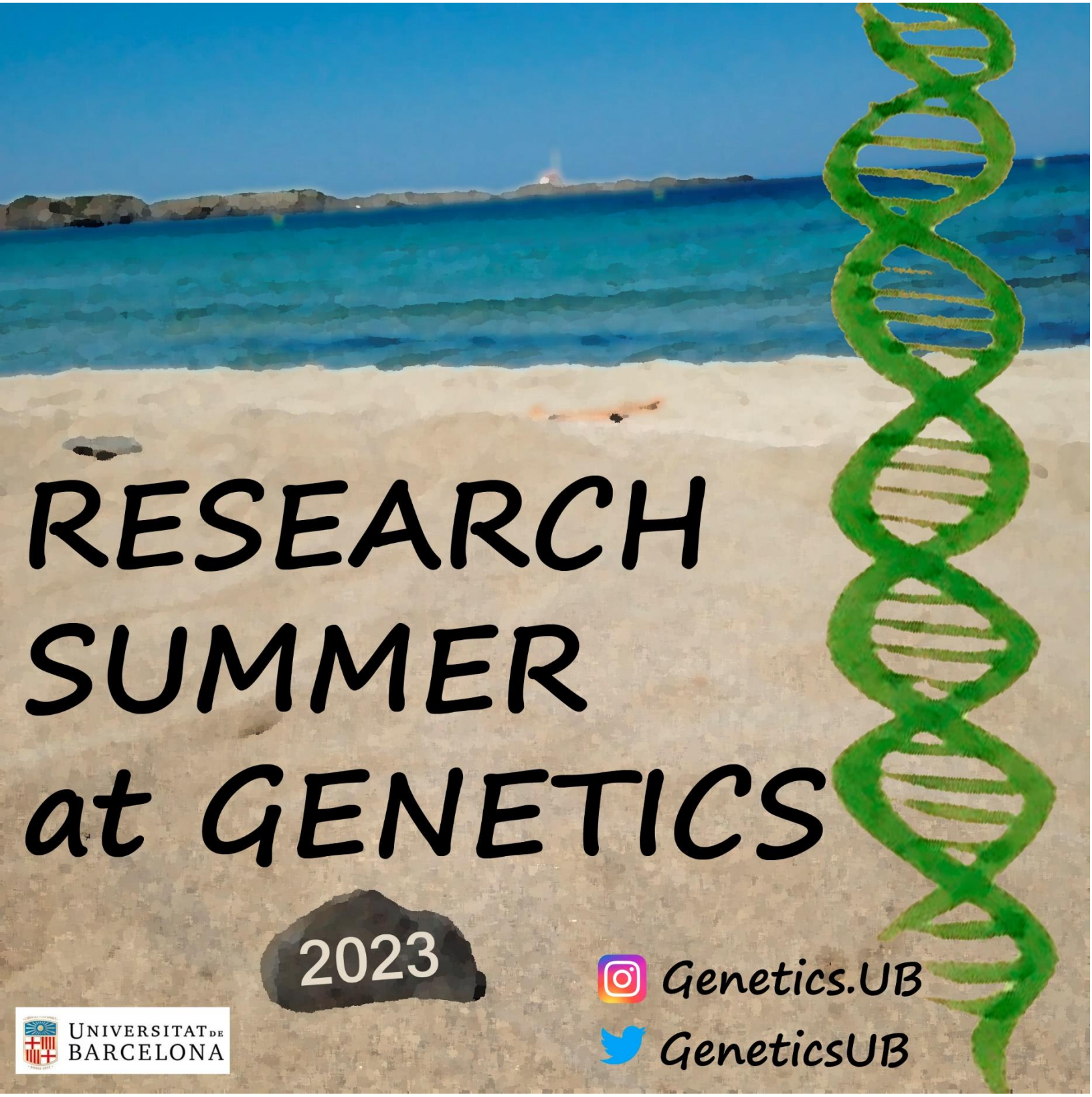


SECTION *of* BIOMEDICAL, EVOLUTIONARY AND DEVELOPMENTAL GENETICS

PRESENTATION

of the SECTION

The Section of Biomedical, Evolutionary and Developmental Genetics (former Department of Genetics until 2016) of the current Department of Genetics, Microbiology and Statistics is one of the most active research Sections at the University of Barcelona (UB). At present, it has 27 professors, which along with postdoctoral and recruited researchers, graduate and undergraduate students, technicians and administrative staff and services, form a group of ~100 people.

