories to which they can submit applications.

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

Last, the masters in Clinical Laboratories (BIOLAC) and Pharmaceutical and Biotechnology Industries of our Department are also valid to continue a PhD program in research, and they offer the possibility of doing a research-related practicum. The admission criteria to these masters do not require the previous acceptance by a research group. We recommend that students who may be interested in biomedical research-related training, but cannot find a laboratory for the BIOMED master, might consider enrolling in the BIOLAC or PHARMA-BIOTECH masters.
“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 usually not financed by the university nor the research center, and they get the money from competitive grants that are given or denied based on publication 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.
Antiprions: a screen for prion mutants interfering with endogenous prion aggregation

Supervisor:
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www.ibmb.csic.es/groups/spatial-control-of-cell-cycle-entry

Summary
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 arresting 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 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.

Specific objectives
We propose to use human prion sequences as initials seeds to perform (1) an extensive and highly sensitive random-mutagenesis based screen to identify antiprion peptides, and (2) a comprehensive functional survey of the isolated candidates as antiprion factors by their ability to counteract aggregation of human prions and their concomitant pathological effects in neurons.
The student will participate in the first objective aiming at the identification of prion mutants with antiprion properties at both cellular and molecular levels.

Selected papers


Project Title:
Study of anti-tumor immune responses in immunotherapy and virotherapy cancer treatments.

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

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Summary of project summary or current research lines (less than 300 words).
Our Cancer Virotherapy Group aims to design and evaluate oncolytic adenoviruses as antitumor agents against different solid tumors. Main areas of research are tumor targeting, intratumoral dissemination through stromal barriers and immunotherapy induced by oncolysis. The group is also involved in other immunotherapy projects based on cancer neoepitopes derived from the mutanome. The group analyzes immune parameters in patients treated in immunotherapy clinical trials and in mouse models of cancer immunotherapy. Some of the techniques applied are: Adenovirus construction by recombineering, immunodeficient and immunocompetent mouse models of cancer, elispot, lymphocyte isolation and cultures, flow cytometry and histology.
Project title (generic): New mechanisms of transcriptional control of inflammatory responses

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

Jose Aramburu or Cristina López-Rodríguez,
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Summary of project summary or current research lines

A main focus of our group is to identify new mechanisms of transcriptional control of inflammatory responses. We study various processes, such as cancer immunotherapy, inflammatory defense against pathogens, and communication between immune cells in transplant rejection.

For more information, see:
https://www.upf.edu/cexs/community/facult/lopez_rodriguez.html
https://www.upf.edu/cexs/community/facult/aramburu.html


The successful candidate will develop a master project aimed at uncovering molecular mechanisms of regulation of immune responses using technical approaches as quantitative analysis of gene expression and chromatin modifications, as well as mouse models of human diseases.

We value a clear motivation for research and a doctorate, as well as the ability to solve problems. We will also consider previous experience in immunology and laboratory training.

Interested candidates, please send your request to Dr. Jose Aramburu or Dr. Cristina López-Rodríguez: cristina.lopez-rodriguez@upf.edu or jose.aramburu@upf.edu, including your CV and the official academic transcript with scores/grades obtained in your university courses.
Project Title:
Negative and positive regulation of the cell cycle by stress.

Project supervisor:
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Summary of current research lines.
Our group is interested in studying the components and molecular mechanisms which regulate the responses to oxidative stress and the control of the cell cycle, using 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 of the group include:


The transitions to enter the S and M phases are tightly regulated upon nutritional and environmental clues. We pretend to characterize the participation of stress signaling cascades in the inhibition of the cycle upon stress imposition and of growth resumption once the stress is over.
Project Title: p27Kip1, an innovative target for Parkinson's disease

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

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

The cyclin-dependent kinase inhibitor p27Kip1 (p27) also behaves as a transcriptional regulator. We recently observed that mouse embryonic fibroblasts lacking p27 have increased levels of α-SYN mRNA and a significant reduction in the mRNA levels of different subunits of the Complex I (CI) of the respiratory chain. These alterations lead to increased accumulation and aggregation of α-SYN, decreased CI activity, reductions in oxygen consumption and generation of oxidative stress, molecular alterations similar to those observed in neurons degenerating in Parkinson's disease (PD). In cells lacking p27 an increased secretion of chemokines as CXCL5 was also observed. These results suggest the intriguing possibility that sporadic PD might arise from a progressive loss of p27 in neurons. The goal of this project is to validate the novel hypothesis that p27, through its non-canonical actions on transcription, plays an active role in the coordinated expression of α-SYN, mitochondrial enzymes and chemokines and that its dysfunction can, therefore, explain the alterations observed in PD patients. To this goal we will use induced pluripotent stem (iPS) cells generated from wild-type and p27 knockout (p27KO) mice or human normal iPS that will be knocked down for p27. These cells will be differentiated to dopaminergic neurons and α-SYN levels, oxidative stress and CXCL5 secretion will be determined. These aspects will be also analyzed in mice brain regions such as the Locus Coeruleus (LC) and the Substantia Nigra (SN). We will also use two conditional p27KO mice strains, one lacking p27 in dopaminergic neurons and the other one with a general p27 deletion to discriminate whether this regulation is cell-autonomous or not. We also aim to analyse the role of the CXCL5 receptor on this regulation and finally, to establish a correlation between p27 levels and these alterations in the LC and SN from PD patients.
Project Title: Role of the transcriptional programs regulated by p27(Kip1) in cancer

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

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

The decrease of nuclear p27, or its cytoplasmic localization, in tumors has been associated with a poor prognosis. The evidence showing that p27 is a transcriptional regulator indicates that these alterations deregulate transcription of its target genes leading to molecular changes that would be associated with poor prognosis.

To raise therapeutic interventions aimed to the functional recovery of p27 in tumors, it is necessary to identify the transcriptional programs regulated by p27 and the mechanisms involved in this transcriptional regulation. Recently, we have described a mechanism through which p27, together with p21, regulates the expression of genes specifically repressed by p130/E2F4 complexes. Moreover, p27 also regulates transcription through its association with other specific transcription factors.

By ChIP-seq and expression microarray analysis the transcriptional programs regulated by p27 have been identified. These programs include cell proliferation, metabolism energetics and cytokine induction. Deregulation of these transcriptional programs is involved in the induction of four of the Cancer Hallmarks. Thus, the decrease of p27 in tumors participates in the generation of Cancer Hallmarks and as a consequence in increasing tumor malignancy. In this project, we aim to analyze the role of p27 in the Cancer Hallmarks generation.

The decreased levels of p27 in tumors, is mainly due to p27 degradation via proteasome. The cytoplasmic retention of p27 occurs by specific phosphorylations of the protein by PI3K/AKT and finally, the inability of p27 to inhibit cyclin-Cdk is produced by specific tyrosine phosphorylation by members of the Src family of protein kinases. Thus, recovering the functionality of p27 in tumors may be achieved by a combination of compounds that attempt to relocate the p27 in the nucleus, to increase their levels and regain their ability to inhibit cyclin-Cdk complexes. The effect of this functional recovery of p27 or tumor development will be analyzed.
Project Title: UNDERLYING BIOLOGY IN LUNG TUMORIGENESIS OF PATIENTS WITH CHRONIC RESPIRATORY DISEASES.

Project supervisor (besides the name, title and position, please include the relevant contact information: e-mail, phone postal address, and webpage).
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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 (163 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). Ongoing research in my group will pursue the identification of novel therapeutic strategies targeted to alleviate muscle mass loss and cachexia in patients with chronic disorders including lung cancer.
**Project Title:** Preventing metastasis initiation by targeting the tumor stroma

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

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 healthy cells activated by tumors that are embedded into the connective tissue surrounding the tumor mass. We have demonstrated that Snail1-expressing CAFs generate a pro-metastatic micro-environment around tumors: the extracellular fibers, such as the fibonectin and collagen fibers, are aligned and the rigidity of the connective tissue is locally higher than that of unaffected tissues.

The master project aims to study how CAFs expressing Snail1 facilities cancer malignance and how their activity can be inhibited.