It can be considered that the Department of Genetics was created in 1963, when Dr. Antoni Prevosti, introducer of this specialty at the University of Barcelona, was awarded Professor of Genetics in the first Spanish call of this discipline. At the time of its formation, the Department pioneered the study of variability in natural populations using Drosophila as a model organism. Nowadays, research and teaching have expanded greatly. Using state of the art molecular tools and the latest generation of genomic approaches, as well as a wide variety of animal models, research in the section addresses the scientific challenges expected to have a major impact on the XXI Century society: Plants Genetics, Development and Regeneration, EVO-DEVO, Genetics and Evolutionary Genomics, and Human Molecular Genetics. Teaching includes courses in the Degrees of Biology, Biomedical Sciences, Biochemistry, Biotechnology and Environmental Sciences, as well as various masters, such as Genetics and Genomics, Biodiversity, Biomedicine, Neurosciences and Molecular Biotechnology. The Department is also responsible for the PhD program in Genetics, which has the quality award of the Ministry of Education.

https://www.ub.edu/portal/web/dp-genmicrostat/grups-de-recerca-de-la-seccio-de-genetica-biomedica-evolucio-i-desenvolupament

PLANTS GENETICS

What pathogens use virulence genes to cause disease in animals and plants? What is the role of resistance to heavy metals in virulence? What genes encode metal resistance proteins? Can we get disease-resistant crops?

The area of Biotechnology of the Department of Genetics includes one research group aimed to study at the genetic and molecular levels (from genomics to proteomics) the mechanisms by which organisms respond and/or defend against various situations of stress, including infections, biological pathogens, such as inorganic - lack or excess metal ions. Knowledge of these processes is later applied in biotechnological strategies to modulate, enhance and optimize the response of organisms to metal homeostasis or plants diseases.

DEVELOPMENT and REGENERATION

How is pattern formation achieved during development and regeneration? How is cell plasticity controlled: genome *versus* epigenome?

The field of DEVELOPMENTAL BIOLOGY studies how a fully formed adult animal arises from a single cell. During this process, distinct tissues, organs and systems develop in a precise spatio-temporal manner to achieve particular morphologies. Some adult animals have the ability to REGENERATE some of these organs and systems after their traumatic loss.

Nowadays, research in development and regeneration focuses on signaling pathways, proliferation, cell death, organogenesis, epigenetics and stem cells. Many phylogenetically- conserved pathways play very similar roles in development, regeneration and the pathogenesis of cancer in various model organisms. To understand the function of these pathways we use Platyhelminthes and Drosophila. Our research spans from pattern formation during development and regeneration, including cell proliferation and differentiation, to studies of neural circuit assembly and synaptic specificity.

The approach to answer our questions is extremely multidisciplinary and takes advantage of state of the art genomic and genetic technologies, as well as the latest imaging methods and computer optimized image analysis.

EVO-DEVO and NEW ANIMAL MODELS

To what extent humans are similar or different to a mouse, a fish or a worm? How do genetic changes during development generate evolutionary innovations and create biodiversity?

The field of EVO-DEVO has been recognized in the MILLENIUM issue of Nature (2000) as one of the 10 disciplines that will have a greater future impact on the society of the XXI Century. EVO-DEVO studies how the evolution of the mechanisms of embryo development at the genetic, molecular, cellular and morphogenetic levels is responsible for the extraordinary diversity generated during the last 1.000 million years of animal and plant diversification.

EVO-DEVO, as we know it today, arises from the intersection of the fields of Genetic and Molecular Developmental Biology, Molecular Evolution and comparative Genomics, and it is nourished by state-of-the-art novel “omic” technologies (genomics, transcriptomics, proteomics, epigenomics) and the recent advances of molecular techniques of Genetic Engineering, transgenesis and gene silencing.

EVO-DEVO research follows comparative developmental approaches using new animal models chosen ad hoc for their key phylogenetic position to illuminate the changes of the mechanisms of development responsible for morphological and functional innovations that might have facilitated the major evolutionary transitions of life forms in our planet.

EVOLUTIONARY GENETICS and GENOMICS

What are the genetic and genomic bases of adaptation and evolutionary novelties? How have genetic changes contributed to the diversity of life? What are the main evolutionary processes that have shaped genetic changes?

Evolutionary Genetics studies the genetic basis and mechanisms determining the adaptive process, the patterns of evolution and biodiversity. Within this general objective, at the Departament de Genètica we perform research in the fields of population genetics and genomics, phylogeography, phylogenetics and comparative genomics. Projects in these fields are conducted in a wide range of taxonomic groups that include both model and non-model species. In our research, we use experimental approaches based on classical methods of molecular biology and on the new "omics" technologies (genomics and transcriptomics), and also bioinformatics, including the development of computational tools and software.

Our research seeks to generate knowledge on fundamental questions in evolutionary genetics. More specifically, we aim to determine: a) the significance of genetic changes in coding and regulatory regions in adaptive evolution; b) the molecular origin of chromosomal inversions, and their role in speciation and adaptation; c) the role of multigenic families and gene networks in the origin of evolutionary novelties; d) the processes leading to population genetic structure and that determine the evolutionary history of species. Our research aims to achieve an inclusive vision of the evolution of populations and species, and the adaptation process, as well as of the acquisition of evolutionary novelties and the origin and maintenance of biodiversity.

HUMAN MOLECULAR GENETICS

What are the genetic basis of hereditary diseases? How can we approach the search of new genes causing lysosomal diseases, blindness, osteoporosis or migraine? How can we delve into the molecular causes of genetic diseases? Can we improve the diagnosis and design of effective therapies for these diseases?

These are scientific questions addressed by the group of Human Molecular Genetics at the Department of Genetics, formed by a large group of researchers who have spent years working to determine the genetic and molecular bases of monogenic diseases from rare neurodevelopmental disorders to hereditary disorders of vision due to retinal degeneration, and complex diseases, most prevalent, such as osteoporosis and neurological disorders (migraine, impaired neurotransmission) and behavioral (drug addictions, ADHD, autism and aggressive behavior).

We aim to answer what genes cause these diseases, which processes are altered when these genes have mutations, how can we diagnose genetic carriers in families, if we can address some cell or gene therapy to alleviate its effects or even if we might someday cure the patients. To achieve these goals, we employ a range of innovative techniques and accurate genetic diagnosis (sequencing exomes and transcriptomes), and define new therapeutic targets by biochemical, genetic and cellular studies that combine the construction of animal models (mouse, zebrafish) as well as cell- based assays (transfected cells, primary cultures, iPS cells, organoids).

RESEARCH PROJECTS *under the* PROGRAM "RESEARCH SUMMER *at* GENETICS"

Development *and* Regeneration

1. Sofia J. Araújo
2. Teresa Adell and Cristina González-Estévez

EVO-DEVO *and* New Animal Models

3. Cristian Cañestro

Evolutionary Genetics *and* Genomics

4. Julio Rozas and Sara Guirao-Rico
5. Alejandro Sánchez-Gracia
6. Marta Pascual, Francesc Mestres, Carlos Carreras and Cinta Pegueroles