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

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**Tridimensional reconstruction of a pro-metastatic extracellular matrix.**

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

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

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**Snail1-expressing CAFs remodel the extracellular matrix, which, in turn, promotes Snail1 expression.** Fibronectin fibers are in pink, Collagen fibers in violet and αSMA-stress fibers in green. Focal adhesions are in red.
Project Title: The role of PDK1 in mediating PI3K actions during neurodevelopment and in mental disease

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

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

PDK1 activates Akt, S6K, RSK, SGK and PKC isoforms in response to growth factors, neurotransmitters and ion channels that signal through PI3K. Two PDK1 knock-in mice avoiding the activation of Akt, or the activation of S6K, RSK, SGK and PKC, were generated in the lab. In the PDK1 L155E mice, the inhibition of the PDK1 pathway with intact Akt signalling caused developmental alterations in progenitor proliferation, neuronal polarity and axon outgrowth, which translated onto abnormal cortical layering and reduced connectivity in the adult brain, leading to disrupted behaviour. We are currently investigating the connexion between the developmental defects and the pathology of the adult brain, with especial attention to the pattern of neuronal migration, and the opportunity that these mice could represent a new model for neuropsychiatric disease of the schizophrenia spectrum. In the PDK1 K465E mice, reduced activation of Akt with intact PDK1 signalling resulted in mild alterations in the timing of differentiation that were however compensated in the adult, which exhibited no overt or adverse phenotypes. Moreover, the reduced activation of Akt had homeostatic consequences and protected neurons against ER stress, TNFα, and amyloid beta peptides. We are currently investigating the role of Akt in controlling TACe and the UPR, and exploring whether the PDK1 K465E mice are protected against Alzheimer Disease.
Project Title:

Cross talk between the c-Jun N-terminal kinase pathway and nuclear receptors: Mechanisms and actions

Project supervisor

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

Carme Caelles’s lab studies the principles that govern the mutual inhibitory cross talk between some of the most relevant signalling pathways and the actions mediated by this interaction. In concret, research efforts are directed to gain a better understan (GR)ding of the molecular mechanisms underlying the pharmacological actions of drugs that are ligands for a set of nuclear receptors, in particular the glucocorticoid receptor, the peroxisome proliferator-activated receptors (PPARs) and liver X receptors. These receptors have in common the ability to inhibit the activation of the c-Jun N-terminal kinase (JNK) pathway which is a well-known mediator of pro-inflammatory signalling. For instance, blockage of JNK activation is crucial not only for the anti-inflammatory action of these molecules, but also for other relevant pharmacological actions, such as for the anti-diabetic action of the PPARγ ligands thiazolidinediones (TZDs). On the contrary, exacerbated JNK activity inhibits the GR functionality and, hence, this pathway is a strong candidate to underlie the failure to glucocorticoid treatment in clinics.

List of relevant publications:


**Project Title**: The causes of non-genetic heterogeneity in death and proliferation

**Project Supervisor**: Lucas Carey  
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Group: Single Cell Behavior  
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**Summary**:  
Single isogenic cells are phenotypically heterogeneous. This is implicit in ideas such as LD50 (the drug concentration that kills 50% of cells): in the absence of variability either 100% would be killed, or none would be. What holds for single cells also holds for organisms: when mice are given a toxin or exposed to a virus some mice survive, while others die immediately, even when the mice have the same genome sequence and share a common environment. The aim of my research group is to determine how brief stochastic events at the molecular level generate heritable phenotypic variability in single cells and in organisms. In other words, in the absence of genetic and environmental variation, what is the reason that some individuals survive and proliferate while others die?
Project Title: Analysis of the molecular mechanisms underlying the induction of metamorphosis in insects.

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

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

Most animals, including humans, undergo major transitions during post-embryonic development until reaching adulthood. In all cases, these transitions are promoted by endocrine changes. Puberty in humans is a clear example of a transition triggered by steroidal hormones. Similarly, insects undergo metamorphosis to reach the adult, and this process is also controlled by two hormones, ec dysone and juvenile hormone. In this context, recent work in our laboratory has shown that two hormonal-dependent events are critical to promote metamorphosis in insects: (i) the up-regulation of transcription factors $E93$ and Broad-Complex, which induce metamorphosis, and (ii) the disappearance of the anti-metamorphic transcription factor $Kr-h1$. Despite the importance of both events, however, it is still unknown how the expression of these three genes is regulated during insect metamorphosis.

Using the fly $Drosophila melanogaster$, as insect model, we plan to characterize in detail, that is at the molecular level, the regulatory mechanisms underlying the expression of such critical metamorphic factors. We will use cellular and biochemical techniques, such as cell culture, Chromatin-immunoprecipitation, co-immunoprecipitation, as well as genetics methodologies with different mutant lines to decipher the regulation of these metamorphic genes.
Project Title:

**Editing C. elegans genomes by CRISPR to model Human Diseases**

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

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

We work with a model organism, the nematode *Caenorhabditis elegans* that is widely used in biomedical research. Scientists working with this model have been awarded with three Nobel prizes, including two Nobel prizes in Medicine and Physiology.

Our laboratory is located within a hospital and therefore it is an extraordinary environment to develop translational project oriented to human diseases. There are two main research lines ongoing in our lab: (i) The first intends to identify genes that provide resistance or sensitivity to chemotherapeutic agents such as Cisplatin. (ii) The second relies on the functional characterization of genes regulating splicing whose human homologs are involved in diseases.

A typical master project in our lab include many techniques as manipulation and maintenance of *C. elegans*, purification of DNA and RNA, molecular cloning to construct transgenes, generation of transgenic animals by CRISPR and mutant strains, RNAi experiments, Immunofluorescence, microscopy, Real-Time PCR, analysis and validation of RNA-seq data..etc..  
We are having lab meetings every week and the official language for these meetings is English.
Project Title
Understanding Glioblastoma from the Perspective of Neural Stem Cell Biology

Project supervisor
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Translational Genomics and Targeted Therapeutics in Solid Tumors Team
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Project summary and current research lines

Our research group is a young, highly motivated team devoted to the study of glioblastoma (GBM) from the perspective of neural stem cell (NSC) biology. GBMs, some the most aggressive human tumors, arise from a rare subpopulation of cells which have stem-like properties such as self-renewal, multipotency and the ability to initiate a tumor upon serial transplantation. These so-called glioma initiating cells (GICs) share specific properties with NSCs. This suggests that factors involved in NSC biology are likely to contribute to the pathogenesis of gliomas.

To identify new candidates involved in NSC/GIC biology, we integrate our previous knowledge on developmental neurobiology and adult NSC biology together with bioinformatic analyses of cancer genome datasets such as TCGA. Our projects are highly multidisciplinary and involve the use of molecular biology, cell biology, and mouse modeling approaches to address fundamental questions relevant to NSC and cancer biology.

Main research lines:
• Study of NSC factors in the context of glioblastoma pathogenesis.
• Identification of mechanisms of radioresistance in GBMs.
• Characterization of the immunological properties of GICs.
• Design of novel therapies targeting GICs.

Dr. de la Iglesia was trained as a postdoctoral fellow in the molecular neurobiology laboratory of Dr. Azad Bonni at Harvard Medical School. She is now the principal investigator of the Glioma and Neural Stem Cell group at Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and Research Associate in the Translational genomics and targeted therapeutics in solid tumors Team. IDIBAPS is in the midst of the Hospital Clinic de Barcelona-Faculty of Medicine complex, which provides an extremely favourable environment for research in the biomedical field. Indeed, we are part of the Medical Oncology department (Hospital Clinic), with the ultimate goal to translate our research from bench to bedside. We are also part of Gliocat, a consortium formed by most of the major hospitals in Catalonia for the RNA sequencing of a large cohort of GBM patients with an extremely rich associated clinical database (funded by la Marató de TV3).
**Project Title**: key determinants of emerging viruses infection and their adaptation to human and insect hosts

**Project supervisor**
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**Summary of project**

Emerging mosquito-borne viruses such as the Chikungunya virus (CHIKV), Dengue virus (DENV) or Zika virus (ZIKV) critically rely on their capacity to multiply in mosquitoes and humans. Elucidating how these viruses adapt to such divergent cellular machineries is essential to understand their biology and to develop novel antiviral strategies. Naturally endemic in tropical regions, both CHIKV and its mosquito vector have dramatically expanded to new geographical areas, including Europe. This poses a threat to public health, as CHIKV infection can cause long-term rheumatic disorders and disabilities and neither a vaccine nor specific antivirals are available. A key first step in CHIKV and other emerging viruses lifecycles is to translate their RNA genomes and to express the viral proteins. For this step, they entirely rely on the cellular translation machinery of their vertebrate and insect hosts. To elucidate how CHIKV adapts to the requirements of such evolutionarily distant translation machineries and how they subvert the host gene expression program, we will use RNAseq and ribosome profiling, a novel and exciting technology that allows for high-precision, quantitative measurements of transcriptome-wide translation at codon resolution.

Our multi-disciplinary approach that combines cutting-edge high-throughput analyses, molecular analysis and in-vivo experiments, is the ultimate effort to get the most comprehensive understanding of how emerging viruses cycle between hosts. Moreover, it will define a paradigm for the analysis of other serious emerging viruses and may provide novel antiviral strategies.
Project Title:
Deregulated Nutrient Sensing in Cancer

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

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

A broad interest in the lab is to understand how cells, tissues, and the whole organism respond to changes in nutrients and hormones. In particular, we want to provide mechanistic understanding of the links between elevated nutrient levels and the development of cancer; and conversely, to gain insight into the mechanisms by which restriction in caloric intake limits tumorigenesis. We have focused on the mechanistic target of rapamycin (mTOR) pathway, a key signaling pathway deregulated in cancer, the obesity state, and in several human syndromes characterized by deregulated growth and cancer. The mTOR kinase responds to changes in local nutrient levels (i.e.: amino acids and glucose) in a cell autonomous manner, and indirectly to changes in organismal nutrients levels via its activation by growth factors. When activated, mTOR drives most anabolic cellular processes such as synthesis of protein, ribosomes, nucleotides, lipids; and suppresses catabolic processes such as autophagy. We study the regulation and consequences of normal and pathological mTOR activation by means of a combination of cellular, metabolomic and biochemical approaches and fundamentally, by studying physiology in the context of genetically engineered mice. Combining these approaches is critical to understand the causes of aberrant regulation of this pathway in the pathogenesis of cancer, but also in the pathogenesis of diabetes and aging, all of which can hardly be modeled without adequate genetic tools in mice.
Project Title: Towards personalized therapies for colorectal cancer patients

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

Dr. Lluis Espinosa, PhD
Head of the Molecular Mechanisms of Cancer and Stemness Group.
Program on Cancer Research, IMIM
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Summary of project summary or current research lines (less than 300 words).

Despite the recent scientific and medical advances, current colorectal cancer (CRC) prognostic and treatment are based on histopathological characteristics, imaging techniques and on the mutational status of KRAS, NRAS and BRAF. In this scenario, a proportion of the patients relapse even when they receive the appropriate treatment. The general objective of this project is to combine the cutting-edge techniques of Patient Derived Orthoxenografts (PDOX), 3D tumoroids and Whole Exon Sequence (WXS) analysis to obtain mutational patterns that predict therapy response. Specifically, we will generate a collection of PDOX from CRC cases and their corresponding cultured tumoroids, and we will characterize them by WXS. We will then perform drug testing on the vitro expanded tumoroids including 40-50 FDA-approved compounds available at Shelleckchem. Most relevant results will then be validated in the PDOX model. In depth analysis of molecular data in combination with drug-response/resistance data will permit the identification of mutational patterns than define therapeutic assignment. The predictive value of our conclusions will be validated in 1) an independent cohort of fresh human tumors and 2) by IHC analysis of candidate driver pathways on a Tissue Microarray containing retrospective CRC samples with available molecular and clinical data. Of note, that our objectives go beyond the current proposal, as all biological material (PDOX and tumoroids) will be deposited in Marbiobanc, and made accessible to the scientific community for future investigations.
Project Title: Innate Immunity against HIV infection

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

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

The result of any viral infection depends largely on innate and adaptive immune responses that accompany it. Innate immune cells such as macrophages are usually the first point of contact with pathogens, including retroviruses. However, there is sufficient evidence to indicate differences in the innate response of patients that could explain the lack of progression or slow progression of human immunodeficiency virus (HIV) infection or effective control of hepatitis virus (HCV or HBV) infections in a group of individuals co-infected with HIV. Our goal is to understand the cellular and molecular basis of induction of innate response to chronic viral infections as a means to establish new strategies to cure HIV infection and AIDS.

The development of this project could lead to the validation of new markers for monitoring and controlling infection in the post HAART era, and identifying strategies to reduce chronic activation in HIV-positive patients.

Recent publications
Project Title: Characterization of the network genes that control metamorphosis

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

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

A great variety of organisms, including humans, undergo major transitions during post-embryonic development. Puberty in humans is associated with major endocrine and phenotypic changes. Likewise, metamorphosis in insects is associated with major physiological and morphological changes. Despite the relevance of these transitions, interesting questions still remain unsolved: at what time in development an organism decides to exit juvenile development to undergo the changes required to become a fully reproductive adult? and, what are the signals that induce such transitions?

To answer both questions, we are currently using the beetle Tribolium castaneum and the fly Drosophila melanogaster as insect models to investigate the factors and the physiological/genetic mechanisms underlying the initiation of major life history transitions, particularly the metamorphic transition. To this aim, we are using RNAi and CRISPR/Cas9 methodologies, as well as different molecular and cellular techniques (immunocytochemistry, in-situ hybridization, qPCRs, among others), to characterize the role of different signaling and endocrine pathways in the control of the metamorphic transition.

Given the conservation, these studies on Tribolium and Drosophila would provide important understanding of how metabolic and endocrine disorders affect the timing of puberty in humans.
**Project Title:**

EFFECT OF THE SYSTEMIC COPD ENVIRONMENT ON THE MYOGENIC FUNCTION OF MUSCLE PRECURSOR CELLS

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

Joaquim Gea

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

Chronic Obstructive Pulmonary Disease (COPD) is a multi-component disease with systemic abnormalities. Skeletal muscle dysfunction and atrophy, particularly of the limb muscles, is one of the most prominent and extensively studied systemic effect, and a major contributor to exercise limitation and impaired quality of life. Moreover, it’s a predictor of morbidity and mortality which is partly independent of the severity of the airflow limitation.

Acute exacerbations of COPD aggravate the extrapulmonary consequences of the disease and contribute to further deteriorate skeletal muscle function. Patients who experience frequent acute exacerbations have more severe muscle wasting and reduced recovery of muscle mass and function after each exacerbation.

Satellite cells (SCs) represent the primary source of myogenic precursor cells contributing to the processes of muscle mass maintenance, hypertrophy and repair after birth. Their myogenic function is very sensitive to microenvironmental factors contained in the so-called SC niche, which arise both, from local and systemic sources.

Bearing all this in mind, the objective of our investigations is to address the possibility that components of the COPD systemic environment could provide an inappropriate environment to SCs, affecting their myogenic efficiency, and contributing to compromise maintenance of peripheral muscle mass.

To carry out our objective, culture of SCs obtained from human muscle biopsy samples are used as model system. SCs are exposed to the serum obtained from control subjects or COPD patients with or without acute exacerbations. We investigate whether different sera affect myoblast proliferation, differentiation and myotube size in SC cultures under growth or differentiation conditions.

Proliferation is measured using a BrdU incorporation assay. Studies for induction into myoblast differentiation pathways include quantification of myogenic markers at the mRNA and protein level by reverse-transcription polymerase chain reaction and Western blot analysis. In addition, microscopic examination of SC cultures and immunofluorescence are used to assess polynucleated myotube formation.

Understanding the molecular mechanisms that govern muscle mass wasting and recovery is crucial to develop proficient intervention strategies in chronic diseases such as COPD.
**Project Title:**
Eukaryotic protein quality control and protein oxidation; effects on aging

**Project supervisor:**
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**Summary of current research lines.**
Our group is interested in studying the components and molecular mechanisms which regulate the responses to oxidative stress and the control of the cell cycle, using 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:


We have isolated 20 genes controlling the fate of oxidized proteins, and therefore contributing to lifespan. The aim of this project will be to characterize several of them, most of which are involved in the ubiquitin-proteasome system and to autophagy.

![S. pombe](image1)  
![Protein carbonyls](image2)  
![Loading control](image3)
**Project Title:** Snail1 function and activated fibroblasts in epithelial tumorigenesis

**Project supervisor:** Antonio García de Herreros, Programa de Recerca en Càncer, IMIM-Hospital del Mar, Parc de Recerca Biomèdica de Barcelona, Room 298.03, agarcia@imim.es, Tel 93 – 3160433.