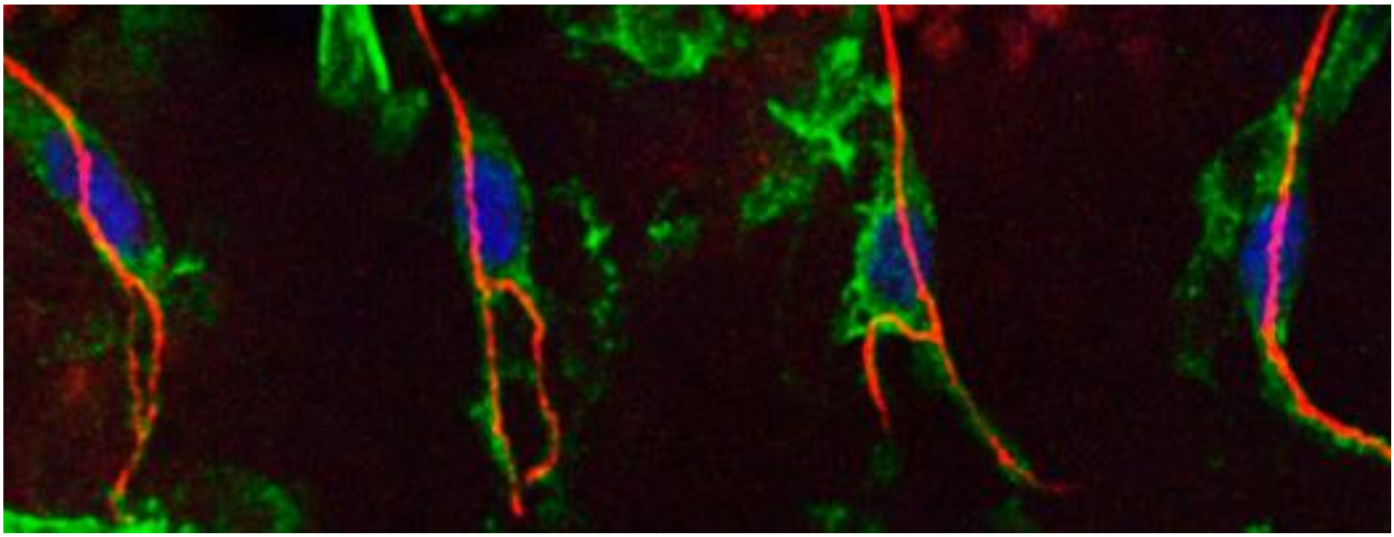
Human Molecular Genetics

7. Susanna Balcells
8. Gemma Marfany
9. Raquel Rabionet

DEVELOPMENT and REGENERATION

Molecular mechanisms of cellular branching

1



Supervisor:

Sofia J. Araújo

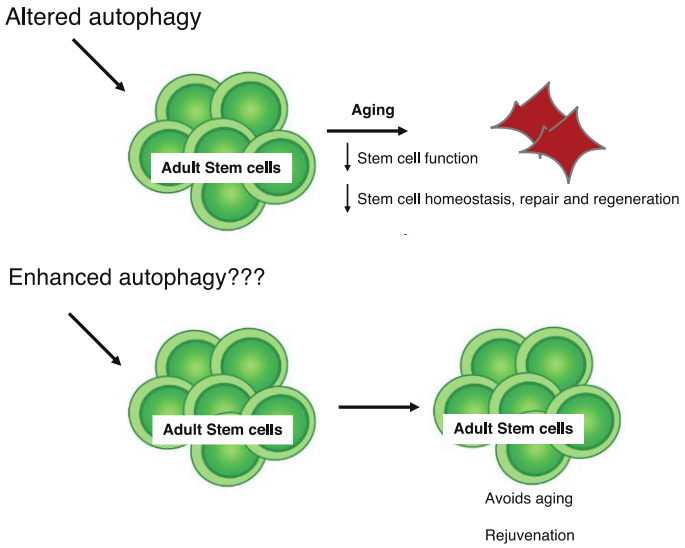
sofiajaraujo@ub.edu

How can a cell break its symmetry and generate a highly branched structure? Branching morphogenesis during development builds the ramified structures of various organs, including the nervous, vascular and respiratory systems. Branching at the single-cell level implies extensive cytoskeletal remodelling and membrane growth and dynamics. Understanding how cells branch at the correct time and place and what are the molecular mechanisms implicated is essential for the modulation of this cell behaviour during development and regeneration. Using Drosophila melanogaster, we will study different cell branching phenotypes using genetic engineering techniques, molecular biology and advanced imaging, in order to unveil new molecules involved in subcellular branching.

DEVELOPMENT and REGENERATION

How to rejuvenate stem cells: the role of autophagy during regeneration

2



Supervisor:

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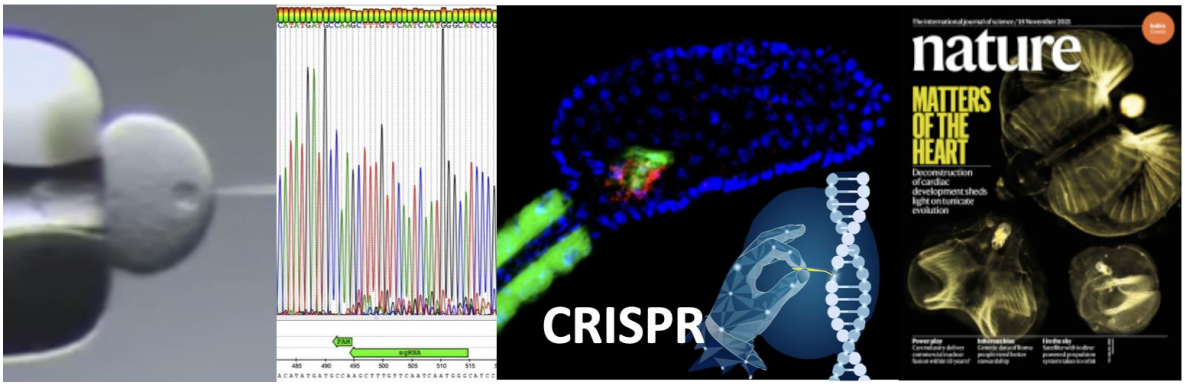
Cristina González-Estévez crisgonzalez@ub.edu

Planarians possess a large population of adult stem cells, which allows them to regenerate any part of their body. They are also able to withstand long periods of starvation while maintaining the stem cell population and their regenerative capabilities. How can they maintain a cell population that proliferates continuously when there is a lack of nutrients? Our research has shown that planarian stem cells increase stress resistance allowing the maintenance of energy levels and preventing genome instability. We have also shown than during starvation planarians rejuvenate their stem cells in terms of telomere length. We are now investigating autophagy, an evolutionary conserved mechanism to maintain tissue homeostasis and a candidate mechanism to be enhancing stem cell function and regeneration during starvation.

EvoDevoEcoGENOMICS & NEW ANIMAL MODELS

EVO-DEVO-GENOMICS, CRISPR & New Animal Models

3



Supervisors:

Cristian Cañestro and Alfonso Ferrández

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Are you interested in Genetics, Transgenesis, Developmental Biology, Genomics, Evolution or Bioinformatics? Would you like to investigate an emergent animal model and to develop new CRISPR tools? If the answer is YES, we invite you to contact us to get to know the research lines of our lab, in which we are investigating:

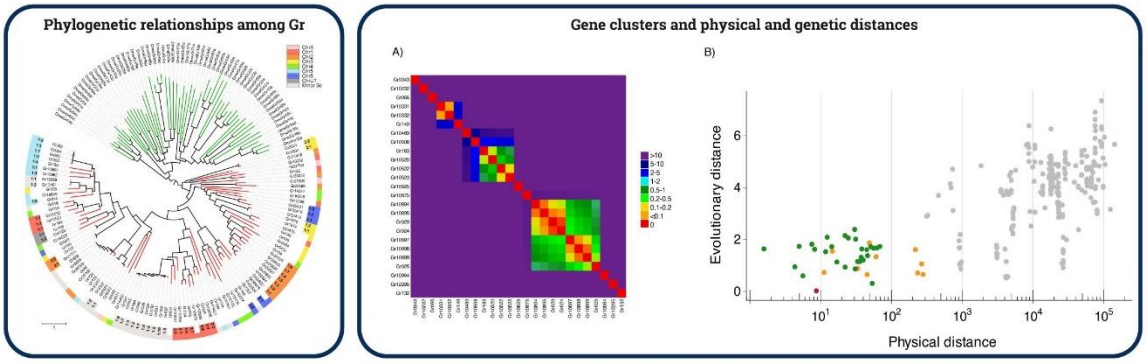
- the impact of gene losses on the evolution of the mechanisms of embryonic development of the heart of chordates, and the development of new animal model for cardiomyopathies
- the adaptive genetic response of marine embryos in the context climate change and ocean's health.
- the development of new CRISPR tools for generating knockouts by targeted insertion

For more info: https://evodevogenomics-unibarcelona.weebly.com/

EVOLUTIONARY GENETICS and GENOMICS

Evolutionary Genomics in Arthropods

4



Supervisors:

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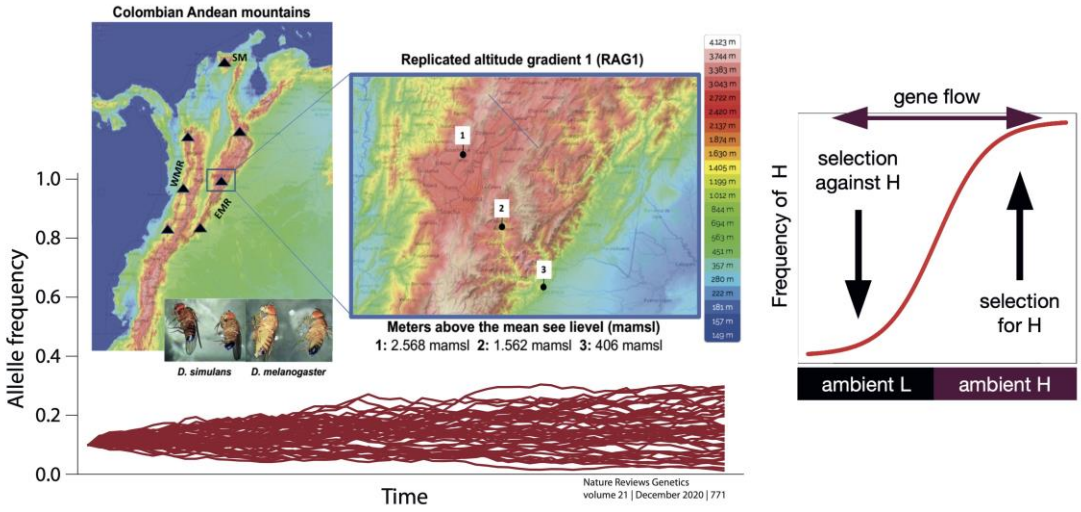
Sara Guirao-Rico sguirao@ub.edu

Our research group seeks to understand the evolution of genes and genomes. To this aim we use bioinformatics tools (some of them developed in our group) to analyze high-throughput sequencing data under the theoretical framework of population genetics and molecular evolution. We are especially interested in the molecular evolution of gene families, especially those encoding the chemosensory (i.e., olfactory and gustatory) proteins in model and non-model organisms. We have identified and studied the chemosensory genes of insects, centipedes, chelicerates, tardigrades and onychophorans, which belong to different arthropod subphyla that colonized the land from an aquatic ancestor independently in different evolutionary periods. We are also investigating the genomic basis of adaptive radiations in the Macaronesia islands using the spider genus Dysdera as a model, and participate in some genome consortia dealing with the analysis of species of commercial interest, or with special ecological or evolutionary relevance.

EVOLUTIONARY GENETICS and GENOMICS

Detecting the genomic signals of polygenic adaptation in natural populations

5



Supervisor:

Alejandro Sánchez-Gracia

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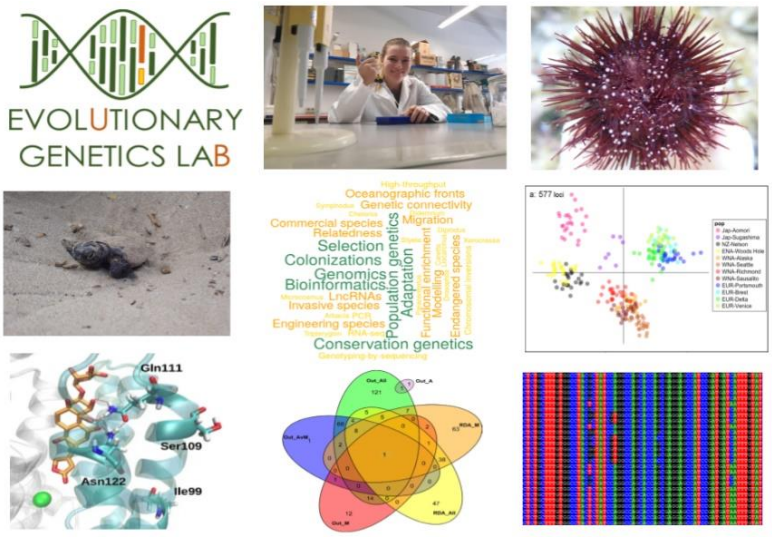
The main goal of our research group is to understand the molecular mechanisms underlying adaptation in natural populations. Our case study are altitude gradients, an ecological limit with important variations in temperature and humidity. Our research model is Drosophila, a model organism with high-quality genome sequences and functional annotations. We are combining high-throughput sequencing data, powerful population genomics and bioinformatics inference, and computer modelling, in an innovative large-scale study across more than 2,500km at Colombian Andes Mountain ranges. We are focusing our study on detecting the characteristic hallmark of polygenic adaptation, i.e., the process in which a population adapts through changes at many genes across the genome (typically hundreds or thousands of genes) in the wild. Our results will contribute new knowledge about how evolution works at the molecular level but also about the factors influencing the response of natural and breeding populations to climate change and global warming.