**Orientative project summary or summary of current research lines:**

Years ago our group reported that Snail transcriptional factor down-regulated E-cadherin expression and induced an epithelial-mesenchymal transition (EMT) in tumor cells (Batlle et al 2000, Nature Cell. Biol. 2: 84-89). Our group has kept working on this transcriptional factor that is the main object of our research, not only as an E-cadherin repressor but also as an inducer of EMT. Therefore we have studied targets of Snail1 relevant for EMT and other effects of Snail1 expression in epithelial cells, such as the induction of invasiveness, resistance to apoptosis or stemness. We have also analyzed in detail the mechanism of epithelial gene repression by Snail1 in genes directly inhibited by this factor, determining how Snail1 modifies epigenetic marks and also characterize the mechanism used to activate mesenchymal genes. We have also studied how Snail1 transcriptional activity is controlled. Recently we have identified two new Snail1 ubiquitin ligases modulated by several cellular stresses and explaining the rapid Snail1 stabilization in these conditions. (Viñas-Castells et al, Nucl. Acids Res. 42, 1079, 2014). Moreover, we have determined that Snail1 protein stability is controlled specifically by Akt2 isoform through the inactivation of GSK3b (Frias et al, Mol. Cell Biol. 2016, 36, 923-940).

The most recent work of the group has been focused on the relevance of Snail1 expression in the tumoral stroma. 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 maintenance of the undifferentiated phenotype of mesenchymal stem cells a cellular entity very similar to cancer activated fibroblasts. Snail1 depletion causes the premature differentiation of these cells to adipocytes or osteoblasts (Batlle et al, 2013, Oncogene 32, 3381). Moreover, our results indicate that activation of mesenchymal stem cells or fibroblasts with TGF-β is impaired in Snail1 KO cells; Snail1 is required for a full transcriptional as well as functional response to this cytokine. Snail1 is also needed for the correct physiological function of activated fibroblasts, either in the pancreas (Loubat et al, 2016, Oncotarget 2016, 7. 4468-4482) or during the process of wound-healing (Stanisavljevic et al 2015, Cancer Res. 75, 284). We are 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 in the presence of fibroblasts the invasive capability of tumoral cells is markedly enhanced, supporting the well-known effect of the stroma on tumor development. Snail1 expression in fibroblasts is required for this supportive effect (Lorena-Castellón et al, Cancer Res., 2016, 76, 6205-6217). The molecular basis of these effects is being investigated, both in vitro assays and in tumor animal models. Our group is also analyzing the role of Snail1 in other cells of the stroma, such as endothelial cell or macrophages that also play a role in the invasion of tumor cancer cells.
Project Title: Molecular basis of cellular memory

Project supervisor: Jordi Garcia Ojalvo
Full Professor of Systems Biology
Group leader, Dynamical Systems Biology
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Summary of project summary or current research lines (less than 300 words).
The goal of this project is to analyze how the structure of cellular regulatory networks determines the ability of cells to store a record of preceding environmental signals, and eventually forecast future conditions. The study will be done on transcriptional, protein-protein and metabolic networks, and will make use of statistical and complex systems methods to examine computationally the structural properties of those networks, and their role in establishing their dynamical behavior.

Project Title: Detecting oscillatory dynamics in single-cell transcriptomics data

Project supervisor: Jordi Garcia Ojalvo
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Summary of project summary or current research lines (less than 300 words).
Our cells contain genetic circuits that generate rhythms of protein expression with a variety of periods ranging from minutes to hours. These oscillations have a variety of physiological functions including reacting to a dynamical environment. Studies of the biomolecular circuitry underlying these oscillators have been restricted so far to low-throughput analyses that are limited to small numbers of genes and do not take into account the intrinsic heterogeneity in cell populations. But the recent development of high-throughput transcriptomics data at the single-cell level is enabling us to address these issues using big-data approaches. The objective of this project is to evaluate and use a variety of statistical analysis and machine-learning methods (including correlation and clustering analysis, information theory and reservoir computing strategies) to provide a time-line to existing single-cell transcriptomics data sets (which are usually time-less). We will use to that end known oscillatory genes as anchors, and will attempt to identify other potential contributors to cellular rhythmicity, and potentially uncover previously unknown effects of these rhythms to the functioning of cells.
**Project Title:**

Exploring the role of Cyclin O in chromosomal instability

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

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**Summary of project summary or current research lines.**

Most human cancers are characterized by being aneuploid (their cells have an abnormal chromosome number) and show an ongoing rate to change their karyotype, a phenomenon known as chromosomal instability (CIN). CIN arises as a consequence of mitotic dysregulation and it is already present in the earliest stages of carcinogenesis. CIN is a prognostic indicator of risk of relapse and/or disease progression in many tumour types.

The segregation of newly replicated chromosomes into daughter cells takes place during the M-phase of the cell cycle and the biochemical machinery involved in the process and its regulation is well characterized. A gene signature which includes the main regulators of the process (CIN70) has been described as being altered in human tumours.

Cyclin O is a member of the cyclin family identified in our laboratory that is involved in the cellular response to DNA damage (Roig et al., 2009 Cell Death Differ. 16:230-243) and in ciliogenesis (Jung et al. submitted). We are interested in studying the regulation of Cyclin O by the tumour suppressor p53 in response to DNA damage and to explore the connection between Cyclin O overexpression in human tumours and centrosome amplification. The centrosome is formed by a centriole and its associated pericentriolar proteins. During the G1 phase of the cell cycle normal cells have a pair of centrioles that are duplicated synchronously with the DNA to allow for the assembly of the mitotic spindle in the M-phase. The centrioles are also the precursor structures of the cilia and Cyclin O regulates centriole amplification in multiciliated cells. Since most tumour cells show centrosome amplification and Cyclin O overexpression, we will explore the regulation of the CIN70 signature by Cyclin O and its putative role in centrosome amplification in non-ciliated epithelial cells.
Project Title:

Cloning, overexpression, purification and functional studies of a proteolytic enzyme

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

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Direct supervision at the bench will be carried out by an experienced member of the hosting lab.

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

For biotechnological applications and assays of enzymes and other proteins it is indispensable to be able to produce sufficient amounts of pure material with which to perform biophysical, biochemical, functional and structural studies. The aim of the present module is to provide students of the BIOMED Master’s Degree with the required practical skills to obtain large amounts (in the milligram range) of purified proteins as part of a wet-lab practicum in a biochemical laboratory dedicated to basic research. For this, the selected student will be introduced into key techniques aimed at cloning, recombinant overexpression, chromatographic purification of proteins, and functional assays under the guidance of an experienced researcher.
Project Title:

Using Drosophila model to understand malignant growth.

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

Prof. Cayetano González https://www.irbbarcelona.org/en/research/cell-division-laboratory
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Summary of project summary or current research lines (less than 300 words).

We model cancer in flies to understand the cellular changes that drive malignant growth and to identify conserved mechanisms that might be relevant for human cancer therapy. We focus on the mechanisms of malignant transformation in larval brains where we have found that neural stem cells can originate tumours if the process of self-renewing asymmetric division is disrupted, and that some tumour types are driven by the ectopic expression of germline proteins. We work on the mechanisms that bring about genome instability in Drosophila tumours and try establishing the actual extent to which such lesions contribute to tumor progression. We develop and make extensive use of advanced microscopy techniques.

The goal of this Master project is the characterisation of genes that we have recently found to be required for malignant growth in our tumour models. The Master student will take part in ongoing molecular, biochemical and microscopy studies.

The Master student is expected to take full part in lab seminars and scientific discussions and will acquire hands on experience in Drosophila research. S/he will also gain training in experiment design.
Project Title:

Chromatin regulation of human and viral gene expression

Project supervisor

Albert Jordan, PhD, Científic Titular CSIC, Group leader
Institut de Biologia Molecular Barcelona IBMB-CSIC, Dept. Molecular Genomics
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Orientative project summary or summary of current research lines

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.

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, in different cell types. 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, with an extensive use of Genomics and Bioinformatics.