EVOLUTIONARY GENETICS and GENOMICS

Genetic connectivity and adaptation in marine organisms

6



Supervisors:

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Carlos Carreras carreras@ub.edu

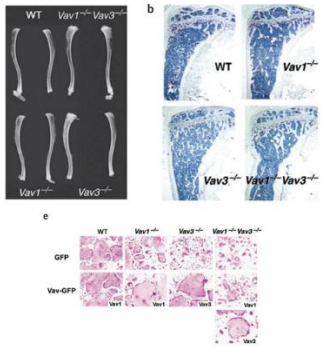
Cinta Pegueroles cpegueroles@ub.edu

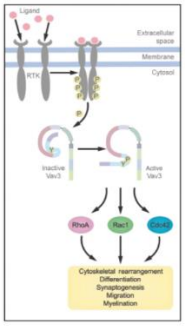
Connectivity and adaptation are fundamental evolutionary processes that shape populations of marine organisms. Our group study these processes in a wide variety of organisms, including commercial, invasive, endangered or ecologically relevant species such as demersal fishes, marine turtles, tunicates, echinoderms or crustaceans. We use genetic and genomic data, sometimes combined with phenotypic and environmental data, to address our research evolutionary questions that also provide a framework for a scientifically based management and conservation of the studied species.

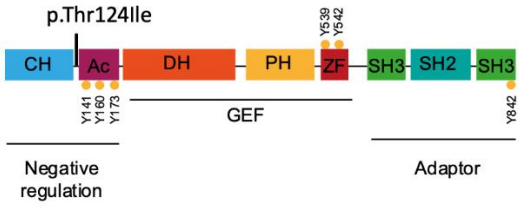
HUMAN MOLECULAR GENETICS

Functional studies of mutations found in patients with rare bone pathologies

7







Supervisor:

Susanna Balcells

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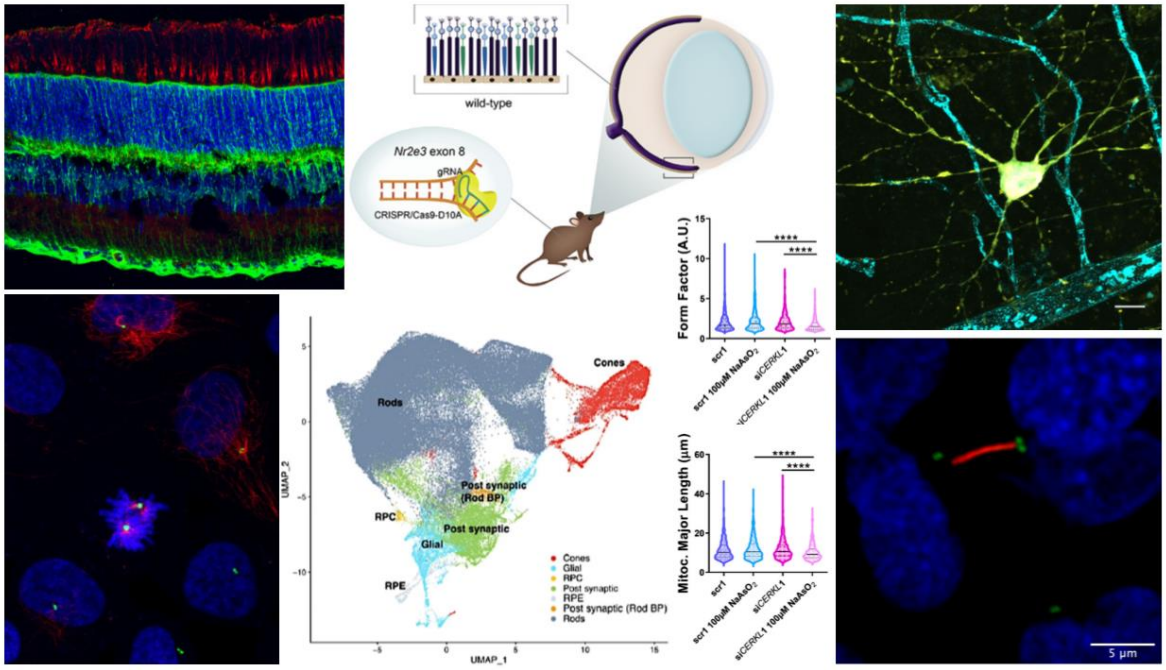
Next Generation massive sequencing allows to address the genetics of patients with rare diseases. However, when the variant filtering process is complete, a small list of possibly pathogenic variants is obtained functional studies need to be done to demonstrate or refute this supposed pathogenicity. In the case of bone pathologies with phenotypes of high bone mass, or conversely, with osteoporosis, it is advisable to study the effect of mutations found in the relevant cell types of bone tissue: osteoblasts and osteoclasts. In our group, we are applying CRISPR/Cas9 to introduce some mutations found in patients, in osteoblasts and osteoclasts. Then, we study the characteristics and behavior of these cells carrying the mutation, comparing them with cells that do not have the modified gene. We want to see if mutated osteoblasts are able to mineralize the extracellular matrix and if they express alkaline phosphatase as unmodified osteoblasts do. We also want to see if mutated osteoclasts are able to resorb the bone matrix and if they express tartrate-resistant acid phosphatase as unmodified osteoclasts do.