In a second line of research, we use an HIV promoter model to investigate the influence of chromatin organization at the integration site on HIV expression, with a focus on the role of heterochromatin and transcriptional interference on the establishment of viral latency. Moreover, we screen for and characterize new HIV latency reactivation drugs.

Please do not exceed 1 page.

Project Title:
Molecular mechanisms underlying defective brain development and neuronal degeneration.

Project supervisor (besides the name, title and position, please include the relevant contact information: e-mail, phone, postal address, and webpage).
Dr. Jens Luders, Group Leader
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required info:
CV, grades, motivation letter

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

During brain development the microtubule (MT) cytoskeleton drives the divisions of neural progenitor cells (NPCs) to increase NPC number, mediates migration of differentiating neurons to allow correct formation of brain architecture, and promotes neuronal morphogenesis by transporting membrane and protein cargo to distinct subcellular compartments. In human patients mutations in genes encoding components of the microtubule cytoskeleton can interfere with any of these processes causing severe nervous system defects such as brain malformation (e.g. microcephaly) or neuron degeneration. Unfortunately, the molecular mechanisms underlying most of these disorders remain poorly understood. While there is currently no therapy aimed at correct neuronal development, recent work has demonstrated that MT-stabilizing drugs can promote axon growth and regeneration in spinal cord neurons after injury. While these studies establish MTs as a prime target for promoting axon regeneration, the use of MT-targeted drugs globally inhibits MT dynamics, impairing neuron homeostasis and leading to severe side effects. Using cultured mouse primary NPCs and neurons as a model, the student will study candidate proteins previously identified in our lab, with the goal of unraveling molecular disease mechanisms and/or identifying targets to promote axon regeneration after injury.
Project Supervisor

Name: Maria J. Macias

Group: Structural characterization of macromolecular assemblies

Dept: Structural & Computational Biology Programme

Institution: Institute for Research in Biomedicine (IRB Barcelona)

web page: maciasnmr.net and irbbarcelona.org

Project Title

Analysis of tumor mutations in Smad proteins and co-factors

Brief Summary (maximum 100 words)

Smads are central mediators of the effects of TGF-β and BMP factors that regulate embryo development, immunity, tissue maintenance, and both, tumor progression and suppression. Our lab is interested in providing new structural information of complexes between Smad proteins, co-factors and DNA, complexes that are key to control stem cell differentiation and that also have implications in the role of TGFβ signaling in tumor suppression.

We have open positions for students to analyze the impact of tumor mutations in the fold and function of Smads proteins -with and without oncogenic mutations, using sequence analysis, molecular and structural biology, (X-ray, NMR).

Master Programmes

Master of Genetics and Genomics, human genetics: Cancer

Master Biomedical Research, BIOMED (UPF)

Master in Biomedicine (UB)

Master in Molecular Mechanisms of Disease (RIMLS)

Master in Omics Data Analysis (UVIC)

Additional information: maria.macias@irbbarcelona.org

Please provide a CV and the academic records
**Project Title**: Insulin and RNAi in insects.

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

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

At present in our group we are working on two related research lines:

- In the first place we are studying the function of the insulin pathway in insects and its relation to different processes, mainly reproduction and growth. To address this issue, different methodologies are used, among them interfering RNA (RNAi) techniques and the analysis of the phenotypes produced by this treatment, using quantitative real-time PCR for quantifying mRNA levels or in vitro incubations for quantifying hormone production.

- Secondly, we are interested in understanding how RNAi works in insects for producing the RNA knock down effect. This study involves the analysis of the characteristics of the dsRNA molecules for producing the maximum effect, how Dicer and Argonaute enzymes contribute to the knock down and which intermediary molecules (small interfering RNAs) are more propitious to be produced. As the model molecule for RNAi treatment we are using the Insulin Receptor, for which we know the phenotype that its knock down produces.

  We use as a model the cockroach *Blattella germanica*, a species with which we have been working for more than twenty years and in which RNAi works extraordinarily well.
Project Title:

**GENETIC CONTROL OF SPINAL CORD MORPHOGENESIS AND GROWTH, A MODEL TO STUDY NEURODEVELOPMENTAL DISORDERS**

Project supervisor:
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Summary of current research lines:

The spinal cord is the anatomically simplest and most conserved region of the vertebrate central nervous system. Moreover, since the spinal cord is generated over an extended period in a head to tail sequence, not only is instrumental in understanding the mechanisms that control the growing organ, but is also essential to approach neuro-developmental disorders. In the lab, we have been working for 15 years on the generation of cell diversity during development of the spinal cord. Recently we have opened new lines aimed at understanding two additional key events; the generation of organ shape and size, two key event with direct implications in human health. Taking advantage of our background on the study of spinal cord development, we now propose to tackle the following general objectives:

- The generation of the Secondary Neural Tube (SNT), a model to study closed spina bifida; development of the posterior spinal cord involves the elongation and cavitation of the tail bud in a poorly understood process called secondary neurulation. Importantly, faulty SN is the cause of closed spina bifida. Here, we propose an approach combining live imaging and data from transcriptomics and functional genetics, to unveil the gene regulatory networks and tissue dynamics of secondary neural tube (SNT) formation and to generate computational models with predictive capabilities.

- The control of cell numbers and organ size at birth, 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. In the course of the previous grant from Plan Nacional, we demonstrated that Sonic hedgehog (Shh) and BMP signalling are required for the expansion of the pool of progenitors by maintaining symmetric divisions. Here we propose and approach combining high resolution imaging and data from transcriptomics and functional genetics, to describe the mechanisms downstream these growth factors that regulate neural stem cell maintenance.
Project Title: Regulation of steroid hormone biosynthesis by signaling pathways in Drosophila

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

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

A critical feature of animal development is that regulatory processes must be tightly timed to coordinate cell growth and differentiation at particular life stages. In humans, for example, transition from adolescence to adulthood is correlated with rapid changes in growth and the acquisition of sexual maturity. Similarly, in insects developmental transitions also occur at regularly defined intervals. A particularly interesting transition in insects is the metamorphic one, in which the immature larva transforms into the reproductively mature adult. Interestingly, the metamorphic transition is mainly controlled by circulating pulses of steroid hormones produced and released from a specific gland, the Prothoracic Gland (PG). Unfortunately, and despite its relevance for the proper development of the insect, little is presently known about the regulatory mechanisms that control ecdysteroid biosynthesis in the PG.

By using the genetic model system Drosophila, and a variety of cellular and molecular techniques (genetics, immunocytochemistry, in-situ hybridization, qPCRs among others) we aim to uncover signaling and neuroendocrine circuits required for the regulation of ecdysteroid biosynthesis during the metamorphic transition, with a particular attention to the role of different signaling pathways.

Given the high degree of conservation, these genetic studies on Drosophila would eventually provide critical insights for understanding how diseases, such as metabolic disorders like obesity and diabetes, affect steroid production in humans and how the timing of puberty is controlled.
Project Title: "Epigenetic defects in intellectual disability: role of histone demethylase PHF8"

Project supervisor:
Group: Signaling to chromatin, IBMB-CSIC, Parc Cientific
Supervisor: Máriam Martínez Balbás (Investigador Científico CSIC); e.mail: mmbbmc@ibmb.csic.es. Phone: 93 4034961/34934020185; Fax: 93 403 4979; Web: http://www.ibmb.csic.es/groups/molecular-signaling-and-chromatin

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

Student Project: Epigenetic mechanisms that regulate the accessibility to the genetic material are the basis of cell differentiation and embryonic development. We are interested on histone H4 methylation of lysine 20 (H4K20me). Recently it has been identified the enzyme responsible for this activity, PHF8, is strongly associated to intellectual disability and autism. However, the PHF8 function and the molecular mechanisms responsible for it role during neurogenesis are not clearly established. In the project the student will help to characterize its function during neural differentiation.
**Project Title:** Pooled Deep Sequencing of Antimalarial Resistance Genes through Next Generation Sequencing

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

Thesis director

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

To adequately address the malaria challenge in Mozambique (where 29% of all deaths are due to malaria), a specific program has been designed by Mozambican Ministry of Health to intensify control measures and introduce new strategies to accelerate the decrease of malaria. The program aims to reduce the parasite prevalence by 90% in the population from Magude district (65000 individuals) of southern Mozambique through several rounds of Mass Drug Administration (MDA) with Dihydroartemisinin plus piperaquine (DHA-PPQ). Although MDA can be effective in treating malaria cases in Magude district but the development of drug resistance (DR) is inevitable. MDA provides the highest possible selective pressure for resistant parasites. The extremely short half-life of DHA, combined with the very long half-life of PPQ will result in monotherapeutic levels of PPQ for several months, potentially leading to resistant parasite selection, thus endangering all the efforts of health care systems to control or eliminate malaria infection. For this reason, we aim to develop a rapid and efficient method using advanced molecular technology such as Next generation sequencing (NGS) to assess and track resistant parasites arise due to MDA, could be useful for the success of malaria control and elimination programs. We will use known molecular markers of DHA-PPQ resistance to develop this assay. Further, we will validate this assay in the field isolates collected before and after MDA.
Project Title: Systemic analysis of virus infection fate regulation

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

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

Viral infections can be fundamentally categorized as acute or persistent according to their temporal relationships with their hosts. Acute infections are usually resolved within a few weeks. By contrast, persistent infections are not resolved and, instead, develop when the immune response is not sufficient to eliminate the invading virus during the primary infection phase. Viruses from both categories continue to threaten human health. Notable examples are Influenza virus and infections with the Human Immunodeficiency Virus or the Hepatitis B and C viruses.

A number of viral and host factors are involved in the fate decision between an acute and a persistent infection outcome. However, the key host sensing system is not known and the relationship between these factors is still poorly understood. A major remaining question is how the host organism senses the balance between all implied components, and how and when it decides whether it is worth continuing the fight against the infecting virus or whether it is better to surrender via downregulating immune effector mechanisms in order to avoid immunopathology.

Aim of the project is to better understand how the outcome of a non-acutely-lethal virus infection is controlled. The underlying hypothesis is: a host organism senses the threat of an infection by means of dynamic virus-host interactions and then decides (i) to keep augmenting antiviral responses until the virus is eliminated, or (ii) to surrender and down-regulate antiviral responses to avoid host damage due to continued inflammatory responses.

To address this fundamental and complex issue we use a virus-infection mouse model system that allows the establishment of acute or persistent infections by inoculating the animals with different virus doses. Bioinformatics systems analysis of spleen-specific transcriptomes of mice with different infection outcomes has allowed generating hypotheses on infection fate regulation. The master thesis will be focused on one of these hypotheses.
**Project Title:**

Drosophila as a model system in cancer biology

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

Marco Milán, IRB Barcelona


marco.milan@irbbarcelona.org

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

Cancer is a multi-hit process involving mutations in oncogenes and tumor suppressors, as well as interactions between the tumor cells and the surrounding stroma. Cancer as a disease is characterized by a series of hallmarks, which include sustained proliferative signalling, resistance to growth suppressors and to cell death, increased replicative immortality, invasiveness and metastasis, energy metabolism reprogramming, genome instability, and inflammation. Our lab is interested in the cellular and molecular mechanisms underlying the regulation of many of these hallmarks, especially the role of Genome Instability in tumourigenesis. The fruit fly, Drosophila, is an excellent, genetically-tractable system for modelling the development of cancer, due to the conservation of signaling pathways, cell proliferation and survival genes between fly and humans, its suitability for genetic and molecular manipulations, and its well-described developmental biology. Working with flies (an in vivo approach) allows the analysis of tumours at the cellular level but also at the systemic level (relationship between tumours and the rest of the body).
Project Title:

Molecular mechanisms of signal integration in tumorigenesis

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

Ángel Nebreda, IRB Barcelona


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

We are investigating molecular mechanisms of tumorigenesis, especially regarding how the p38 MAPK signalling pathway regulates cell viability, proliferation and invasion, using a combination of biochemical approaches and studies in human cancer cell lines. An important question is how this signalling pathway contributes to the ability of tumor cells to bypass normal controls. We also use genetically modified mice, which allow the inactivation of this pathway in a regulated and tissue-specific manner, and chemical inhibitors to investigate physiological functions of p38 MAPKs and their role in lung, colon and breast cancer, as well as the connection between inflammation and tumorigenesis. We are very interested in the identification of therapeutic opportunities based on the modulation of p38 MAPK signalling. Moreover, we are studying the regulation and functions of a new family of proteins named RINGO that can activate the cell cycle kinases Cdk1 and Cdk2.
Project Title: Understanding stress adaptation

Project supervisor: Dr. Francesc Posas / Dr. Eulàlia de Nadal

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Summary of project summary or current research lines

The main focus of our group is to understand how cells detect and respond to environmental changes. We have focused our studies on the characterization of the stress signal transduction pathways, especially those controlled by MAP kinases of the Hog1/p38 family, also known as the Stress Activated Protein Kinases (SAPK). We study the molecular mechanisms required to respond to changes in the extracellular environment and the adaptive responses required for cell survival. Proper adaptation to stress involves the modulation of several basic aspects of cell biology, such as the control of cell cycle progression and regulation of gene expression. We also analyze the basic signaling properties of the HOG pathway using single cell analysis and how to engineer it, based on quantitative data collection and mathematical modeling. Moreover, our studies on signal transduction processes include the assessment of single cell transcription and cell cycle analyses to understand cell-to-cell variability in stress adaptation.

References:
Gene Regulation in Cell Differentiation and Cancer

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Summary of project summary or current research lines

ZEB proteins (ZEB1 and ZEB2) regulate key master genes during development, cell differentiation, tumor invasiveness and metastasis (reviewed in EMBO Rep 11:670; Cell Mol Life Sci, 69:3429). ZEB1 is also involved in regulation of normal cell differentiation in skeletal muscle (Mol Cell Biol 33:1368). Over the last few years ZEB1 and ZEB2 have gained great relevance in cancer biology as inducers of an epithelial-mesenchymal transition (EMT), thus promoting tumor invasiveness and metastasis (Genes & Dev 22:894; Nat Cell Biol 11:1487; Oncogene 29:3490; PNAS 108:19204; Clin Cancer Res 19:1071; Cell Death Differ 21:247; Gut 66:665). Recent work by our group and others indicate that ZEB proteins also regulate earlier stages of cancer development. On the one hand, ZEB1 and ZEB2 determine phenotypic and functional stemness in normal and cancer stem cells as well as the resistance of cancer cells to chemotherapy drugs (Nat Cell Biol 11:1487; Cell Stem Cell 4:336; Nature Neurosci 12:1369; Cell Stem Cell 6:59; Cell 154:61). On the other hand, ZEB proteins act as both tumor suppressors as well as mediating oncogenic transformation and benign-malignant transition induced by signalling pathways such as Wnt, Ras, Notch and p16/Rb (Cell 47:382, PNAS 108:19204, Mol Cell 38:114, Cancer Cell 15:489; Nature Comunications 4:2650; Nature Commun 5:5660; Oncogene, 34:5760).

See https://www.icrea.cat/Web/ScientificStaff/antonio-postigo-379 for selected publications by the group

The selected candidate(s) would have the opportunity not only to develop his/her own research Master Project but also to get involved in other research lines currently ongoing at the lab, participate in publications and learn a wide range of molecular and cellular biology techniques using in vitro and animal models with the eventual goal of entering a PhD program.

Requirements: Bachelor in Biology, Biotechnology or related biomedical-related discipline. Candidates with a strong academic record (higher than 2.8/4.0 or 8.6/10), previous lab experience and interested in pursuing later a PhD will receive special consideration in the selection process.

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 or research performance to idibaps.postigo2@gmail.com indicating “Master UPF
Please do not exceed 1 page.

**Project Title:**
Deciphering how cell diversity is generated in the developing hindbrain.

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

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

The Central Nervous System is initially subdivided into regions with distinct identity that underlies the generation of a specific set of cell types, each of which must arise at the right time and place and in the correct proportions for normal development and function. We focus our studies on the embryonic development of the hindbrain, as a model to study how cellular compartments operate during brain development, and how cell diversity is generated. Our goals are to unveil when and how brain progenitors commit to a given fate, how they behave once committed, and how cell fate decisions are regulated to generate the distinct cell lineages.

The main aim of the project is to study how cell diversity is generated in the developing hindbrain. We want to understand how the neurogenic/gliogenic capacity is allocated to specific regions of the hindbrain. We combine high-resolution in vivo imaging and gene transcriptional activation signature analyses.