HUMAN MOLECULAR GENETICS

Why mutations in retinal dystrophy genes cause blindness?

8



Supervisors:

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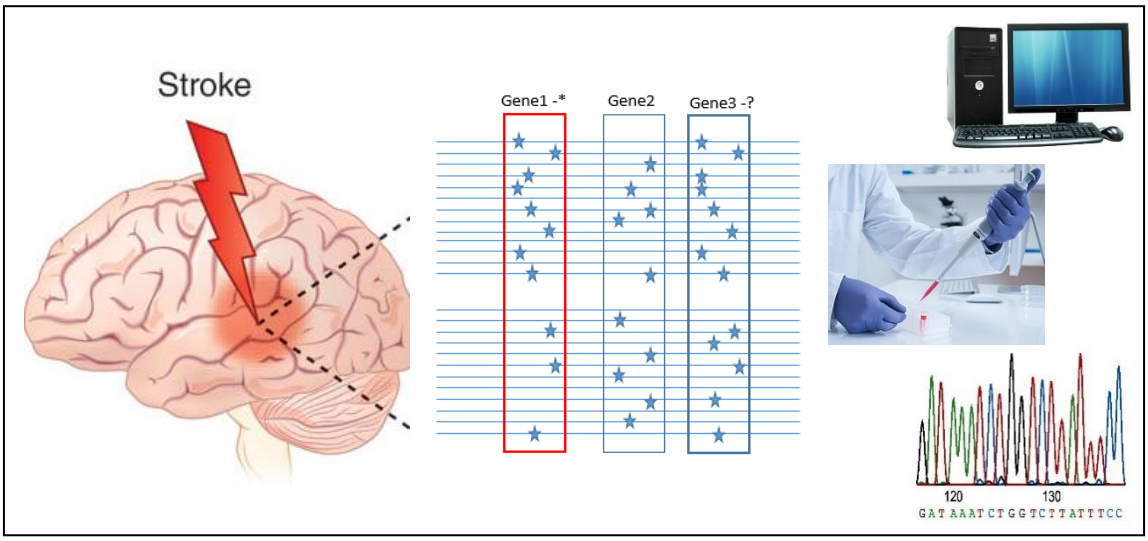
Retinal dystrophies (RD) are the main cause of hereditary blindness in the adult. Mutations in more than 300 hundred genes cause RD, but the precise function in the retina is for many still unknown. We use transfections in cultured cells, primary cultures of neurons, explants of mouse retinas, genome editing in mouse and retinal organoids to generate cell and animal models to address the functional characterization of RD genes.

HUMAN MOLECULAR GENETICS

Genetic factors in stroke recovery

9



Supervisor:

Raquel (Kelly) Rabionet

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The recovery process after a stroke leads to differences in the functional outcome of the patient. Genetic variants in the genes in involved in recovery pathways may influence this functional outcome. In a collaborative study, we explored the contribution of rare, exonic variants that affect protein function, observing several genes that could be involved in the recovery. We have a few candidate genes and mutations that we intend to validate through functional analysis.