Our model system is the zebrafish embryo because it permits to combine genetic tools with high resolution imaging approaches. The candidate will be involved in the generation of different transgenic lines by the genome editing system CRISP/Cas9, and in the cell lineage analysis of rhombomeric cell populations.
Project Title:
Why some individuals are strongly resilient to develop cancer?

Project supervisor.
Miquel Angel Pujana
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Summary of project summary or current research lines.

The study of the genetic basis of hereditary cancer has been commonly focused on understanding molecular perturbations in affected individuals. Thus, many genetic risk factors have been discovered in the past years. However, understanding why individuals at high risk (i.e. carriers of germline mutations with large effects) do not develop cancer remains an unexplored fundamental subject. The identification of strongly protective alleles or mutations for specific cancer syndromes, such as breast and ovarian cancer, will revolutionize cancer prevention and treatment. Here, we propose a multidisciplinary research project aimed at identifying such mutations and genes.
**Project Title**: DISCOVERING THE FUNCTION OF NEW GENES INVOLVED IN PANCREATIC AND BLADDER CANCER IDENTIFIED THROUGH MASSIVE PARALLEL SEQUENCING

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

Francisco X. Real  
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Universitat Pompeu Fabra, Barcelona  
and  
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Project to be conducted at the CNIO, Madrid

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

Massive parallel sequencing (MPS) provides unprecedented opportunities to identify new cancer genes. We have applied MPS to urothelial bladder cancer gene identification and are now assessing the role of candidate genes at various levels. Some of these genes, and others that we have identified through other strategies, play also a role in pancreatic cancer.

These are some of the questions we tackle:

1) **the genetics**: how prevalent are the mutations? where in the gene/protein do they occur? are they restricted to specific tumor subtypes? are they specific to discrete tumor progression pathways?
2) **the biology**: how do these genes contribute to cancer development/progression? we use a variety of strategies including knockdown/CRISPR/overexpression and phenotypic analysis in vitro and in vivo;
3) **the clinical application**: can the gene mutations identify patients with distinct outcome? can they be applied to the detection of the tumor in urine or plasma?
4) **the therapy**: can these genes be targeted therapeutically? are there drugs available? can in vitro or in vivo models be used to assess the therapies? can synthetic lethality strategies be used to target tumors harbouring these mutations?

If you want to contribute to answering them, you can work together with students and postdocs in the group to move the story forward!

**Recent publications related to this project**
**Project Title:** New therapeutic targets for acute myeloid leukemia stem cells

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

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

Acute myeloid leukemia (AML) is a neoplasia characterized by the rapid expansion of immature myeloid blasts in the bone marrow. The course of the disease is marked by poor prognosis, frequent relapse, and high disease-related mortality. As such, new therapeutic approaches are required for remission induction and prevention of relapse. The difficulty in treating AML is thought to arise from a chemoresistant subpopulation of leukemia stem cells (LSCs) that are capable of maintaining and reinitiating disease. Our research program focuses on the development of therapeutic strategies for targeting LSCs.

Due to the higher chemotherapy sensitivity and limited life span of more differentiated AML blasts, differentiation-based combinatorial therapies that eliminate blasts are a promising therapeutic approach. As LSCs display the highest differentiation capacity due to the tightly regulated balance between self-renewal and differentiation, a therapy that favours differentiation would potentially also exhaust this population and eradicate the cells responsible for the initiation and maintenance of AML. An in silico screening was performed to search for already FDA-approved drugs that may induce LSC differentiation and spare healthy hematopoietic stem cells (HSCs). The drugs identified are been validated in vitro and ex vivo. The mechanism of action of these drugs on AML-LSCs will be characterized and their potential clinical use for leukemia will be studied. Additionally, new therapeutic targets from the signalling pathway identified will be evaluated. While describing the signalling pathway implicated in the block of differentiation will increase the knowledge of the biology that drives the leukemogenesis process, searching for new drugs that disrupt this intracellular signalling will allow new biomarkers and therapeutic targets to be defined for AML, and especially LSCs.
Project Title:

Study of endocannabinoid biomarkers in cell cultures of olfactory epithelium pro-neurons associated with neurocognitive alterations in mental disorders

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

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

The overall objective of our project is to implement a platform of neuronal precursor cell cultures from olfactory epithelium tissue to develop diagnostic biomarkers in different types of psychiatric diseases such as schizophrenia, bipolar disorder and depression. Current evidence has put forward the involvement of the endocannabinoid system in the cognitive and affective alterations associated with these mental disorders. Thus, we will investigate the differential changes in endocannabinoid biomarkers such as AEA and 2-AG and CB1 and CB2 receptors in pro-neurons of the olfactory epithelium and associate them with the cognitive and affective dysregulations observed in patients affected by these pathologies. In order to understand the impact of long-term treatment on these biomarkers, we will also study psychotic patients treated with antipsychotics for a short period of time and compare them with chronic schizophrenic patients of whom we already have cell cultures and cognitive functional data. In parallel pre-clinical studies we will evaluate the expression and functionality of the CB1-5HT2A heteromers after a chronic treatment with classical (typical, atypical) antipsychotics and with cannabidiol in animal models of psychosis. In addition, since CB1 receptors modulate both GABA and glutamate release in the brain, and it is known that the deleterious effects of cannabis on long-term memory are mediated by the action of these receptors on GABAergic neurons of the hippocampus, we propose to determine the differential localization of the CB1-5HT2A heteromers in the brain using transgenic mice deficient in CB1 receptors in GABAergic neurons and in mice deficient in CB1 receptors in glutamatergic neurons. In these models, we will also investigate the involvement of these receptors with specific localization in the pro-psychotic behaviours and the cognitive alterations induced by a chronic treatment with PCP.
Please do not exceed 1 page.

Project Title:

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

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

We are interested in understanding how cells control the machinery that allows them to divide. Specifically, we study how different protein kinases control the organization and function of the centrosomes and the mitotic spindle through the specific modification of different proteins. For this we use genetically modified animals and cells as well as a range of molecular biology and biochemical techniques, including these related to the production and culture of cells, CRISPR/CAS9, RNAi, FACS, live cell microscopy, western blot, immunoprecipitation, immunofluorescence, proteomics etc.

Ongoing research lines in the lab study:

- the different functions performed by the NIMA-family of protein kinases during spindle formation and chromosome segregation in mitosis.
- the importance of Nek9, Nek6 and Nek7 during development and their possible implication in the onset of different pathologies (such as, yes, cancer).
- the phosphoregulation of different molecular motors and associated proteins during G2 and mitosis and its importance for correct chromosome segregation.

We are looking for students that are highly motivated to do research (and possibly obtain a PhD), and able to work well in a team. Previous experience with mouse models, cell culture or immunological techniques will be valued. If you are interested send us a CV, academic records and a short letter of interest.
Project Title: ZEB1 role in oncogenic transformation and tumorigenesis of CRC by Wnt, KRAS and BRAF pathways

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

Group: Transcriptional regulation of Gene Expression during Cell Differentiation and Cancer

Ester Sánchez Tilló – PhD, Miguel Servet I principal investigator – IDIBAPS – CELLEX P1B, Facultat de Medicina, Universitat de Barcelona-Hospital Clínic de Barcelona, c/Casanova 143, 9333275400, ext 3325, Barcelona. esanche3@clinic.ub.es

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

The group investigates the regulation of gene expression at the transcriptional level during cell differentiation and cancer. As molecular model we use the ZEB family of transcription factors. ZEB1 (also known as delta-EF1, zfhx1a) and ZEB2 (SIP1, zfhx1b) that regulate key genes during embryonic development, cell differentiation and cancer. Depending on the tissue and gene, ZEB proteins function as either transcriptional repressors or activators. ZEB factors inhibit normal cell differentiation and maintain stemness in normal and cancer stem cells. This project focuses on the role of ZEB1 in the main molecular pathways involved in colorectal cancer (CRC): accumulation of genetic changes in intestinal cells altering Wnt pathway and activating KRAS or BRAF oncogenes, among others, involve the formation of aberrant crypt foci that can develop adenomas and evolve to carcinomas which can invade and metastasize to secondary tissues. ZEB1 is a key promoter of tumor invasiveness and metastasis in CRC, being expressed in invasive cancer stem cells inducing epithelial-mesenchymal transition (EMT). Our study is to determine the role of ZEB1 as effector of these pathways in the early steps of CRC progression, in normal-to-adenoma-to-carcinoma transition. Research will aim at the study of upstream signaling pathways regulating ZEB1; the molecular mechanisms involved in ZEB1 mediated transcriptional regulation of gene expression and new gene targets regulated by ZEB1 during cell differentiation and CRC oncogenic transformation. Additionally, ZEB1 implication in cancer stem cell phenotype and resistance to CRC chemotherapy will be investigated. Study of ZEB1 in CRC involves the use of human primary CRC samples, cell-based systems and in vivo transgenic models that will help to evaluate the extent of the disease, patient survival and their response to future chemotherapy treatments.
**Project Title:** Epigenetic dynamics during normal myogenesis and muscle tumorigenesis

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

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**Summary of project summary or current research lines**

Epigenetic regulation is key to establish the cellular differentiation processes. Mature muscle cells acquire specific functions controlled by transcription factors in association with changes in chromatin structure. In the laboratory, we are analyzing the dynamics of the histone modification profiles and DNA methylation patterns during the myogenic differentiation process in physiological and pathological conditions, such as rhabdomyosarcoma tumors, using *in vitro* and *ex-vivo* cellular models. Recently, we have identified a Pax7-mediated muscle-specific DNA demethylation signature required to acquire and maintain muscle-cell identity, although the underlying mechanism is yet unknown.

In addition, we are studying the role of histone deacetylases in muscle differentiation and growth, in primary muscle cell lines and in animal models. Preliminary results suggest that certain HDACs can regulate sarcomere assembly modulating muscle contraction. Globally, a better understanding of the epigenetic mechanisms underlying muscle-lineage determination and terminal differentiation is extremely relevant for reprogramming cells with biomedical and therapeutic purposes in chronic muscle pathologies, as well as in cancer.

*Contact: send CV to Mònica Suelves, email:msuelves@igtp.cat*
Project Title: Climate change and brain development: the effects of ambient temperature on brain functioning.

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

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

Climate change is the major global health threat in the XXI century. Increase of temperature and in particular of the extreme heat conditions could have a noticeable health impact. Among the observed effects there is a raise of mortality for psychiatric diseases and car accidents (in part due to cognitive function impairments). My group is focused on the environmental early life origins of brain development. We have demonstrated the adverse effects of traffic pollution on the development of several cognitive functions and brain function in neuroimaging studies in infants and schoolchildren. We have also shown beneficial impacts of green spaces on these functions. The aim of the project is to assess, for the first time, whether ambient temperature during gestation is related with the brain development and whether the daily variations in outdoor and indoor ambient temperature is related with daily variations in brain functioning. The studies will be conducted in two population-based cohorts: the INMA project, a birth cohort including more than 2,000 pregnant followed for the whole pregnancy and their children examined almost yearly until pre-adolescence; and, the BREATHE project a longitudinal study of around 3000 schoolchildren in Barcelona followed during 3 years. The brain development has been measured with psychometric assessment, exams using computerized tests and MRI imaging. The tasks for the 6 months period will be to review the knowledge, to select one of the research questions, and to answer that question in the INMA or BREATHE studies. The final aim is to prepare a manuscript. This project could be expanded with a PhD thesis.
Project Title:
Dissecting the biology of brain metastasis through epigenetic regulators

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

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

The Brain Metastasis Group (BMG) was established in 2015 with the goal of discovering critical aspects of the biology of brain metastasis in order to develop new therapeutic opportunities. To reach this goal the laboratory is validating novel brain metastasis mediators, characterizing the brain microenvironment, improving experimental models by incorporating therapies and exploring novel ways to target established brain metastasis. We have an extensive cellular collection of experimental models from breast and lung cancer and melanoma, which is being complemented with novel GEMM and PDX. We use a variety of in vitro, ex vivo and in vivo approaches that allow us to develop a broad validation of our hypothesis before we seek confirmation partnering with our established clinical collaborators.


The student will join our young, enthusiastic and ambitious lab to work in an on-going project together with a senior PhD student. We have identified a critical role of a linker histone in brain metastasis. The project aims to elucidate its function in the epigenetic regulation of brain metastasis initiation and progression. Interestingly the histone is required when metastatic cells are challenged in assays involving the ability to initiate growth (but not under regular culture conditions), suggesting potential links to metastasis initiating properties. This cellular phenotype will be evaluated by the student simultaneously to the molecular links with proteins of the Polycomb group and downstream effects on histone marks and gene expression.
Project Supervisor:
Name: Josep Vilardell
Group: pre-mRNA splicing
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Project Title: Molecular Strategies for pre-mRNA Recognition

Summary: With exceedingly few exceptions, all human pre-mRNAs are processed by
the spliceosome to get their introns removed and the remaining exons spliced together
into mRNAs. In contrast to their obvious significance, exons could be seen as an oddity
in many pre-mRNAs. Most of them are <200-nt long, surrounded by introns that can be
hundreds of kilobases long. Yet, a splicing error of a single base could be lethal. In
additions, many pre-mRNAs include "cassette-exons", which may be either included or
skipped in the product mRNA. How is this controlled?
The notion that there is a mechanism to properly identify exons in pre-mRNAs, and that
it is regulated, is clearly supported by data. However, we know little on the
spliceosomal interactions that take place, and we lack a good experimental model to
analyze them. It is believed that cross-exonic interactions require additional factors,
because the spliceosome 'core', in charge of identifying and processing the intron,
does not recognize exons. This is view is consistent with what we know from yeast, a
great working model to study the properties of the core spliceosome. Yeast has a
relatively (compared to us) simple transcriptome, with most genes lacking introns.
Accordingly, the yeast spliceosome machinery is reduced to the basic components,
and it appears to just recognize introns. Work from others and us has helped to
decipher the code of this intronic recognition to a great extent.
However, an initial Bioinformatics analysis of the yeast genome taking into account all
what we know on intron recognition, suggests that even the core spliceosome can
"sense" some exons. This, if confirmed, would support the possibility that the core
spliceosome is capable of at least some exon-definition interactions. These would have
then expanded during evolution to the complexity of mammalian splicing. Thus, the
question here is whether the core spliceosome has the capability to define exons,
Specifically, the tasks for this part of the project would involve to design and develop
genes with introns (known and predicted) in several positions and document their
splicing in vivo and in vitro. The aims would be (1) determine which exonic parameters
(if any) affect the splicing of the intron being tested and (2) suggest spliceosomal
components that may be responsible.

References:
* Yan C, Hang J, Wan R, Huang M, Wong CC, Shi Y. "Structure of a yeast spliceosome at 3.6-angstrom
* Devillers H, Morin N, Neuvéglise C. "Enhancing Structural Annotation of Yeast Genomes with RNA-
* Meyer M, Plass M, Pérez-Valle J, Eyras E, Vilardell J. "Deciphering 3'ss selection in the yeast genome
* Bitton, D. A., et al. (2014). "LaSSO, a strategy for genome-wide mapping of intronic lariats and branch
  points using RNA-seq." Genome Res 24(7): 1169-1179..
* Plass, M., et al. (2012). "RNA secondary structure mediates alternative 3'ss selection in
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Project Title: Do the nucleosome and the spliceosome talk? Epigenetics and control of pre-mRNA splicing.

Summary: The majority of our pre-mRNAs are subjected to pre-mRNA splicing, a process that greatly expands the genetic and coding capabilities of our genome. A novel exciting area of research is being developed studying the impact that chromatin has in the splicing pattern of nascent transcripts. While it is becoming increasingly clear that epigenetic marks such as histone post-translational modifications can modulate splicing, how this is happening at molecular level is not understood. Recent results in our laboratory indicate that the connection between the spliceosome and the nucleosome happens as well in the yeast model system, where we investigate the regulation of the spliceosome assembly on the RPL30 nascent transcript. We have found that this assembly is affected by some histone mutations and therefore offers an opportunity to investigate the role of chromatin in splicing. Specifically, the aims of this project are (1) Determine which histone marks have a greater impact on spliceosome assembly on the RPL30 transcript. For this we will take advantage of the collection of yeast histone mutants. (2) Suggest possible spliceosomal factors sensitive to histone modifications, which would point to possible mechanisms. (3) Validate our findings with data from human cells.

Further Reading: