Annual Report 2009

INSTITUT de BIOLOGIA EVOLUTIVA

ANNUAL REPORT 2009

INSTITUT de BIOLOGIA EVOLUTIVA

CSIC UPF

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INDEX

FOREWORD

by the Director of the IBE, Xavier Bellés

Only during the past 500 years or so have they [human beings] begun to be, in the biological sense, a success… We cannot point to a single definitive solution of any one of the problems that confront us. We are still beginners, and for that reason may hope to improve. To deride the hope of progress is the ultimate fatuity, the last word in poverty of spirit and meanness of mind.

Peter Medawar. *Pluto's Republic* (Oxford, 1982)

There are few jobs more rewarding than doing scientific research, either in the field or at the bench. One of them is launching a new institute of research, just because it can serve as a tool for many others to do scientific research, so the reward has a multiplicative effect. This has been the idea underlying the onset of the Institute of Evolutionary Biology (Institut de Biologia Evolutiva, IBE); an idea supported by the young, creative, bright and enthusiastic team of people that is the main foundation of the new institute.

Formally, the IBE was created in July 2008, so it is a bit more than 1-year-old. During 2009, in addition to solve lots of administrative duties derived from the creation, many other things happened. From a logistic point of view, the members of the Department of Physiology and Molecular Biodiversity, formerly working at the Institute of Molecular Biology of Barcelona (CSIC) and one of the founder groups of the IBE, moved to the CMIMA, a CSIC building next to the "Parc de Recerca Biomèdica de Barcelona" (PRBB), where the other IBE founder group, the Evolutionary Biology Unit of Pompeu Fabra University, was already placed.

One of the first organizational objectives, then, was to constitute a truly operative administrative unit for the IBE. This objective was completed by mid 2009 with the incorporation of a General Manager (UPF) and a Vicemanager (CSIC) who completed the administrative core. Another important step on IBE organization was the participation of the Institute on the General CSIC Strategic Plan 2010-2013. The Plan organized the scientific activity of the IBE into four

programs, and reflected the objectives to be covered within the next 4 years. It was approved by the CSIC and UPF, and envisages the CSIC investment for 33 new positions, including permanent positions, predoctoral grants, post-doctoral contracts, and technician posts.

From the scientific point of view, it is worth mentioning that on 14th and 15th December, the IBE organized its Annual Retreat, which took place in the Monastery of Avellanes (Balaguer). The Retreat grouped 84 IBE members around a rich and varied scientific program, including 49 scientific posters and 6 general lectures. Social activities played also an important cohesive role, including a thorough visit to this famous monastery founded in 1195, an excursion to the surrounding mountains, and a nocturnal and lengthy informal discussion in the underground cellar.

In spite of being a sort of transitional year, with plenty of time spent on collateral duties, we still had time to do research. The publication of a total 53 international papers gives an overview on the global scientific IBE production during 2009. It is worth to remark the high general quality of the journals used and the remarkable percentage of internalization of IBE collaborations and papers, with 70% of them published in co-authorship with other international institutions.

The year 2009 was the bicentennial of Charles Darwin's birthday, and sesquicentennial of publication of his book *The Origin of Species*. As it could not be otherwise, the IBE celebrated Charles Darwin with multiple activities. These included the organization of meetings and conferences, publication of works on popularization of Darwin's scientific legacy, participation and advice in public exhibitions, translation of some of the Darwin's works, etc. Darwin's year gave us quite a lot of work, but served to refresh our ideas, to read Darwin again and, especially, to gain new colleagues and to strengthen friendship with the old ones.

Besides the things that happened, there were also things that did not happen and are still pending. Among these, and perhaps the most urgent, is the formalization of an External Advisory Board, which must be a key IBE structure. Moreover, we aim at adding a new program on complex systems, and at recruiting new good scientists to increase the critical mass and to foster the 4 + 1 IBE programs. The consolidation of the planning and schedule for the new IBE building is also an important issue. All these, and many other still unexpected challenges, will be faced in 2010. The recent past times and those that are immediately coming, immersed into a general economical crisis, are probably not the best in the world to achieve all these things. However, we seniors have a long practice in surviving the worst conditions. In the end, as Vivian Greene said, life isn't about waiting for the storm to pass... It's about learning to dance in the rain.

INTRODUCTION TO THE IBE

A SHORT HISTORY OF THE IBE

The first ideas about the possibility of creating an Institute of Evolutionary Biology (Institut de Biologia Evolutiva, IBE) originated during the preparation process of the CSIC Strategic Plan 2006-2009. While analysing the work carried out at the Department of Physiology and Molecular Biodiversity (DPMB) of the Institute of Molecular Biology of Barcelona (IBMB) it became clear that its research lines would be better developed in an institute of evolutionary biology. This, and the CSIC strategy of establishing new cooperative links with emerging universities, led to the first meetings with the Evolutionary Biology Unit (UBE) of the Pompeu Fabra University (Universitat Pompeu Fabra, UPF), in order to explore the possibilities of creating a joint CSIC-UPF research institute in Catalonia.

At that time, the approximately dozen of group leaders from both DPMB (CSIC) and UBE (UPF) covered research topics on a variety of lines around Evolutionary Biology subjects, which was considered enough to start. Therefore, in May 2007, a team formed by three researchers from the CSIC and three from the UPF prepared a formal Scientific Project for a new institute, the IBE, which was submitted to the CSIC and to the UPF. After a number of iterations, the Scientific Project was approved by the CSIC in March 2008 and by the UPF in May 2008. On July 16th, 2008, a formal Agreement for the Creation of the IBE was signed by the President of the CSIC and the Vicechancellor of the UPF. On July 24th, 2008, the Governing Committee of the CSIC, after receiving the favourable report from the Ministry of Science and Innovation, officially approved the creation of the IBE as a joint CSIC-UPF new institute of research.

SCOPE AND GENERAL GOALS

Evolutionary biology aims at studying the processes and mechanisms generating biodiversity. After the Human Genome project, the description and comprehension of biodiversity is one of the most important scientific challenges of the XXI century, and coping to this challenge requires the methods and concepts of evolutionary biology. In particular, we need to understand the genetic basis of the difference among species (divergence) as well as within every species (variation, polymorphism), paying special attention at how differences are fixed and how are distributed, transmitted, maintained and how they interact with the environment. The description of genomes and the understanding of genomic differences in organisms are of paramount importance to understand the basic mechanisms of life and to place biodiversity into a robust evolutionary frame.

The general objective of the IBE is to work on these contexts using all the available new tools, experimental and computational, to understand the basic functioning of life, to describe and put in context their diversity, to unveil the mechanisms generating biological innovations and evolutionary changes and, finally, to preserve biodiversity and to promote its use in a sustainable way. In particular, the basis of the IBE, and its main peculiarity, is the capacity to face biodiversity studies describing genomic and functional evolution at any observational scale: molecular, biochemical, physiological or morphological. The IBE aims at becoming an international reference in these subjects.

GENERAL STRUCTURE

In addition to the classical figures of Director and Vicedirector, and the Executive board, the IBE counts with the important managing structures of the Board of Trustees and the Scientific Advisory Board.

BOARD OF TRUSTEES

IBE main managing structure is the "Board of Trustees" composed by two representatives of both partner Institutions (CSIC-UPF):

Luis Calvo
- CSIC Institutional Coordinator in Catalonia

Teresa García Milà
- UPF Vicechancellor of Scientific Policy

Francisco Montero
- CSIC Vicepresident of Institutional Relationships and Organisation

Francesc Posas
- CEXS-UPF Department Director

SCIENTIFIC ADVISORY BOARD (SAB)

The IBE Scientific Advisory Board (SAB) committee will be composed by 6-8 scientific experts with international recognition in the Evolutionary Biology field. Its main task will be to help the IBE in the definition of new research lines and strategies and in the best ways to recruit talent and widen the scientific strength of the Institute. At this moment the SAB is under constitution process. It is planned that can be officially constituted during 2010.

EXECUTIVE BOARD

The IBE Executive Board is composed at the moment by 7 members:

IBE Director

- Xavier Bellés

IBE Vicedirector

- Arcadi Navarro (acting also as the Coordinator of the *"Comparative and Computational Genetics"* Program)

Current Members

- Jaume Bertranpetit
- José Castresana (acting also as the Coordinator of the *"Animal phylogeny and Systematics"* Program)
- David Comas (acting also as the Coordinator of the *"Population genetics"* Program)
- Maria-Dolors Piulachs (acting also as the Coordinator of the *"Functional Evolution in Insects"* Program)

General Manager and Board Secretary

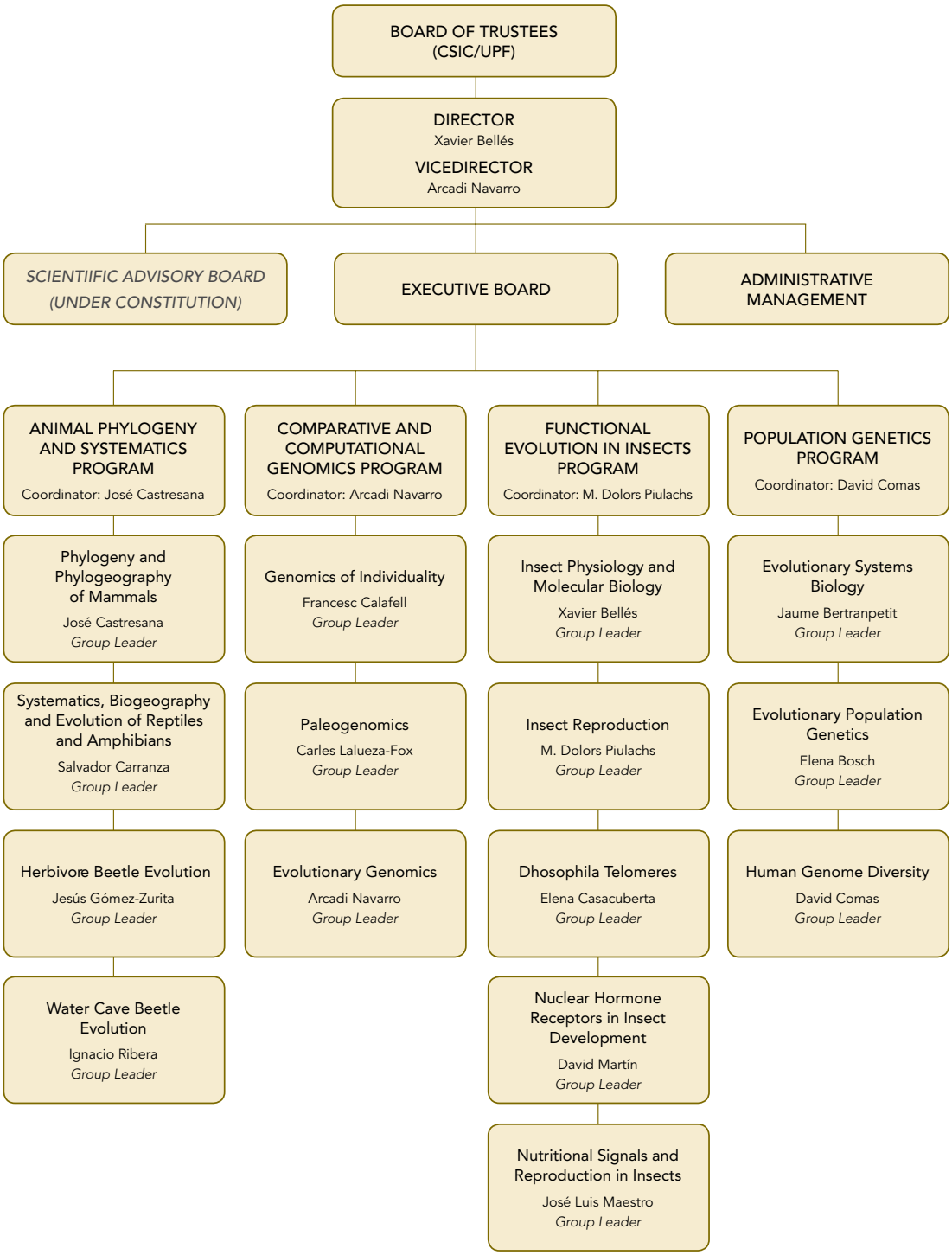
- Anna Pérez-Lezaun

SCIENTIFIC STRUCTURE

The scientific structure of the IBE is composed by fifteen different groups under a single Department of Molecular Biodiversity and Evolution, and four Scientific Programs:

- Animal Phylogeny and Systematics
- Comparative and Computational Genomics
- Functional Evolution in Insects
- Population Genetics

IBE ORGANISATION CHART



SERVICE UNITS

In support of the IBE scientific structure three service units have been planned. The first one is the "Administrative Unit", which is already functional. The other, more technical units, one on "Bioinformatics" and the other one on "Experimental Techniques", are under constitution process.

ADMINISTRATIVE UNIT

The IBE central administrative unit was formally constituted by mid 2009 with the incorporation of an IBE General Manager from the Pompeu Fabra University and a Vicemanager from the CSIC.

Nowadays, the IBE administrative unit is composed by 5 people:

ADMINISTRATIVE UNIT

General Manager

Anna Pérez-Lezaun | UPF

Vicemanager

Rita Arias | CSIC

Administrative Support

Emiliano González | CSIC

Blanca Álvarez | CSIC

Judit Sainz | UPF

RESEARCH ASSISTANTS

Apart from the mentioned formal units, the IBE also counts with four laboratory technicians that give scientific key support to the IBE programs:

RESEARCH ASSISTANTS

Rocío Alonso, JAETEC-CSIC Contract | Animal Phylogeny and Systematics Program

Cristina Olivella, Technical Staff CSIC | Functional Evolution in Insects Program

Olga Rubio, JAETEC-CSIC Contract | Functional Evolution in Insects Program

Mónica Vallés, Technical Staff UPF | Population Genetics and Comparative and Computational Genomics Programs

PERSONNEL

At the end of 2009, the IBE counted with 92 members (Table 1) with a ratio men/women close to 50%.

Table 1. IBE personnel distribution by categories. December 2009.

Faculty	16
Long-term Researchers*	3
Postdoctoral Researchers	17
Predoctoral Researchers	33
Support Personnel	
Laboratory Technicians	4
Bioinformatics	4
Administrative Staff	5
Others	2
Long-term Visitors	8
TOTAL	92

*Marie Curie or ICREA JUNIOR researchers

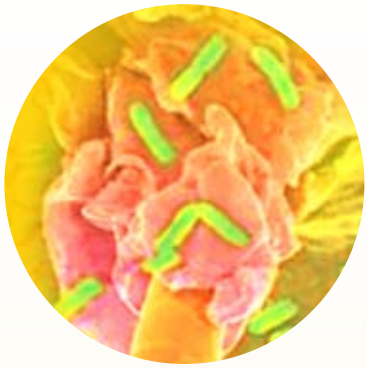
There is a remarkable level of personnel internationalisation, especially in the pre-doctoral level, where a 30% of the students come from a number of European and American countries.

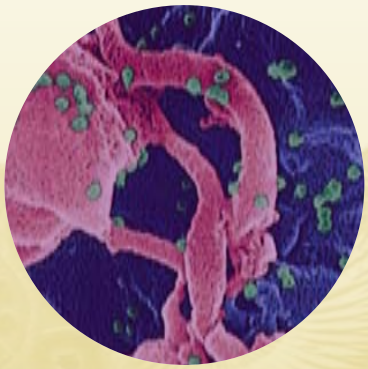
LOCALISATION

While not having an own specific building, whose construction is planned towards 2012, the IBE has two different headquarters:

IBE at the CMIMA building:
Passeig Marítim de la Barceloneta, 37-49.
08003 Barcelona, Spain
IBE at the PRBB building:
C/ Dr. Aiguader, 88.
08003 Barcelona, Spain.

IBE RESEARCH PROGRAMS





PROGRAM animal phylogeny and systematics

RESEARCH GROUPS

Phylogeny and Phylogeography of Mammals Lab
José Castresana, *Group Leader*

Systematics, Biogeography and Evolution of Reptiles and Amphibians Lab
Salvador Carranza, *Group Leader*

Herbivore Beetle Evolution Lab
Jesús Gómez-Zurita, *Group Leader*

Water Cave Beetle Evolution Lab
Ignacio Ribera, *Group Leader*

Members of this research program carry out research on animal biodiversity from a phylogenetic perspective with the aim of gaining further insight into the tree of life. The program's specific research interests include the origin and distribution of biodiversity (whether morphological, genetic, ecological or functional), systematics of certain groups, speciation, hybridization, diversification, biogeography, evolutionary ecology and phylogenetic methodology. Program members are not only working on the systematics and phylogenetic relationships among certain groups of organisms, but also on the evolutionary processes that gave rise to current biodiversity patterns. The main groups studied are mammals, reptiles, amphibians and Coleoptera, thus including a broad variety of animal taxa. A wide range of techniques are covered, from field work and morphological analysis to genetic studies, genomic data mining and software development. We are increasingly using large-scale phylogenetic analyses (both in terms of species considered and sequenced data) in order to obtain more robust phylogenies and evolutionary conclusions. Phylogenetic trees are a common framework for many evolutionary studies and therefore this research program provides many points of contact with other programs at the IBE.

GROUP

PHYLOGENY AND PHYLOGEOGRAPHY OF MAMMALS LAB

GROUP MEMBERS

José Castresana, Group Leader

| Research Scientist, CSIC

Alejandro Sánchez-Gracia, Post-doc | Juan de la Cierva Contract

Javier Igea, PhD Student | JAEPRE-CSIC Fellowship

Ana Rodríguez-Prieto, PhD Student | FPI Scholarship, MICINN

Víctor Soria-Carrasco, PhD Student | FPI Scholarship, MICINN

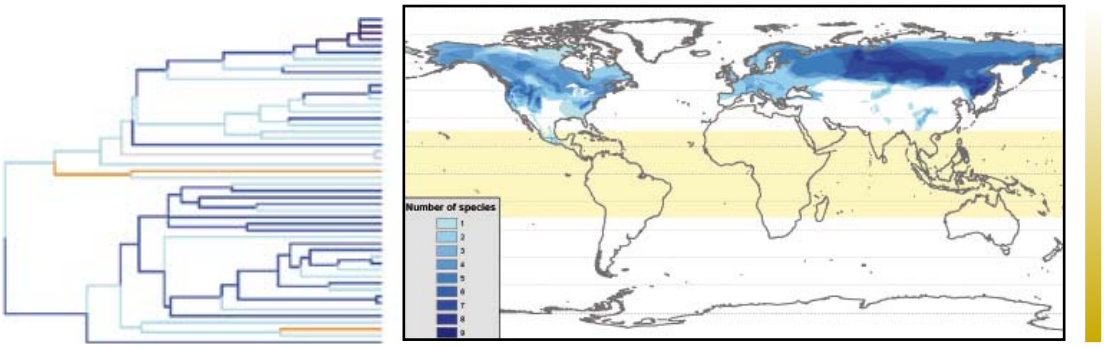
RESEARCH OUTLINE

Our main goal is the application of phylogenetic analyses to study animal biodiversity and its evolution. We have been working on several groups of organisms but our research is currently concentrated on mammals. We are particularly interested in the study of global diversification patterns in mammals and in the analysis of the factors that affect the next generation of species in different groups and biogeographic regions. We are also interested in the interphase between phylogenetics and population genetics, which may shed light on the analysis of speciation. Since phylogenies are one of the main tools of our work, we are always trying to improve phylogenetic analyses by introducing new methodologies and programs. Our research involves large-scale computational analyses as well as sequencing and analysis of novel genetic markers in particular species.

RESEARCH SUBLINES

1. Phylogeny, genetic diversity and speciation of mammals studied with multiple markers

Gene trees of closely related species can be used to infer the species tree, to understand how and when speciation occurred, and to delimit species in cryptic species complexes. However, stochastic effects due to incomplete lineage sorting may affect shallow phylogenies and therefore multiple genetic markers are necessary to resolve the species tree. We have analyzed the available mammalian genomes to compile new sets of intronic markers that may help in these works. We are currently sequencing these markers together with mitochondrial genes in different mammalian species (mainly insectivores and rodents) to better understand the patterns of genetic variability and gene flow within species. We are particularly interested in detecting cryptic lineages with the help of both mitochondrial and the novel intronic markers. By analyzing closely related species with the same genes, we also try to understand the scenarios and models under which speciation occurred. The use of multiple nuclear markers in a coalescent framework is a novel and promising area of phylogenetic and phylogeographic research in which we are actively working.



2. Analysis of species diversification in mammals

Species-level phylogenies contain important information in their patterns of branch splits. For example, current statistical techniques make possible to estimate rates of diversification from phylogenetic trees that have an adequate sampling of species. It is also possible to study the variability of diversification rates along the evolution of a group. The availability of a large amount of sequences in databases allows us to perform large-scale phylogenetic analyses with the aim of studying global diversification patterns in mammals.

3. Methodological aspects of phylogenetic reconstruction

Phylogenetic trees are essential in evolutionary biology and therefore understanding their potentials and limitations is important to make better use of them. With this aim, we are working on different aspects of tree reconstruction and on the detection of artifacts that may affect phylogenetic analyses. We are interested in all the steps of these analyses, including the generation of alignments, the reconstruction of phylogenetic trees, and the comparison of these trees. More recently, we have become interested in methodologies used at the interphase between phylogenetics and population genetics. Methods and software that we develop are made available online.

PUBLICATIONS 2009

- Esteban, R., Olano, J.M., Castresana, J., Fernández-Marín, B., Hernández, A., Becerril, J.M., García-Plazaola, J.I. 2009. Distribution and evolutionary trends of photoprotective isoprenoids within the plant kingdom. *Physiologia Plantarum* 135: 379-389.
- Ramírez, O., Gigli, E., Bover, P., Alcover, J.A., Bertranpetit, J., Castresana, J., Lalueza-Fox, C. 2009. Paleogenomics in a temperate environment: Shotgun sequencing from an extinct Mediterranean caprine. *PLoS ONE* 4, e5670.
- Sánchez-Fernández, D., Bilton, D.T., Abellán, P., Picazo, F., Ribera, I., Velasco, J., Millán, A. 2009. Los coleópteros acuáticos como indicadores de la biodiversidad. *Quercus* 275: 22-27.

FUNDED PROJECTS

Project Title: *Distribution and genetic diversity of the Iberian desman (Galemys pyrenaicus) in the Spanish Network of National Parks*
Financed by: *Ministerio de Medio Ambiente y Medio Rural y Marino. Network of National Parks Research Funds (014/2008).*
Years: *2009-2011*
PI: *Joaquim Gosálbez*

Project Title: *Grup de recerca en sistemàtica i evolució zoològica - ZOOSYSEVO*
Financed by: *Generalitat de Catalunya (2009 SGR 1462)*
Years: *2009-2013*
PI: *Salvador Carranza*

Project Title: *Phylogeny and speciation of mammals studied with multiple nuclear markers*
Financed by: *Ministerio de Ciencia e Innovación (GL2008-00434/BOS)*
Years: *2009-2011*
PI: *José Castresana*

GROUP

SYSTEMATICS, BIOGEOGRAPHY AND EVOLUTION OF REPTILES AND AMPHIBIANS LAB

GROUP MEMBERS

Salvador Carranza, Group Leader

| Tenured Scientist, CSIC

Josep Roca, Technician | Project Contract

Joan García-Porta, PhD Student | JAEPRE-CSIC Fellowship

Margarita Metallinou, PhD Student | FPU Scholarship, MEC

Raquel Vasconcelos, PhD Student co-supervised with Dr. D.J. Harris, CIBIO, Portugal | FCT Scholarship, Portugal

Catarina Rato, PhD Student co-supervised with Dr. D.J. Harris, CIBIO, Portugal | FCT Scholarship, Portugal

Mafalda Barata, PhD Student co-supervised with Dr. D.J. Harris, CIBIO, Portugal | FCT Scholarship, Portugal

Elisa Mora, MSc Student | Master in Biodiversity, UB

RESEARCH OUTLINE

Our research focuses on the application of phylogenetic analyses of reptiles and amphibians to understand how biodiversity is generated and maintained. Moreover, we are also interested in inferring the biogeographic and evolutionary patterns of the different groups studied, to revise their taxonomy and to use all this information to address conservation issues. Although our investigations include the study of many different reptile and amphibian groups, our main research sublines focus mainly on the faunas of the Mediterranean Basin and Arabia, including some oceanic and continental island, as for instance the Canary and the Cape Verde islands in the Atlantic Ocean and the archipelago of Socotra in the Indian Ocean.

RESEARCH SUBLINES

1. Historical biogeography and evolution of the reptiles and amphibians around the westernmost Mediterranean

Our main objectives are: 1) infer the geographical history and evolution of the reptiles and amphibians around the westernmost Mediterranean basin; 2) characterize and compare the molecular evolutionary rates of reptiles and amphibians; 3) identify using phylogenies the possible existence of Pliocene fossil islands in the area of study; and 4) test the current taxonomy of the groups concerned.

2. Uses of phylogenies to study evolutionary, ecological and biogeographical processes: the North African and Arabian arid reptile faunas

In this project, we are using molecular phylogenies from multiple reptile taxa to address a whole range of evolutionary, ecological and biogeographic questions. The main objectives of the project are: 1) to understand how deserts gain and maintain their endemic faunas; 2) to infer the age of the Sahara and Arabian deserts; 3) to compare the diversification rates of several desert lineages; and 4) to test and improve the current taxonomy of the groups concerned.

3. Island biogeography and evolution

The main goal of this research line is to take advantage of the excellent experimental conditions of the island systems to try to understand how biodiversity is generated and maintained. Island systems offer great opportunities to study evolution, and are especially attractive environments for several reasons: 1) they present discrete geographical entities within defined oceanic boundaries; 2) gene flow between individual islands is reduced by oceanic barriers; 3) their often small geographical size has made the cataloguing of flora and fauna easier than continental systems; 4) despite their small geographical size they can contain a diversity of habitats; and 5) they are often geologically dynamic with historical and contemporary volcanic and erosional activity. At the moment we are investigating both oceanic and continental reptile islands faunas from several places in the world including the Canary Islands and Cape Verde in the Atlantic Ocean and the Socotra archipelago in the Indian Ocean.

4. Distribution and genetic diversity of the Iberian desman (*Galemys pyrenaicus)* in the Spanish Network of National Parks (In collaboration with José Castresana)

PUBLICATIONS 2009

- Arnold, E.N., Robinson, M.D., Carranza, S. 2009. A preliminary analysis of phylogenetic relationships and biogeography of the dangerously venomous Carpet Vipers, *Echis* (Squamata, Serpentes, Viperidae) based on mitochondrial DNA sequences. *Amphibia-Reptilia* 30: 273-282.
- Mateos, E., Cabrera, C., Carranza, S., Riutort, M. 2009. Molecular analysis of the diversity of terrestrial planarians (Platyhelminthes, Tricladida, Continenticola) in the Iberian Peninsula. *Zoologica Scripta* 38: 637-649.
- Van der Meijden, A., Chiari, Y., Mucedda, M., Carranza, S., Corti, C., Veith, M. 2009. Phylogenetic relationships of Sardinian cave salamanders, genus *Hydromantes,* based on mitochondrial and nuclear DNA sequence data. *Molecular Phylogenetics and Evolution* 51: 399-404.
- Vasconcelos, R., Rocha, Ss, Brito, J.C., Carranza, S., Harris, D.J. 2009. First report of introduced African Rainbow Lizard *Agama agama* (Linnaeus, 1758) in the Cape Verde islands. *Herpetozoa* 21: 183-186.

FUNDED PROJECTS

Project Title: *Distribution and genetic diversity of the Iberian desman* (Galemys pyrenaicus) *in the Spanish Network of National Parks*
Financed by: *Ministerio de Medio Ambiente y Medio Rural y Marino (014/2008)*
Years: *2009-2011*
PI: *Joaquim Gosàlbez*

Project Title: *Sistemática, biogeografía y evolución de diversos grupos de reptiles de las Indias Occidentales*
Financed by: *CSIC ("Proyectos Intramurales Especiales")*
Years: *2008-2009*
PI: *Salvador Carranza*

Project Title: *Systematics, biogeography and evolution of some selected herpetofauna of the West Indies*
Financed by: *Ministerio de Ciencia e Innovación (2008301031)*
Years: *2009*
PI: *Salvador Carranza*

Project Title: *Using phylogenies to study evolutionary, biogeographic and ecological processes: the North African and Arabian arid reptile faunas*
Financed by: *Spanish Ministry of Science and Education (CGL2008-00827/BOS)*
Years: *2009*
PI: *Salvador Carranza*

Project Title: *Zoological Systematics and Evolution Research Group – ZOOSYSEVO*
Financed by: *Generalitat de Catalunya (AGAUR) (2009SGR1462)*
Years: *2009-2013*
PI: *Salvador Carranza*

GROUP

HERBIVORE BEETLE EVOLUTION LAB

GROUP MEMBERS

Jesús Gómez-Zurita, Group Leader

| Tenured Scientist, CSIC

Anabela Cardoso, Research Assistant | CSIC

Tinguaro Montelongo, PhD Student | FPI Scholarship, MEC

RESEARCH OUTLINE

We are interested in the systematics of beetles, the analysis of geographic and ecologic speciation and of the spatial structure of genetic diversity within a temporal framework (phylogeography), as well as the study of biological processes such as hybridization, unisexuality and insect-plant associations from an evolutionary perspective. The basic approach we follow to tackle this broad spectrum of research topics is a phylogenetic framework based upon information provided by DNA sequences. The focus of our research is a megadiverse group of herbivorous beetles, the Chrysomelidae, popularly known as leaf beetles. With well over 35,000 known species, from the arctic tundra to remote Pacific islands, the Chrysomelidae cover a wide range of life histories, offering suitable models to investigate any of the general evolutionary topics outlined above.

RESEARCH SUBLINES

1. Evolution of reproductive strategies: the role and importance of hybridization

The leaf beetle genus *Calligrapha* has both bisexual and unisexual species, whereby the latter seem to be the result of historical interspecific hybridization events. We study these events with a historical, phylogeographic perspective, but also from a genomic point of view, investigating molecular signatures of the hybrid origin of unisexual taxa. We are also interested in ecological aspects of this system, investigating performance and niche characteristics of sympatric bisexual and unisexual species, relevant to understand their interaction and respective evolutionary advantages.

2. Biodiversity and conservation of the tropical dry forest in Nicaragua

Tropical dry forests are one of the most threatened ecosystems on the planet. In this project we implement molecular tools to investigate both the inventory and the interactions sustained by this habitat in Nicaragua. Diagnostic DNA sequences are used for rapid biodiversity assessment of flowering plants and two groups of megadiverse phytophagous beetles, the Chrysomelidae and the Curculionidae, but also the host plants of the beetles by PCR-amplifying DNA remains of their diet to compare them with the local genetic database for the flora. This strategy will hopefully speed up considerably the much-needed tasks of inventorying and trophic networking compared to traditional approaches to the same problems.

3. Evolution in Pacific Islands: diversity and diversification of New Caledonian Chrysomelidae

New Caledonia is a continental fragment of Gondwana that isolated from other continental land masses by the end of the Cretaceous, and remained isolated since that period. It hosts a singular biota with high endemicity and in some cases purportedly very ancient, perhaps relicts of Gondwanian origin. However, this ancient origin is contentious and it was recently proposed that the island would have been colonized recently, after periods of underwater submergence in the Oligocene. The Chrysomelidae fauna in New Caledonia is very rich, with over 200 species described, mostly endemic. In this project, we aim at characterizing their species diversity using morphology and molecular markers, but also to

investigate their origin, age and diversification using molecular phylogenetics, as well as their ecologies, based on field observations and the use of molecular markers *(see Project 2)*.

4. Climate and speciation: European species complexes of *Cryptocephalus*

Cryptocephalus (Chrysomelidae) includes two closely related species complexes in the Western Palaearctic, the *C. sericeus*-complex and the *C. hypochaeridis*-complex, which include several species in mountainous areas, mainly in the Pyrenees and the Alps, and offer important taxonomic problems, including clinal variation of characters and possible hybrids. These are suggestive of recent, incomplete speciation and secondary contacts due to range changes, possibly related to climate oscillations during the Quaternary. We investigate these species complexes using a combination of phylogeographic approaches with nuclear and mitochondrial markers to delimit evolutionary units and recognize putative hybrids, as well as molecular phylogenetic analyses to time their diversification.

5. Systematic revision of Central and South American *Calligrapha*

The genus *Calligrapha*, with over 100 species in the American continent, is focus of our research on the evolution of reproductive strategies and host associations. Unfortunately, the taxonomy of the group has only been revised recently for North American species, including some 30 taxa. In order to clarify the systematics of the group as a guide for our molecular phylogenetic work, we are finishing now the revision of the bulk of the genus in its southern Nearctic and Neotropical distribution.

PUBLICATIONS 2009

- Cardoso, A., Serrano, A., Vogler, A.P. 2009. Morphological and molecular variation in tiger beetles of the *Cicindela hybrida* complex: is an 'integrative taxonomy' possible? *Molecular Ecology* 18: 648-664.
- Jurado-Rivera, J.A., Vogler, A.P., Reid, C.A.M., Petitpierre, E., Gómez-Zurita, J. 2009. DNA barcoding insect-host plant associations. *Proceedings of the Royal Society of London* 276: 639-648.

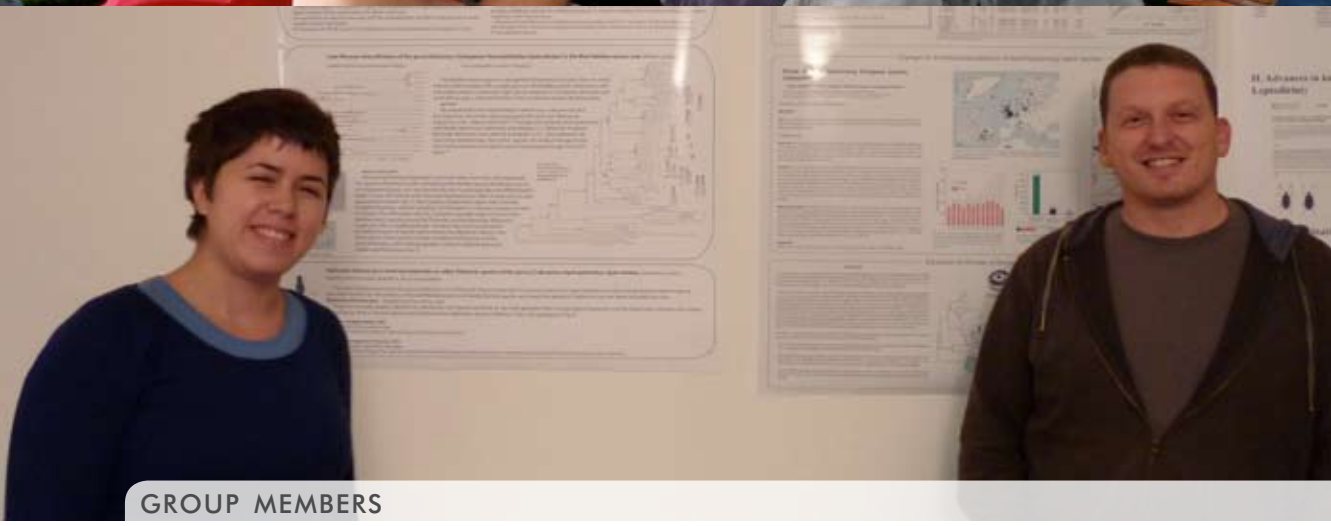
FUNDED PROJECTS

Project Title: *Evolución sin sexo: Circunstancias históricas e implicaciones ecológicas del origen híbrido de insectos unisexuales*
Financed by: *Ministerio de Ciencia e Innovación (CGL2008-00007)*
Years: *2009-2011*
PI: *Jesús Gómez-Zurita*

Project Title: *Sincronización rápida de Inventario e Interacciones en estudios de Biodiversidad: Herramientas moleculares al servicio del conocimiento y conservación del bosque seco tropical en Nicaragua*
Financed by: *Fundación Banco Bilbao Vizcaya*
Years: *2009-2012*
PI: *Jesús Gómez-Zurita*

GROUP

WATER CAVE BEETLE EVOLUTION LAB



GROUP MEMBERS

Ignacio Ribera, Group Leader

| Tenured Scientist, CSIC

Pedro Abellán, Postdoctoral Researcher | Postdoctoral Felloship Fundación Séneca

Arnaud Faille, Postdoctoral Researcher | CSIC contract

Amparo Hidalgo-Galiana, PhD Student | FPI Scholarship, MICINN

Valeria Rizzo, PhD Student | Scholarship Università La Sapienza, Roma

RESEARCH OUTLINE

We are interested in the origin and distribution of biodiversity, whether morphological, genetic, ecological or functional. Our model groups are different lineages of aquatic and subterranean Coleoptera, mostly (but not exclusively) focused on the Holarctic, and specially the Mediterranean. Main current research topics include: 1) systematics and biogeography of different lineages of water beetles; 2) evolution of "subterraneity" in Mediterranean cave and endogean beetles; 3) the effect of habitat constraints in the macroecology and macroevolution of freshwater invertebrates; and 4) the evolution of the size of the geographical range, including the use of comparative proteomics in closely related non-model species.

RESEARCH SUBLINES

1. The evolution of geographical ranges

We try to understand the reason behind differences in the size of the geographical range among closely related species. For that we use a combination of phylogenetic, ecological and physiological data, avoiding the use of statistical correlations to infer causality.

2. Conservation and biogeography of Iberian aquatic beetles

We are currently collaborating with the "Ecología acuática" group of the Universidad de Murcia in a project to assess the effectiveness of the network of Spanish National Parks in protecting a representative sample of the taxonomic and phylogenetic diversity of the Iberian fauna of aquatic beetles.

PUBLICATIONS 2009

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- Faille, A., Bourdeau, C., Fresneda, J. 2009 Eskualdunella delespierrei Coiffait, 1950: la clé inattendue d'une énigme biogéographique (Coleoptera, Leiodidae). *Bulletin de la Société entomologique de France* 114: 469-473.
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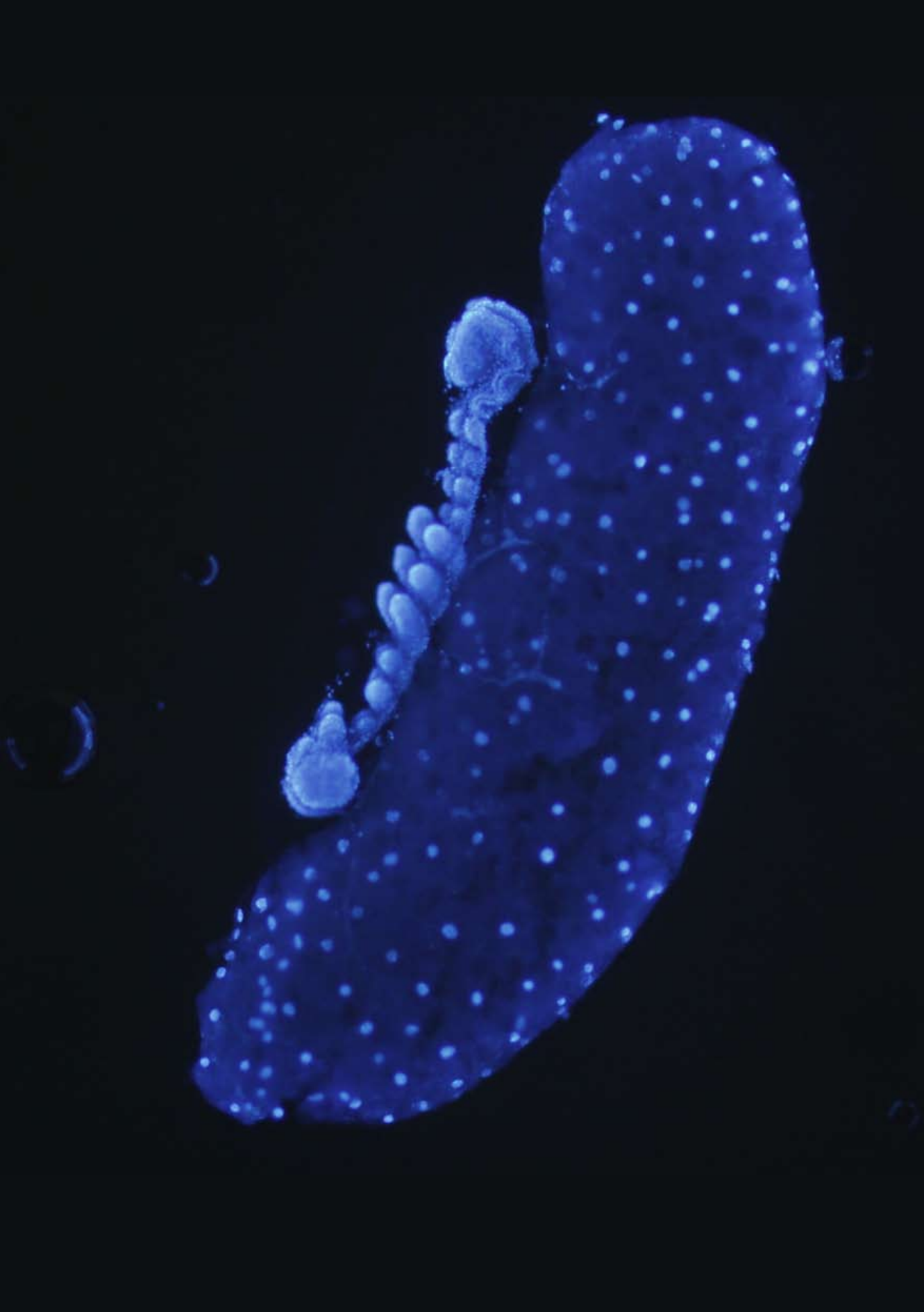
FUNDED PROJECTS

Project Title: *Effectiveness of the peninsular National Park Net in the conservation of aquatic biodiversity*
Financed by: *Ministerio de Ciencia e Innovación. Research program on National Parks (Ref. 023/2007)*
Years: *2007-2010*
PI: *Andrés Millán (Universidad de Murcia)*

Project Title: *The evolution of the size of the geographical range as a key factor in the generation of biodiversity*
Financed by: *Ministerio de Ciencia e Innovación (CGL2007-61665)*
Years: *2007-2010*
PI: *Ignacio Ribera*



PROGRAM comparative and computational genomics

RESEARCH GROUPS

Genomics of Individuality Lab
Francesc Calafell, *Group Leader*

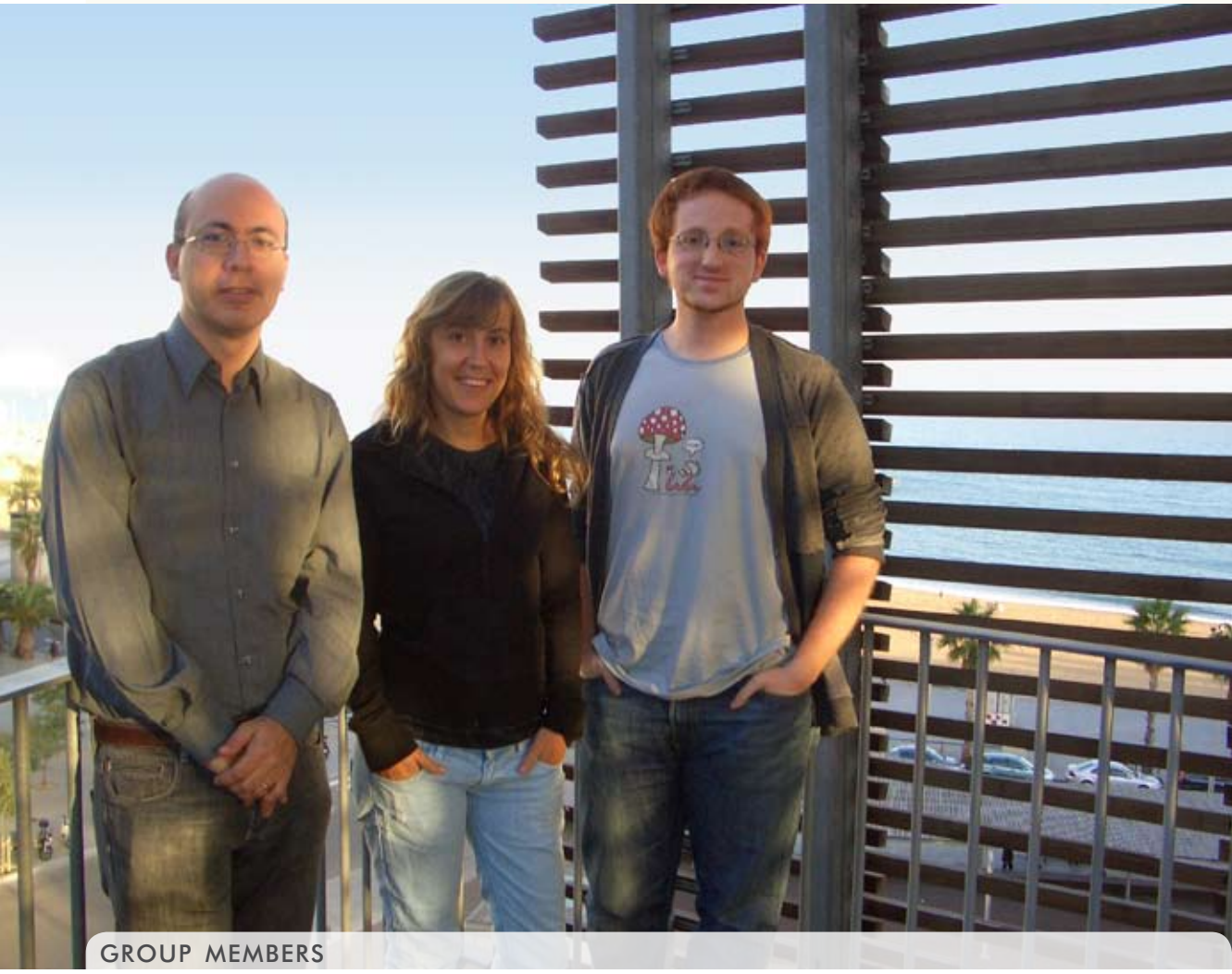
Paleogenomics Lab
Carles Lalueza-Fox, *Group Leader*

Evolutionary Genomics Lab
Arcadi Navarro, *Group Leader*

In the Comparative and Computational Genomics program, genomes are compared at the intra and inter-specific levels with the general aims of understanding genome dynamics, reconstructing the evolutionary processes that generate biodiversity and linking genomic and phenotypic differences between individuals and species. To achieve these goals, we deploy both experimental and theoretical/numerical approaches, with an strong emphasis in computational techniques. Genomes contain a wealth of information, not only about how phenotypes are shaped in interaction with the environment, but also about the evolutionary history of the species these genomes come from. Studying full genomes is, thus, key to answer the basic questions posed eight decades ago by the research paradigm created by the Synthetic Theory of Evolution: How much adaptation can we detect in nature? In addition to the study of adaptation, genomics allows us to answer questions about other crucial evolutionary phenomena such as speciation or the dynamics of horizontal transfer of information within the genome itself. Understanding these phenomena is key to link genotypes and phenotypes, with all the implications of such knowledge in shedding light in issues such as hominization or the genetic architecture of complex phenotypes.

GROUP

GENOMICS OF INDIVIDUALITY LAB



GROUP MEMBERS

Francesc Calafell, Group Leader

| Associate Professor, UPF

Marta Melé, PhD Student | FI Scholarship, MEC

Marc García, PhD Student | FU Scholarship, MEC

RESEARCH OUTLINE

The general topics that interest us revolve around the genomics of individuality: what is there in our genomes that makes us the way we are? What does it tell about our ancestry? How does it affect our susceptibility to diseases? How can this be applied in practical settings, i.e., in forensic genetics? This is implemented in practice in three main projects: 1) we are trying to detect past recombination events in current sequences and use them as phylogenetic markers; 2) we are characterizing the skin microbiome in healthy and psoriatic skin to reveal whether psoriasis has a microbial trigger; and 3) we are working in a case-control association study to detect any host genetic determinant of a poor progression in 2009 A(H1N1) influenza.

RESEARCH SUBLINES

1. Human populations genetics and recombination

Recombination is a problem often cited to shun autosomal genetic diversity when reconstructing population history, which is mostly carried out with the non-recombining portion of the Y chromosome and mitochondrial DNA. We are trying to turn this argument around and using recombination events as phylogeographic markers. We are working with Laxmi Parida and Asif Javed to develop software that will detect chromosomes that are descendants from recombination events. This information can be recoded into recotypes and analyzed in the same way as haplotypes are. We expect to add a new tool to analyze autosomal diversity in population genetics, but it could also be applied to detect natural selection and to understand recombination itself. This is basically the work of Marta Melé, and is carried out in collaboration with Jaume Bertranpetit.

2. The skin microbial flora in health and disease

How the human body works cannot be understood without its relationship with its associated bacterial and viral flora. Human genomic diversity can be extended to encompass the genomic diversity of the microbes living with us. We are studying the skin microbial flora to try to comprehend the skin as a complex ecosystem. We are characterizing bacterial and retroviral diversity, as well as performing bacterial metagenomics in samples from healthy individuals. We seek to establish a baseline and detect how it is affected in individuals with skin conditions such as psoriasis. This is Marc García's project, in collaboration with Marta Ferran at Hospital del Mar.

3. Genetic susceptibility factors in poor influenza progression

Little is known about the possible genetic susceptibility factors for infectious diseases beyond some classical examples in malaria. Taking the opportunity created by the 2009 A(H1N1) influenza pandemic, we are collecting confirmed influenza cases that required hospitalization and had no obvious risk factors, and comparing them with milder cases. By genotyping a whole genome array, we hope to discover genetic susceptibility factors for poor progression in influenza. The case and control collection is part of a much wider project led by Ángela Domínguez (UB), and we are collaborating with Fernando González-Candelas (UV).

PUBLICATIONS 2009

- Berniell-Lee, G., Calafell, F., Bosch, E., Heyer, E., Sica, L., Mouguiama-Daouda, P., Van der Veen, L., Hombert, J-M., Quintana-Murci, L., Comas, D. 2009. Genetic and demographic implications of the Bantu expansion: insights from human paternal lineages. *Molecular Biology and Evolution* 26: 1581-1589.
- Bosch, E., Laayouni, H., Morcillo-Suárez, C., Casals, F., Moreno-Estrada, A., Ferrer-Admetlla, A., Gardner, M., Rosa, A., Navarro, A., Comas, D., Graffelman, J., Calafell, F., Bertranpetit, J. 2009. Decay of linkage disequilibrium within genes across HGDP-CEPH human samples: most population isolates do not show increased LD. *BMC Genomics* 10:338.
- Casals, F., Ferrer-Admetlla, A., Sikora, M., Ramírez-Soriano, A., Marquès-Bonet, T., Despiau, S., Roubinet, F., Calafell, F., Bertranpetit, J., Blancher, A. 2009. Human pseudogenes of the ABO family show a complex evolutionary dynamics and loss of function. *Glycobiology* Jun. 19: 6:583-91. Epub Feb. 13. PMID: 19218399.
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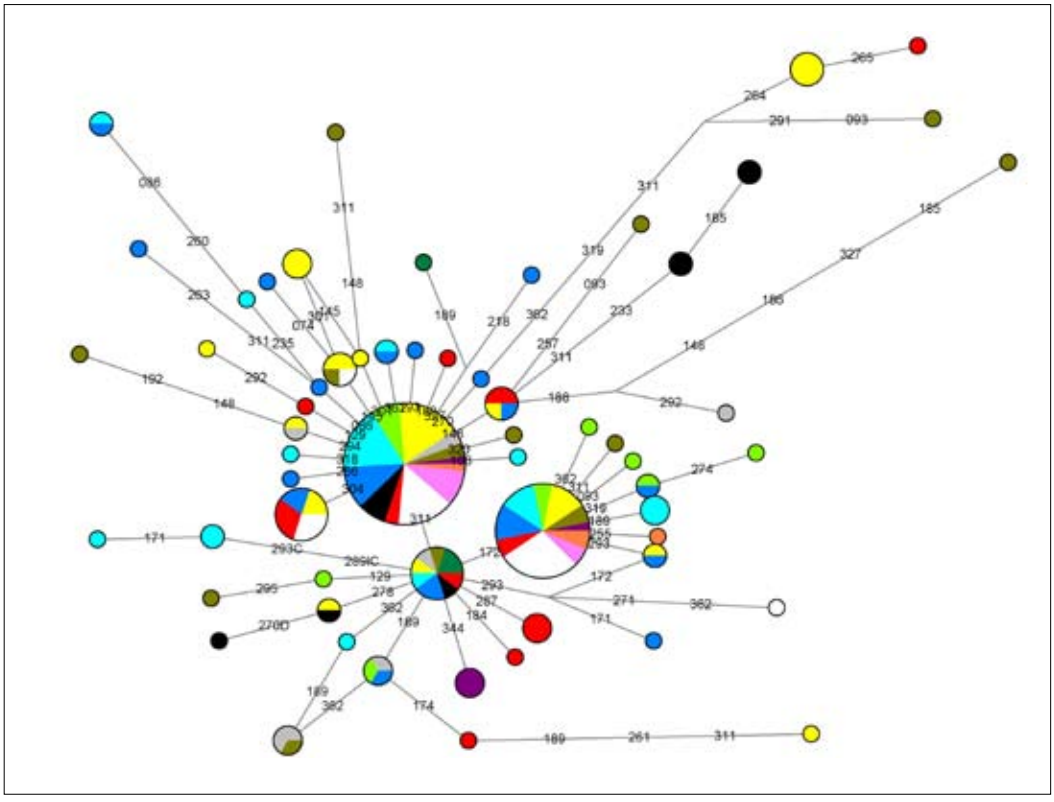
- Garagnani, P., Laayouni, H., González-Neira, A., Sikora, M., Luiselli, D., Bertranpetit, J., Calafell, F. 2009. Isolated populations as treasure troves in genetic epidemiology: the case of the Basques. *European Journal of Human Genetics (EJHG)* 17: 1490-1494.
- Moreno-Estrada, A., Tang, K., Sikora, M., Marquès-Bonet, T., Casals, F., Navarro, A., Calafell, F., Bertranpetit, J., Stoneking, M., Bosch, E. 2009. Interrogating 11 fast-evolving genes for signatures of recent positive selection in worldwide human populations. *Molecular Biology and Evolution* 26: 2285-2297.



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- Sandoval, K., Buentello-Malo, L., Peñaloza-Espinosa, R., Avelino, H., Salas, A., Calafell, F., Comas, D. 2009. Linguistic and maternal genetic diversity are not correlated in Native Mexicans. *Human Genetics* 126: 521-531.
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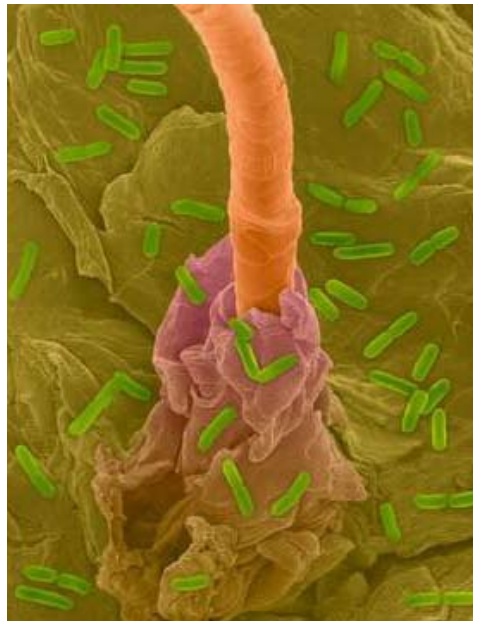
- Tofanelli, S., Bertoncini, S., Castrì, L., Luiselli, D., Calafell, F., Donati, G., Paoli, G. 2009. On the origins and admixture of Malagasy: new evidence from high-resolution analyses of paternal and maternal lineages. *Molecular Biology and Evolution* 26: 2109-2124.

FUNDED PROJECTS

Project Title: *Dinámica de la Recombinación en el genoma humano*
Financed by: *Ministerio de Ciencia e Innovación (REF:BFU2007-63657)*
Years: *2008-2010*
PI: *Francesc Calafell*

Project Title: *Grup de Recerca Consolidat-SGR*
Financed by: *Generalitat de Catalunya (2009 SGR-1101)*
Years: *2009-2013*
PI: *Jaume Bertranpetit*



GROUP

PALEOGENOMICS LAB

GROUP MEMBERS

Carles Lalueza-Fox, Group Leader

| Research Scientist, CSIC

Oscar Ramírez, Visitant Professor, UPF

Elena Gigli, PhD Student | FPI Scholarship, MICINN

Federico Sánchez, PhD Student | FPI Scholarship, MICINN

RESEARCH OUTLINE

Our research group focuses on paleogenomics, the study of structure, function and organization of ancestral genomes. We are interested in different evolutionary problems that can be answered with ancient DNA data, involving human evolution, population dynamics, phylogenetics, phylogeography and adaptive processes. We work with different animals, including mammoths, cave bears, *Myotragus balearicus* and lynxs, but also with an extinct hominin species, the Neandertals. With regard to Neandertals, we are collaborating with the Neandertal Genome consortium in the generation of a genomic draft. In our group we are basically investigating in: 1) the genetic basis of phenotypical traits associated to the individualisation and its diversity among Neandertals; 2) the genetic relationships within a Neandertal family group from El Sidrón site (Asturias, Spain); and 3) the functional implications of genetic variants exclusively found in Neandertals.

RESEARCH SUBLINES

1. Adaptive traits and evolutionary history of Neandertals

We are currently retrieving genes related to different aspects such as physiology, cognition, phenotype and metabolism that can be of evolutionary interest. Also we are trying to obtain genetic information from different Neandertals to unravel their possible phylogeographic structure.

2. Genetic diversity within a Neandertal family group

We are analyzing all the individuals from El Sidrón site in Asturias, Spain. This is a family group of at least 10 Neandertal individuals that became accidentally accumulated in a single, synchronic event within a subterranean karstic system. El Sidrón offers the unique opportunity of knowing which was the genetic diversity within a single Neandertal family and therefore, of making inferences about their demography.

3. Phylogenetics, phylogeography and adaptation in extinct species

We are studying different extinct species, including *Puffinus,* lynx, *Myotragus balearicus,* and mammoths, to answer specific questions about their phylogeny, adaptation and evolution. We are particularly interested in studying some insular endemics and the genomic basis of some common adaptive patterns observed among them such as body size reduction.

PUBLICATIONS 2009

- Briggs, A.W., M. Good, J., E. Green, R., Krause, J., Maricic, T., Stenzel, U., Lalueza-Fox, C. et al. 2009. Targeted retrieval and analysis of five Neandertal mtDNA genomes. *Science* 325: 318-321.
- Gigli, E., Rasmussen, M., Civit, S., Rosas, A., de la Rasilla, M., Fortea, J., Gilbert, MTP, Willerslev, E., Lalueza-Fox, C. 2009. An improved PcR method for endogenous DNA retrieval in contamined Neandertal samples based on the use of blocking primers. *Journal of Archeological Sciences*. 36: 2676-2679.
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- Ramírez, O., Gigli, E., Bover, P., Alcover, J.A., Bertranpetit, J., Castresana, J., Lalueza-Fox, C. 2009. Paleogenomics in a temperate environment: Shotgun sequencing from an extinct Mediterranean caprine. *PLoS ONE* 4, e5670.

FUNDED PROJECTS

Project Title: *Diversidad genética y adaptación en Neandertales*
Financed by: *CSIC ("Proyectos Intramurales Especiales")*
Years: *2008-2009*
PI: *Carles Lalueza-Fox*

Project Title: *Neandertal genome diversity analyzed by ultrasequencing techniques (REF: BFU2009-06974)*
Financed by: *Ministry of Science and Innovation, Spain*
Years: *2010-2012*
PI: *Carles Lalueza-Fox*

GROUP

EVOLUTIONARY GENOMICS LAB

GROUP MEMBERS

Arcadi Navarro, Group Leader

| Professor, UPF – Research Professor, ICREA

Tomàs Marquès, Senior Scientist | Marie Curie Fellow
Elodie Gazave, Post-doc | Project Contract
Fleur Darre, Post-doc | Project Contract
Natalia Petit, Post-doc | Project Contract
Olga Fernando, PhD Student | FCT Scholarship
Belén Lorente, PhD Student | UPF Contract
Urko Martínez, PhD Student | UPF Scholarship
Carlos Morcillo, Project Manager | INB (National Bioinformatics Institute)
Ángel Carreño, IT technician | INB (National Bioinformatics Institute)
Txema Heredia, IT Technician | INB (National Bioinformatics Institute)
Fernando Muñiz, IT Technician | INB (National Bioinformatics Institute)
Rui Faria, Visiting Scientist | FCT Fellowship
Graciela Sotelo, Visiting Scientist | UPF Contract

RESEARCH OUTLINE

Life as we see it in our planet today has been shaped by many different biological processes during billions of years. These processes leave a signature in our genomes in the form of differences between species, or between individuals of the same species. Interrogating these patterns of genome diversity we can infer what are the forces that affect living organisms, how and when they act and how do they affect such various things as biodiversity, human emotions or the differential susceptibility of different persons to certain diseases. All this knowledge empowers us to control our future but, above all, it is fun to obtain.

In practical terms, there are two main kinds of research we do in our group. First, we develop and analyze models that help to answer questions concerning chromosomal evolution, genome dynamics, speciation, comparative gene expression and the genetic architecture of complex human traits (including disease). The tools we use for these research lines include analytical and simulation studies, together with data mining and analysis. Second, we also carry out wet-lab research. Lately, we have focused on array CGH of primate genomes to study the evolution of copy-number variation and Genome-Wide Association Studies of human socio-economic traits.

RESEARCH SUBLINES

1. Chromosomal evolution and speciation

We study how large chromosomal rearrangements affect many aspects of genome structure and evolution, including how they may drive the generation of new species.

2. Segmental duplications and copy-number variation in primates

The genomes of humans and other primates show an enrichment in Segmental Duplications (SDs) with high sequence identity. SDs are fundamental for the creation of novel genes and may have been key in the evolution of our lineage.

3. Detecting positive selection in the human lineage

We try to detect the signature of adaptive changes out of single-copy protein-coding regions. We focus in how natural selection my have shaped regulatory regions and the functional content of SDs.

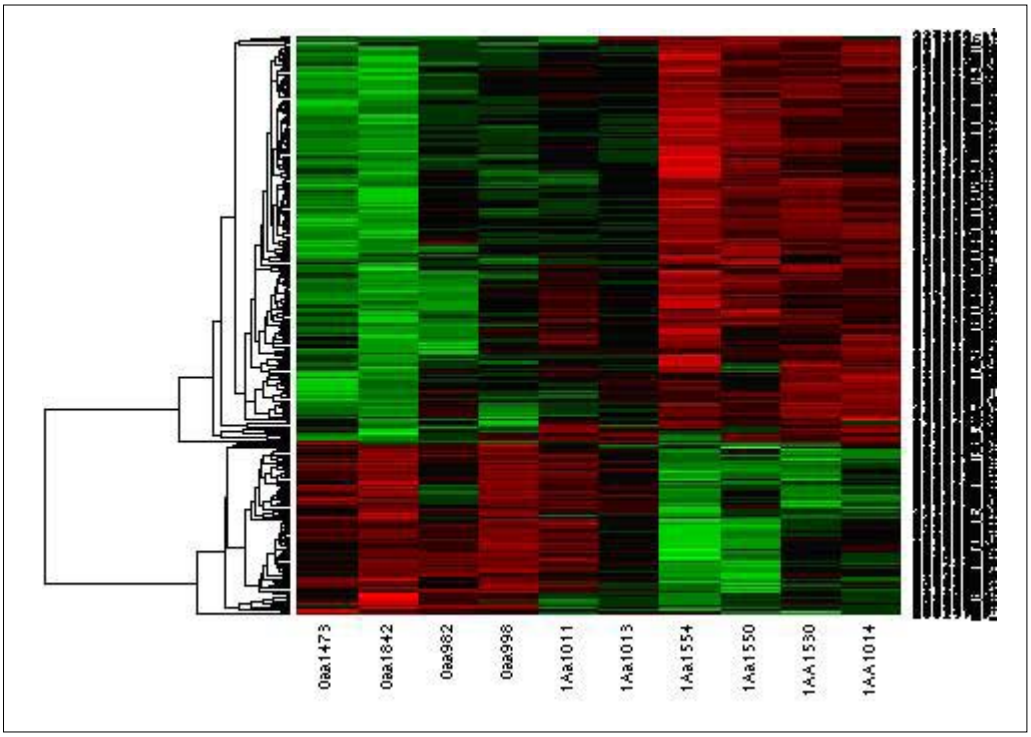
4. The world-wide distribution of human disease

We study world-wide patterns of disease susceptibility distribution to ascertain how these may have been influenced by recent human evolution.

5. Genoeconomics

Complex human traits that are exclusive of our lineage are the basis of our societies and have huge socio-economic impact. We deploy the latest tools of genomics for the dissection of human economic traits.

- Atran, S., Navarro, A., Ochsner, K., Tobeña, A., Vilarroya, O. 2009. Foreword: Values, empathy, and fairness across social barriers. *Annals of the New York Academy of Sciences* 1167: 1-4.
- Bekpen, C., Marquès-Bonet, T., Alkan, C., Antonacci, F., Leogrande, M.B., Ventura, M., Kidd, J.M., Siswara, P., Howard, Jonathan C., E. Eichler. E. 2009. Death and resurrection of the human IRGM gene. *PLoS Genetics* 5: e1000403.
- Bosch, E., Laayouni, H., Morcillo-Suárez, C., Casals, F., Moreno-Estrada, A., Ferrer-Admetlla, A., Gardner, M., Rosa, A., Navarro, A., Comas, D., Graffelman, J., Calafell, F., Bertranpetit, J. 2009. Decay of linkage disequilibrium within genes across HGDP-CEPH human samples: most population isolates do not show increased LD. *BMC Genomics* 10:338.
- Camiña-Tato, M., Morcillo-Suárez, C., Navarro, A., Fernández, M., Horga, A., Montalbán, X., Comabella, M. 2009. Genetic association between polymorphisms in the BTG1 gene and multiple sclerosis. *Journal of Neuroimmunology* 213: 142-147.



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- Marquès-Bonet, T., Ryder, Oliver A., Eichler, Evan E. Sequencing primate genomes: what have we learned? *Annual Review of Genomics and Human Genetics* 10: 355-386.

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- Moreno-Estrada, A., Tang, K., Sikora, M., Marquès-Bonet, T., Casals, F., Navarro, A., Calafell, F., Bertranpetit, J., Stoneking, M., Bosch, E. 2009. Interrogating 11 fast-evolving genes for signatures of recent positive selection in worldwide human populations. *Molecular Biology and Evolution* 26: 2285-2297.
- Navarro, A. 2009. Genoeconomics: promises and caveats for a new field. *Annals of the New York Academy of Sciences*. 1167: 57-65.
- Ogorelkova, M., Navarro, A., Vivarelli, F., Ramírez-Soriano, A., Estivill, X. 2009. Positive selection and gene conversion drive the evolution of a brain-expressed snoRNAs cluster. *Molecular Biology and Evolution* 26: 2563-2571.
- Palacios, R., Gazave, E., Goñi, J., Piedrafita, G., Fernando, O., Navarro, A., Villoslada, P. 2009. Allele-specific gene expression is widespread across the genome and biological processes. *PloS One* 4 (1): e4150.

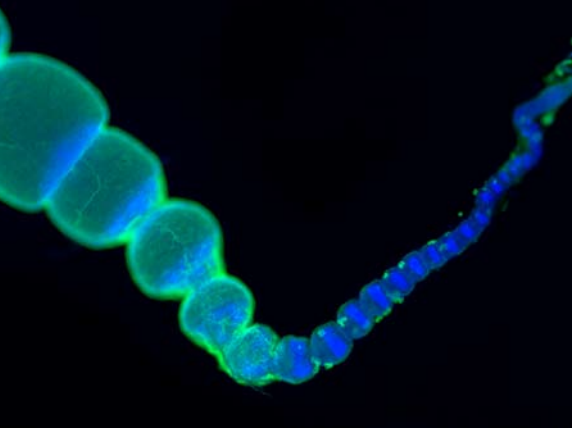
FUNDED PROJECTS

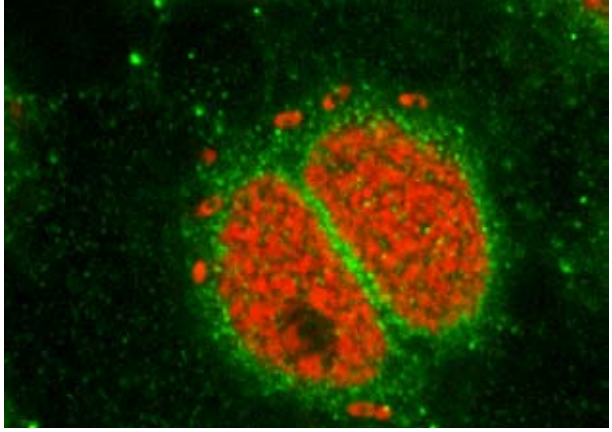
Project Title: *Exploring the behavioral genetics of Trade and Cooperation*
Financed by: *Ministerio de Educación y Ciencia (MEC-SEJ2007-30267-E/SOCI)*
Years: *2008-2011*
PI: *Arcadi Navarro*

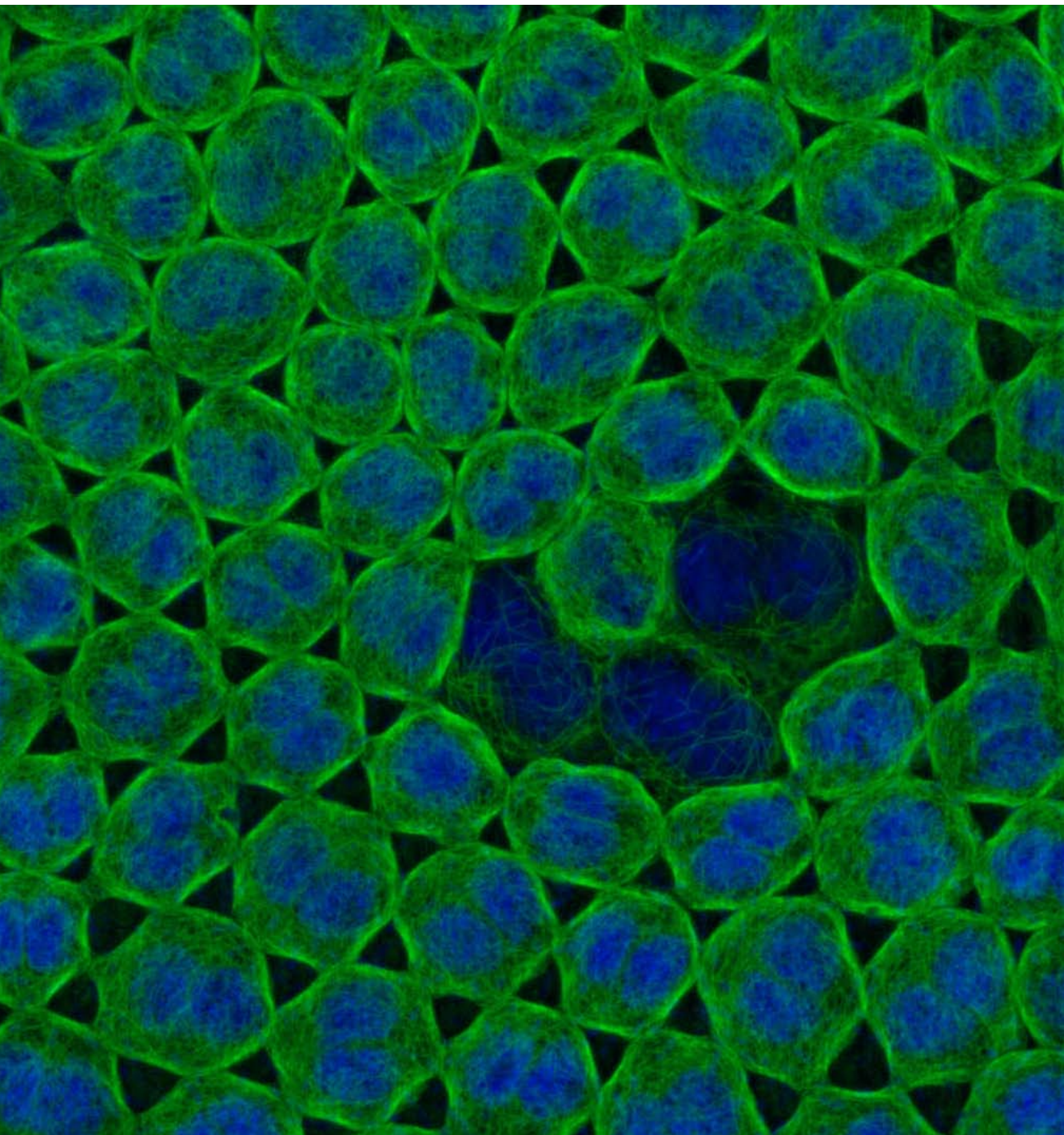
Project Title: *IMID-Kit*
Financed by: *Ministerio de Educación y Ciencia (MEC-PSS-010000-2008-36)*
Years: *2008-2009*
PIs: *Arcadi Navarro and Jaume Bertranpetit (coordinator: S. Marsal)*

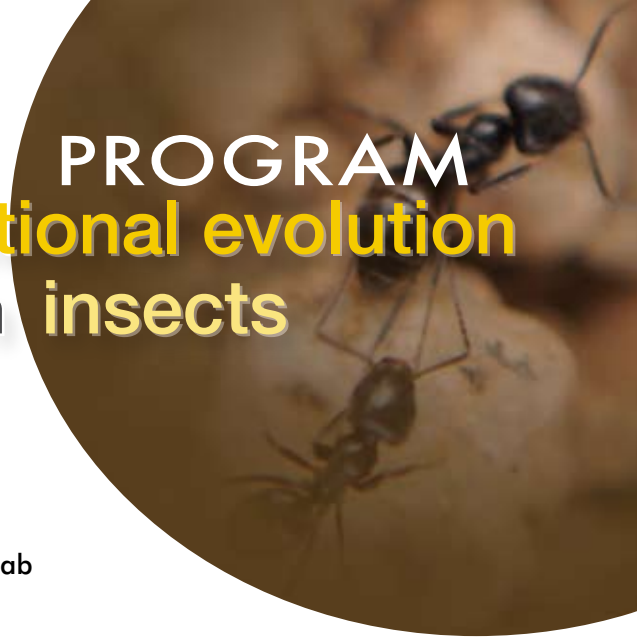
Project Title: *INB GN8*
Financed by: *Genoma España (Instituto Nacional de Bioinformática)*
Years: *2003-2009*
PI: *Arcadi Navarro*

Project Title: *Red Española de Esclerosis Múltiple*
Financed by: *Ministerio de Ciencia e Innovación. Instituto Carlos III (ISCIII-RD07/0060/2021)*
Years: *2009*
PI: *Arcadi Navarro*









PROGRAM functional evolution in insects

RESEARCH GROUPS

Insect Physiology and Molecular Biology Lab
Xavier Bellés, *Group Leader*

Insect Reproduction Lab
Maria-Dolors Piulachs, *Group Leader*

Dhosophila Telomeres Lab
Elena Casacuberta, *Group Leader*

Nuclear Hormone Receptors in Insect Development Lab
David Martín, *Group Leader*

Nutritional Signals and Reproduction in Insects Lab
José Luis Maestro, *Group Leader*

This program aims at studying fundamental processes in animal life, like metamorphosis, reproduction, development, cell division or telomere regulation, from a comparative perspective and in an evolutionary frame. Studies are focused on invertebrates, especially in insects, and they are largely based on functional genomics approaches. Until now, the models used have been insects, in particular cockroaches *(Blattella),* moths *(Spodoptera),* bees *(Apis)* and flies *(Drosophila),* and works have been directed to study processes like moulting, oogenesis, vitellogenesis or telomere replication. In most cases, the endocrine regulation of these processes has been also an important subject of study, and methodologies have covered practically all scales, from morphological to molecular. At present, we have privileged the use of RNA interference (RNAi) techniques to study gene functions, given our interest to compare non-model species, which very often are not easily transformable from a genetic point of view. In these cases, RNAi offers an unique way to face functional genomics on these species. This line combines gene sequence analysis and experimental approaches to unveil gene functions, with the aim of understanding the evolution of biological processes. In the context of the general project of the IBE, it affords the tools of experimental biology, which are of paramount importance to understand the adaptative mechanisms of evolution.

GROUP

INSECT PHYSIOLOGY AND MOLECULAR BIOLOGY LAB

GROUP MEMBERS

Xavier Belles, Group Leader

| Research Professor, CSIC

Eva Gómez-Orte, Post-doc | JAEDOC-CSIC Fellowship

Ferran Borràs, PhD Student | FPI Scholarship, MEC

Mercedes Rubio, PhD Student | JAEPRE-CSIC Fellowship

Alba Herráiz, PhD Student | JAEPRE-CSIC Fellowship

Jesús Lozano, PhD Student | FPI Scholarship MICINN

RESEARCH OUTLINE

The interests of the group have been traditionally diverse, trying to embrace a number of subjects around the physiology of the insect. In general, research has dealt on insect physiological processes regulated by hormones, especially metamorphosis. We use every scale of observation, from morphology to biochemistry and molecular biology, although the molecular scale tends to dominate in our most recent work. Thus, high throughput sequencing (for small RNA catalogues and for transcriptomes) has become a powerful source of information, whereas interference of RNA (RNAi) came to be a key tool for functional studies. We are interested in processes (especially metamorphosis), not only from a mechanistic point of view but also from an evolutionary perspective. Given that most information available has been obtained in highly modified insect species (especially in the omnipresent fruit fly, *Drosophila melanogaster*), we currently use a poorly modified, hemimetabolan insect species, the German cockroach *Blattella germanica*, as the main model.

RESEARCH SUBLINES

At present, we work on four main lines: Insect metamorphosis, Juvenile hormone (JH) action, Small RNAs, and Stress response.

1. Insect metamorphosis

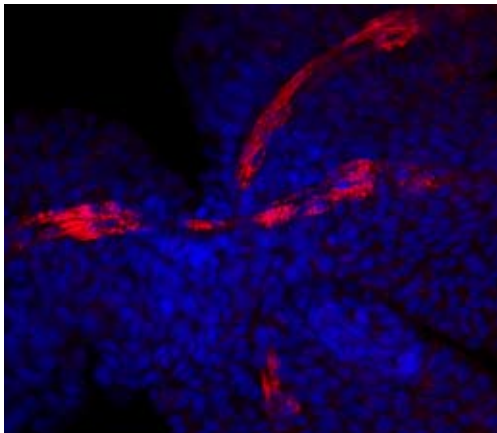
We use the hemimetabolan *Blattella germanica* as the main model. We aim at elucidating the mechanisms regulating the metamorphosis in this species, and then to compare them with those operating in holometabolans. The idea is to infer the evolutionary history underlying the transition from hemimetaboly to holometaboly.

2. Juvenile hormone action

Our aim is unveiling factors involved in juvenile hormone signaling in *Blattella germanica*. Firstly, studying in this cockroach those factors discovered in holometabolan models, then, searching new signaling factors in the juvenile hormone hierarchy in *B. germanica*. Information from the molecular action of ecdysone will be inspiring, given that signaling networks of ecdysteroid hierarchy can show common or interacting elements with those of juvenile hormone.

3. Small RNAs

The idea is to study the possible regulatory role of microRNAs in metamorphosis, juvenile hormone signaling and stress response. Moreover, we are also interested in investigating the basic biochemical machinery involved in the RNAi process and microRNA generation.



4. Stress response

We work on the finding of molecular markers of early signs of water stress in insects. The study of the effects of decreasing water availability in model species *(Blattella germanica, Tribolium castaneum)* would lead to find suitable markers. Then the study of these markers in natural populations of other species submitted to water stress could serve to validate the markers.

PUBLICATIONS 2009

- Bellés, X. 2009. Origen y Evolución de la Metamorfosis de los Insectos. In: Evolución y adaptación. 150 años después del origen de las Especies (H. Dopazo, A. Navarro eds.), pp. 191-199. Sociedad Española de Biología Evolutiva.
- Bellés, X. 2009. Spider beetles (Coleoptera, Ptinidae) from the Socotra Archipelago. *Fauna of Saudi Arabia* 24: 145-154.
- Gómez-Orte, E., Bellés, X. 2009. MicroRNA-dependent metamorphosis in hemimetabolan insects. *Proceedings of the National Academy of Sciences of the United States of America* 106: 21678-21682.
- Irles, P., Bellés, X., Piulachs, M.D. 2009. Brownie, a Gene Involved in Building Complex Respiratory Devices in Insect Eggshells. *PLoS ONE* 4 (12): e8353. doi:10.1371/journal.pone.0008353.
- Irles, P., Bellés, X., Piulachs, M.D. 2009. Identifying genes related to choriogenesis in insect panoistic ovaries by Suppression Subtractive Hybridization. *BMC Genomics* Apr. 30: 10:206.
- Maestro, J.L., Cobo, J., Bellés, X. 2009. Target of rapamycin (TOR) mediates the transduction of nutritional signals into juvenile hormone production. *Journal of Biochemical Chemistry* 284, 5506-5513.
- Revuelta, L., Piulachs, M.D., Bellés, X., Castañera, P., Ortego, F., Díaz-Ruíz, J.R, Hernández-Crespo, P, Tenllado, F. 2009. RNAi of *ace1* 1 and *ace2* in *Blattella germanica* reveals their differential contribution to acetylcholinesterase activity and sensitivity to insecticides. *Insect Biochemistry and Molecular Biology* 39: 913-919.

FUNDED PROJECTS

Project Title: *Global change and physiological diversity*
Financed by: *International Laboratory of Global Change (LINC Global), CSIC (Spain)-PUC (Chile)*
Years: *2009*
PIs: *Xavier Bellés and Francisco Bozinovic*

Project Title: *Silencing the silencers. Mechanistic bases of metamorphosis regulation in insects*
Financed by: *Ministerio de Ciencia e Innovación. Consolider program. (CGL2008-03517/BOS).*
Years: *2009-2013*
PI: *Xavier Bellés*

GROUP

INSECT REPRODUCTION LAB

GROUP MEMBERS

Maria-Dolors Piulachs, Group Leader

| Research Scientist, CSIC

Erica D. Tanaka, Post-doc | JAEDOC-CSIC Fellowship Contract

Paula Irles, PhD Student | JAEPRE-CSIC Fellowship

Alba Herráiz, PhD Student | JAEPRE-CSIC Fellowship • LINCGlobal

RESEARCH OUTLINE

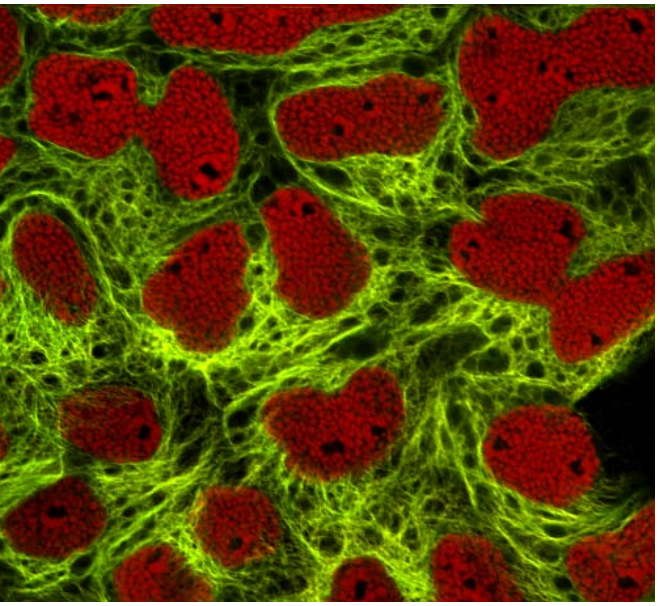
Our aim is to understand how the oogenesis in insects is regulated, considering the structural diversity of ovary types and their respective evolutionary history. Until now, ovarian maturation has been studied in detail only in the dipterans *Drosophila melanogaster* and *Aedes aegypti*, which are highly modified species, with meroistic ovaries regulated by ecdysteroids. In our case, we use as model the cockroach *Blattella germanica*, which is an hemimetabolan species with panoistic ovaries, whose vitellogenesis and oocyte growth are regulated by juvenile hormone. Our working hypothesis is that some genes will be conserved in structure and function in panoistic and meroistic ovaries, whereas other genes will be specific to one of these types or will have different functions in the two ovarian types. The approach is to study the genes that are inducible by JH in the ovary of *B. germanica* and their functions, and to establish how many of these genes and functions are conserved in other insect species with different ovary types.

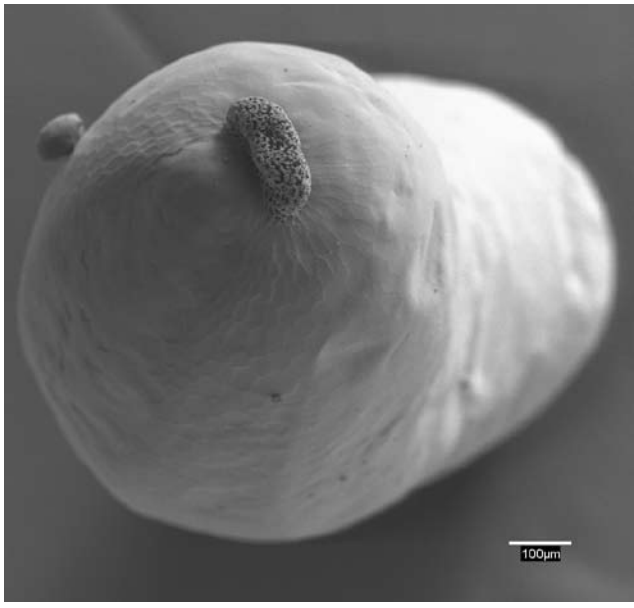
RESEARCH SUBJECTS

Our research focuses on three main subjects:

1. Vitellogenesis

Is the most important process in oocyte maturation and with apivotal role in insect reproduction. We like to understand the mechanism of vitellogenin synthesis induced by JH and to elucidate the mechanisms regulating the expression of the involved receptors.





2. Regulation of oogenesis in panoistic ovaries

We study ovarian maturation, focusing our research in oocyte capacitation and previtellogenesis, oocyte development in vitellogenesis, and chorion synthesis. Attention is also paid to the role of miRNA in regulating oogenesis.

3. Evolution of ovarian structure and function

The idea is to study the function of genes expressed in the ovary of *B. germanica* and to establish how many of these genes and functions are conserved in meroistic models. Data obtained might suggest functional scenarios underlying the transition between the panoistic and the meroistic type.

PUBLICATIONS 2009

- Irles, P., Bellés, X., Piulachs, M.D. 2009. Brownie, a Gene Involved in Building Complex Respiratory Devices in Insect Eggshells. *PLoS ONE* 4 (12): e8353. doi:10.1371/journal.pone.0008353.
- Irles, P., Bellés, X., Piulachs, M.D. 2009. Identifying genes related to choriogenesis in insect panoistic ovaries by Suppression Subtractive Hybridization. *BMC Genomics* Apr. 30: 10:206.
- Revuelta, L., Piulachs, M.D., Bellés, X., Castañera, P., Ortego, F., Díaz-Ruíz, J.R, Hernández-Crespo, P, Tenllado, F. 2009. RNAi of *ace1* 1 and *ace2* in *Blattella germanica* reveals their differential contribution to acetylcholinesterase activity and sensitivity to insecticides. *Insect Biochemistry and Molecular Biology* 39: 913-919.

FUNDED PROJECTS

Project Title: *Endocrine keys in the structural evolution of insects ovaries*
Financed by: *Ministerio de Ciencia y Innovación (BFU2008-00484)*
Years: *2009-2011*
PI: *Maria-Dolors Piulachs*

Project Title: *Global change and physiological diversity*
Financed by: *International Laboratory of Global Change (LINC Global), CSIC (Spain)-PUC (Chile)*
Years: *2009*
PIs: *Xavier Bellés and Francisco Bozinovic*

GROUP

DROSOPHILA TELOMERES LAB

GROUP MEMBERS

Elena Casacuberta, Group Leader

| Tenured Scientist, CSIC

David Piñeyro, Postdoctoral Researcher | CSIC contract

Rute Sousa, PhD Student | PhD fellowship, Fundaçao para a Ciência e tecnologia, Portugal

Elisenda López Panadès, PhD Student | CSIC contract

María Lucena Pérez | Undergraduate student

RESEARCH OUTLINE

Our group focuses on the study of how transposable elements interact with the eukaryote genome and how these interactions can actively contribute to evolution. To study this we use the telomeres of *Drosophila* as a model.

Although the telomeres of *Drosophila* are functionally equivalent to telomerase telomeres, they are maintained by an alternative mechanism. Instead of telomerase, *Drosophila* uses three non-LTR retrotransposons, HeT-A, TART and TAHRE to elongate the end of the chromosomes when needed. These very special retrotransposons maintain their personality as transposons but at the same time are committed to maintain the telomeres in *Drosophila*. The study of telomere maintenance from an evolutionary perspective can help us to understand crucial processes such as aging, tumorogenesis and genome stability.

RESEARCH SUBLINES

1. Host and Retrotransposon requirements for telomere elongation in Drosophila

HeT-A, TART and TAHRE must be integrated in the cellular pathways controlling telomere length and genome stability. Understanding the regulation of the telomeric transposons will shed light in both telomere length control as well as transposon regulation in *Drosophila*.

2. Transition between the Telomerase and the Retrotransposon mechanism of telomere maintenance

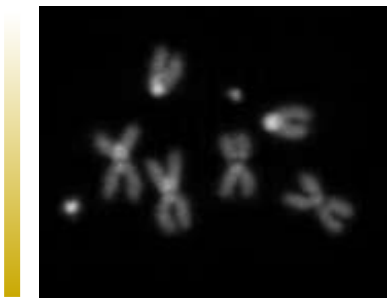
Drosophila shares ancestors with insects with telomerase. We are studying a possible evolutionary intermediate, the silk moth *Bombyx mori* in order to obtain experimental proofs of the telomerase-retrotransposon transition.

3. Evolution of the telomere retrotransposons

The sequences of HeT-A and TART, although linked to an essential cellular role are allowed to change at a fast rate. Studying the level of variability of the telomere retrotransposons is important to better understand their dynamics and the forces that are driving their evolution.

4. Variability within the telomere retrotransposons

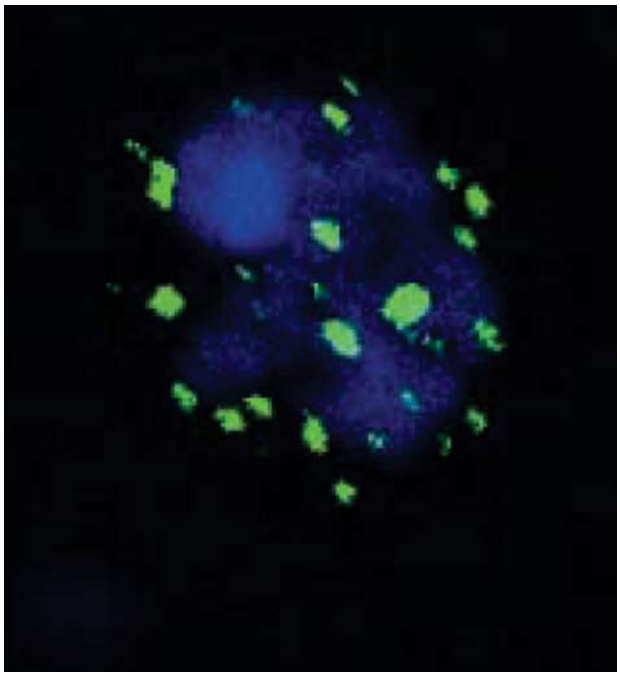
The different copies of each telomeric retrotransposon can be divided in different subfamilies. We are investigating if this variability is due to different necessities in telomere elongation or as a response to specific mutations.



FUNDED PROJECTS

Project Title: *Estudio Análisis de la biología telomérica de* Drosophila *mediante técnicas de RNA de interferencia*
Financed by: *CSIC ("Proyectos Intramurales Especiales")*
Years: *2008-2009*
PI: *Elena Casacuberta Suñer*

Project Title: *Estudio de los Telomeros de Drosophila; relación evolutiva y funcional con los Telomeros de Telomerasa. Los retrotransposones HET-A y TART y su relación con otros componentes teloméricos.*
Financed by: *Ministerio de Ciencia e Innovación (BFU2006-13934)*
Years: *2006-2009*
PI: *Elena Casacuberta Suñer*



GROUP

NUCLEAR HORMONE RECEPTORS IN INSECT DEVELOPMENT LAB

GROUP MEMBERS

David Martín, Group Leader

| Tenured Scientist, CSIC

Josefa Cruz, Post-doc | Project Contract, MEC

Cristina Manjón, Post-doc | Juan de la Cierva Contract, MEC

Ferran Borràs, PhD Student | FPI Scholarship, MEC

Enric Ureña, PhD Student | JAEPRE-CSIC Fellowship

RESEARCH OUTLINE

Our group studies the hormonal control of insect embryogenesis, post-embryonic growth, molting and metamorphosis, particularly the roles of ecdysteroids and juvenile hormone. We are also interested in the hormonal basis of the evolution of metamorphosis. In insects, the steroid hormone 20-hydroxyecdysone (20E) triggers major developmental transitions. The regulatory activity of this hormone is mediated by a genetic cascade of transcription factors that belong to the Nuclear Hormone Receptor superfamily (NRs). Whereas great deal of research has been devoted to uncover the molecular mechanisms regulating 20E-triggered cascade in holometabolous insects *(Drosophila melanogaster),* little understanding has been achieved regarding how these mechanisms operate in more primitive hemimetabolous insects. To solve this, our research group is working to characterize the mechanisms of 20E action in the hemimetabolous insect, *Blattella germanica.* During the last years, we have cloned the entire repertoire of NRs that form the 20E-triggered genetic cascade in *B. germanica* and we have characterized their functional properties during embryonic and nymphal development by using RNAi in vivo and parental RNAi procedures. Furthermore, we are also working to uncover the molecular mechanism underlying Juvenile Hormone action, another important hormone that coordinates multiple developmental and physiological processes ranging from molting to reproduction and aging.

RESEARCH SUBLINES

1. Nuclear Hormone Receptors during development and the evolution of metamorphosis

The major goal of this project is the characterization of the regulatory role of the entire set of nuclear hormone receptors belonging to the 20E-triggered genetic cascade during the post-embryonic development of *B. germanica.* Currently, we are analyzing the function of each nuclear receptor during nymphal and adult stages by using RNAi in vivo techniques. These studies have already demonstrated the critical role of these transcription factors on ecdysteroid production, programmed cell death, tissue growth, ovary follicle proliferation and molting behavior.

2. Embryonic development in short germ band insects

The main goal of this project is to characterize the major morphogenetic events during the early-embryogenesis of *B. germanica,* analyzing the role of each 20E-dependent nuclear hormone receptor on these morphogenetic events. This project will provide a valuable model to understand the molecular basis for how shifts in the hormonal context can lead to the creation of different body forms.

3. Control of developmentally regulated programmed cell death by steroids and the hippo pathway

In holometabolous insects, complete metamorphosis is based on the destruction of larval tissues by programmed cell death (PCD) to accommodate the growth of new adult structures. However, given that metamorphosis arose from a hemimetabolous ancestor, it would be interesting to study whether the mechanisms that coordinate stage-specific PCD were already present in

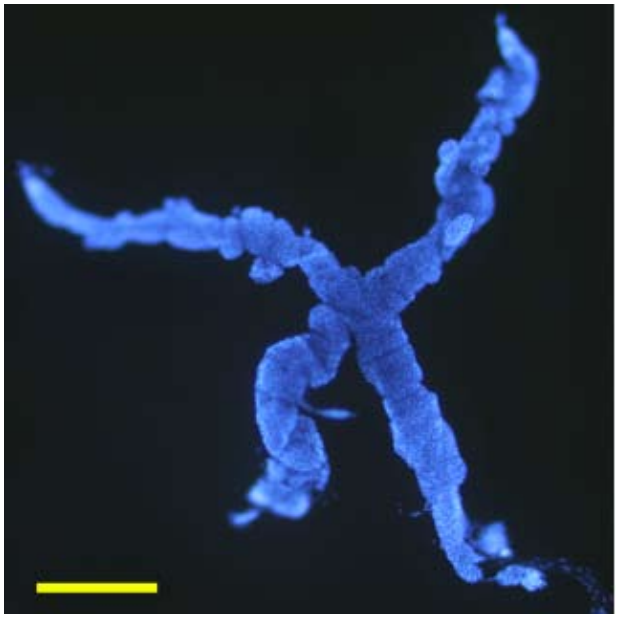
more primitive hemimetabolous insects or they are a novelty of holometabolous species. Using reverse genetic studies, we are carrying out a detailed functional analysis of the 20E-mediated death of the prothoracic gland of *B. germanica,* which undergoes PCD just after the imaginal molt. Furthermore, we are also characterizing in detail the relationship between the tumor-suppressor network, the hippo pathway, and PCD in *B. germanica.*

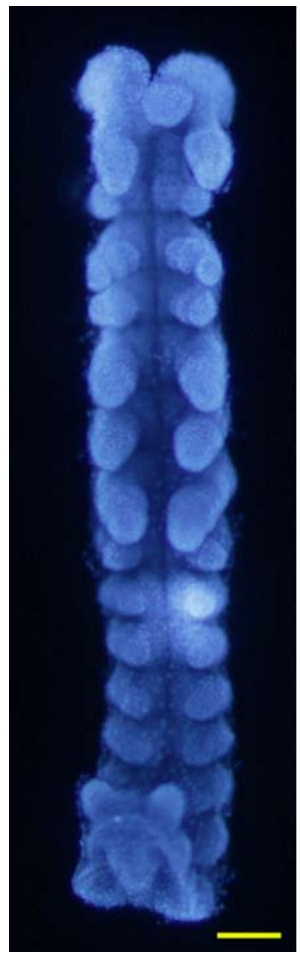
4. Sumoylation and development

Post-translational modification with small ubiquitin-related modifier, SUMO, is a widespread mechanism for rapid and reversible changes in protein function, especially in nuclear hormone receptors. In this project, we are addressing the functional analysis of sumoylation on the development of our model insect, *B. germanica,* and its relationship with nuclear hormone receptor function.

FUNDED PROJECTS

Project Title: *Characterization of the genomic response to 20-hydroxyecdysone during the development of the hemimetabolous insect* Blattella germanica *(Ref. BFU2006-13212)*
Financed by: *Ministerio de Ciencia e Innovación*
Years: *2007-2009*
PI: *David Martín*





GROUP

NUTRITIONAL SIGNALS AND REPRODUCTION IN INSECTS LAB

GROUP MEMBERS

José Luis Maestro, Group Leader

| Tenured Scientist, CSIC

Songül Süren-Castillo, Post-doc | JAEDOC-CSIC Fellowship

Marc Abrisqueta Carol, PhD Student

RESEARCH OUTLINE

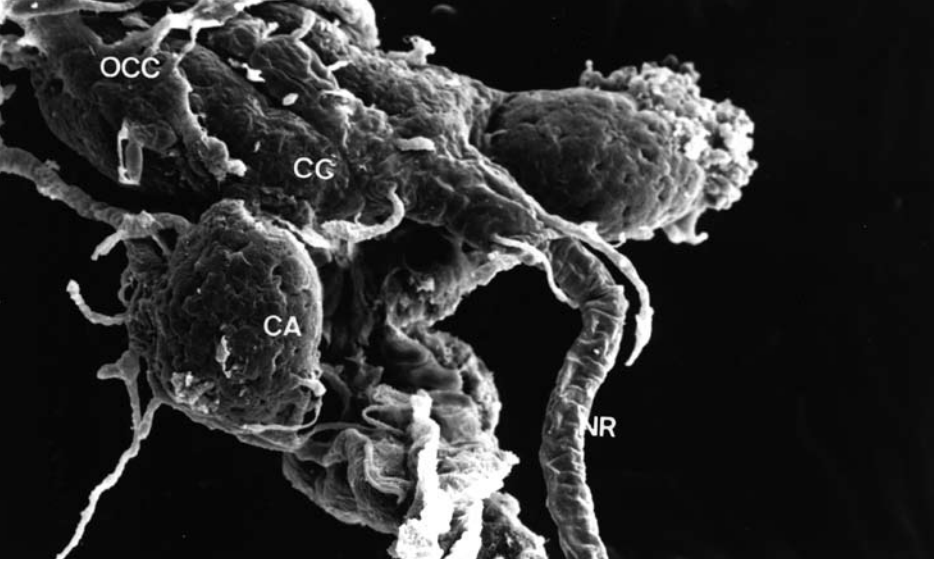
Why only female mosquitoes bite? The adult female mosquito has to bear a reproductive process energetically very costly, where they must quickly produce large numbers of eggs. Therefore, she does not initiate physiological and endocrine processes that lead to reproduction until she had made a blood meal. This type of reproductive strategy called anautogeny is also found in other insects. For example, the cockroach *Blattella germanica* also needs to eat to trigger endocrine mechanisms that produce the onset of the breeding cycle. This cockroach is a very good model of insect reproductive physiology because their reproduction is governed, as in most insects, by juvenile hormone (JH), and not by ecdysteroids as it only happens in dipterans (flies and mosquitoes). Thus, in anautogenous organisms there must exists some nutritional signals to inform the organs involved in reproduction that a meal took place. Two of the pathways that contribute to the nutritional signal transmission, in insects and other organisms, are the insulin receptor/phosphatidylinositol-3-kinase (InR/PI3K) and "target of rapamycin" (TOR) pathways. They are involved in detecting nutritional signals and activating different processes, such as growth, cell proliferation, longevity and cancer. Our group studies these pathways in *B. germanica* and their relationships to the activation of reproduction. We are conducting studies using different experimental models, including fed and fasted individuals and specimens in which we manipulate the expression of different proteins, such as InR itself, TOR, the kinase of the ribosomal protein S6 (S6K) and the FOXO transcription factor, among others.

PUBLICATIONS 2009

- Maestro, J.L., Cobo, J., Bellés, X. 2009. Target of rapamycin (TOR) mediates the transduction of nutritional signals into juvenile hormone production. *Journal of Biochemical Chemistry* 284, 5506-5513.

FUNDED PROJECTS

Project Title: *Nutritional signals and reproduction. Insulin receptor and TOR pathways in insects*
Financed by: *Ministerio de Ciencia e Innovación (BFU2006-01090)*
Years: *2007-2009*
PI: *José Luis Maestro*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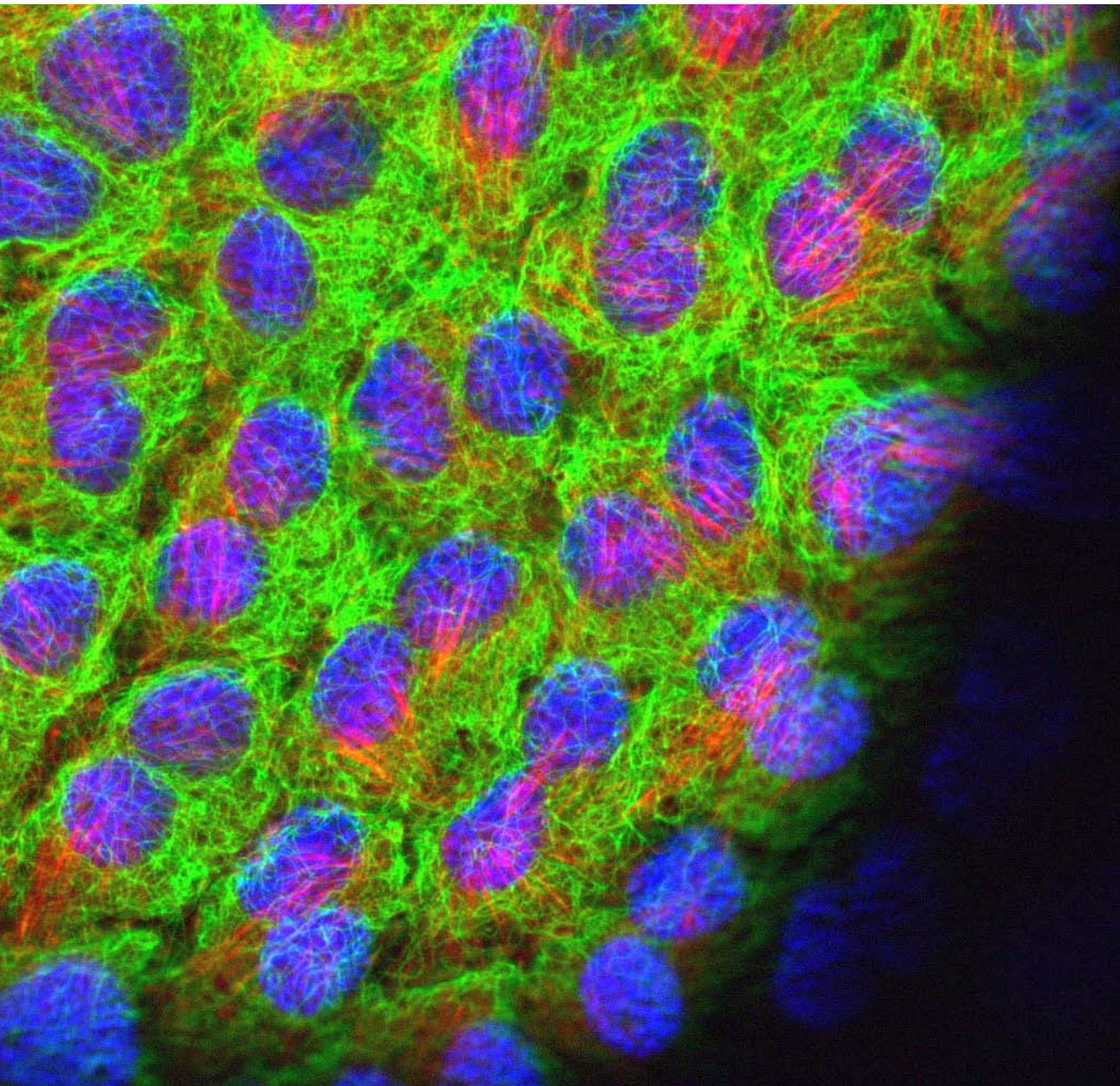
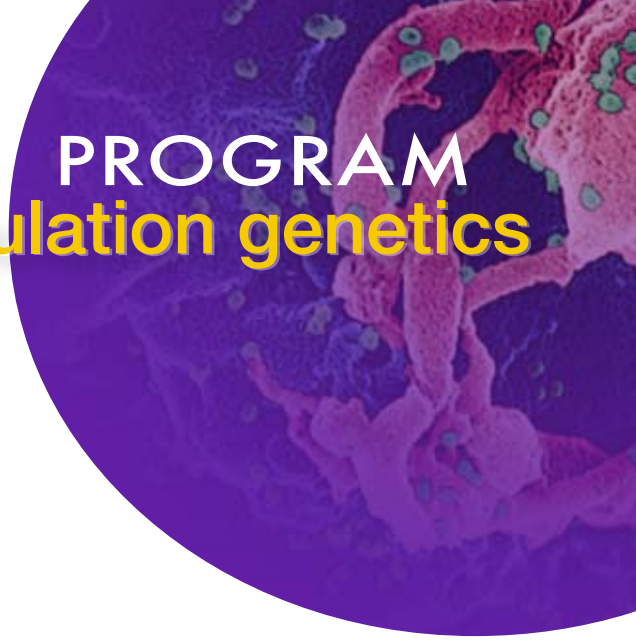




PROGRAM
population genetics

RESEARCH GROUPS

Evolutionary Systems Biology Lab
Jaume Bertranpetit, *Group Leader*

Evolutionary Population Genetics Lab
Elena Bosch, *Group Leader*

Human Genome Diversity Lab
David Comas, *Group Leader*

In the population genetics line, within-species diversity is interrogated with the general aim of reconstructing the processes that created such diversity. Genetic diversity is the result of the intricate interaction of different processes: some are embedded in the genome, such as mutation and recombination; others are absolutely independent from the genome and affect its entirety, such as demographic events; finally, other processes result from the exposure of the genetic diversity to the environment, such as natural selection. Within this line, we are interested in all three types of processes in humans. Namely, we investigate how recombination can be affected by genetic differences between populations; the demographic histories of particular populations or population groups, such as the Bantu expansion; and the extent of the adaptation of humans to their pathogen entourage.

GROUP

EVOLUTIONARY SYSTEMS BIOLOGY LAB

GROUP MEMBERS

Jaume Bertranpetit, Group Leader

| Professor, UPF

Hafid Laayouni, Senior Scientist | CIBEResp Researcher

Ludovica Montanucci, Post-doc | UPF Contract

Martin Sikora, PhD Student | FU Scholarship, MICINN

Marta Melé, PhD Student | FU Scholarship, MICINN

Giovanni dall'Olio, PhD Student | FI Scholarship, MICINN

Brandon Invergo, PhD Student | Project Scholarship

Pierre Luisi, PhD Student | Project Scholarship

RESEARCH OUTLINE

Our main research focuses on how to use molecular pathways to understand the biology of adaptation through the measures of natural selection in genes and other genomic regions. The different forms of selection (purifying, balancing and positive) are analyzed at two levels: among human populations in order to detect population-specific adaptations, and among primates in order both to recognize species-specific adaptive selection and to measure the relative strength of purifying selection. We have also ongoing work in understanding recombination and in reconstructing population history by studying human genetic diversity. We are also collaborating with Carles Lalueza-Fox in ancient DNA studies and with Elena Bosch in detecting positive selection.

RESEARCH SUBLINES

1. Footprints of adaptation in humans and purifying selection in higher primates

The action of natural selection is at the base of different amounts of genetic dispensability or relative importance (in cases of negative or purifying selection) or of adaptation (in cases of positive selection and in the special case of balancing selection) that will be population-specific (in the case of human diversity) or species-specific (in the case of genetic divergence). The action of selection is measured and understood not in terms of single lists of genes, but integrated in molecular physiological pathways or networks and the aim is, in a given pathway, to understand the complex basis of adaptation and how networks have been shaped by natural selection. The final goal is, on one hand, to understand in specific pathways how evolution has taken place, where positive selection (and balancing selection) has taken place and where purifying selection has been shaping the genome, and on the other, to obtain possible general patterns of evolution in molecular pathways and networks.

Data is retrieved mostly from pre-existing databases but, in cases of doubt, low quality or low density, we produce our own (sequences and SNPs). Inter-specific data include the sequences of several primates and intra-specific databases include: HapMap, in versions 2 and 3; SNP analysis of the HGDP panel with the 650k array of Illumina; and Re-sequencing projects (like Seattle-SNP) 1000 genomes. The pathways that we are analyzing are: N-glycans; integration of all glycosylation pathways; innate immunity; skin pigmentation; visual perception and obesity through adiposity signals.

2. Malaria

Taking also a pathway approach we are studying the genetic susceptibility to placental malaria in a case-control setting in a population in Manhiça, Mozambique. This project is in collaboration with Pedro Alonso and other members of the Barcelona Center for International Health Research (CRESIB). High throughput genotyping data has been generated and the analysis has been centered mostly in innate immunity and glycosylation.

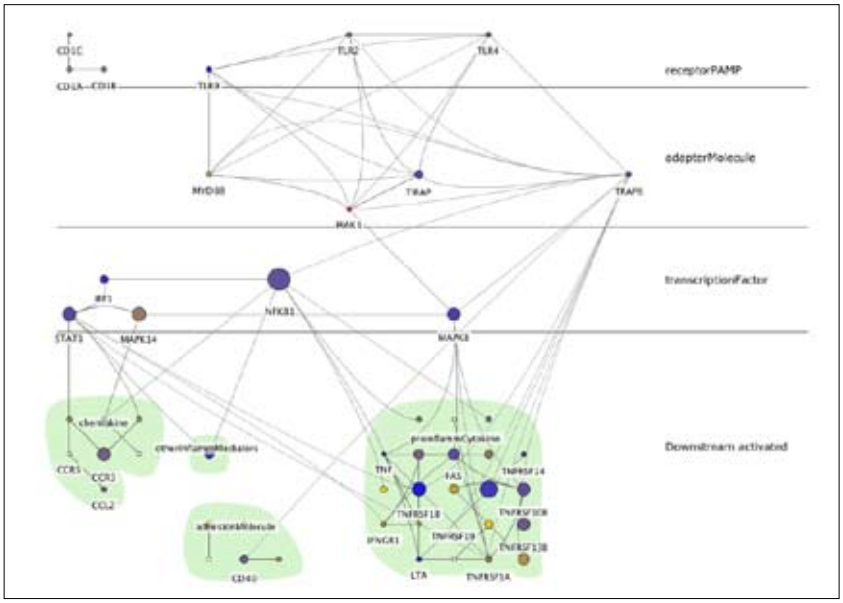
3. Human populations genetics and recombination

Recombination is a main force shaping genome diversity. In collaboration with Laxmi Parida (Computational Biology Center, IBM T J Watson Research, Yorktown, USA), we have developed an algorithm, implemented in the IRiS

program, to detect past recombination events in extant sequences, with specificity of parental and recombinant sequences. The algorithm detects recombination events from tree incompatibilities found along the sequence. We have validated and calibrated the algorithm for the human genome given human demographic history and the human recombination model by means of coalescent simulations implementing a standard model of human demography. In this project is also involved Francesc Calafell; We are also interested in the evolution of recombination and differences in rates among human populations and have demonstrated that there is stratification in the recombination rates among human populations strongly related to genetic distances. In collaboration with Elena Bosch we have shown that most isolated populations do not show a special pattern of linkage disequilibrium.

4. Human genetic diversity and population history

In collaboration with David Comas we are participating in the Genographic Project promoted by National Geographic and IBM as responsible for Central and Western Europe and participating in a variety of population specific studies (including Basques, North African, South Saharian and others).



PUBLICATIONS 2009

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- Ferrer-Admetlla, A., Sikora, M., Laayouni, H., Esteve, A., Roubinet, F., Blancher, A., Calafell, F., Bertranpetit, J., Casals, F. 2009. A natural history of FUT2 polymorphism in humans. *Molecular Biology and Evolution* 26:1993-2003.
- Garagnani, P., Laayouni, H., González-Neira, A., Sikora, M., Luiselli, D., Bertranpetit, J., Calafell, F. 2009. Isolated populations as treasure troves in genetic epidemiology: the case of the Basques. *European Journal of Human Genetics (EJHG)* 17: 1490-1494.
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FUNDED PROJECTS

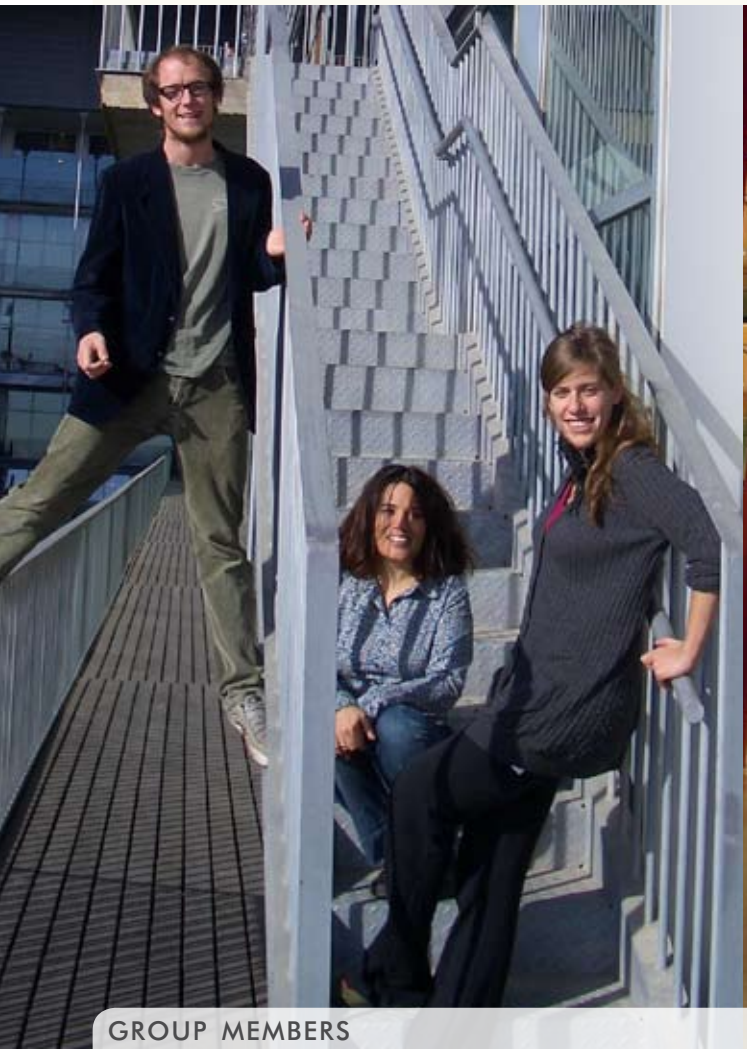
Project Title: *Factores de riesgo genético en la Malaria*
Financed by: *Ministerio de Educación y Ciencia (MEC-SAF2007-63171)*
Years: *2007-2010*
PI: *Jaume Bertranpetit*

Project Title: *Grup de Recerca Consolidat-SGR*
Financed by: *Generalitat de Catalunya (2009 SGR-1101)*
Years: *2009-2013*
PI: *Jaume Bertranpetit*

Project Title: *The Genographic project: Western/Central Europe region*
Financed by: *National Geographic and IBM*
Years: *2006-2010*
PIs: *Jaume Bertranpetit and David Comas*

GROUP

EVOLUTIONARY POPULATION GENETICS LAB



GROUP MEMBERS

Elena Bosch, Group Leader

| Professor, UPF

Andrés Moreno-Estrada, PhD Student | CONACYT Scholarship, Mexico (only until April 09)

Johannes Engelken, PhD Student | Volkswagenstiftung Scholarship, Germany

Elena Carnero, PhD Student | UPF Teaching Scholarship

RESEARCH OUTLINE

Our research focuses on investigating human genetic adaptation, that is, identifying traits that have undergone positive selection during human evolution in order to understand the adaptive events that have shaped our genomes. The search of genetic signatures of selection are pursued at two levels: 1) using comparative data, which will allow us to detect genetic variants that were selected during the process of hominization and thus could provide valuable insights into understanding human-specific traits; and 2) exploring intraspecific diversity patterns within humans populations, which may allow us to detect examples of differential natural selection across human populations. In those genomic regions where the imprint of selection is confirmed we aim to determine the molecular bases of the functional adaptation by the in silico detection of functionally relevant variants around each gene region and by functionally assaying those genetic variants potentially underlying the basis of adaptation. The integration of the different levels of functional variation on several candidate genes related to a particular putatively selected trait will allow us to explore the complete impact of selection on such particular human trait.

RESEARCH SUBLINES

1. Highly divergent genes between humans and chimpanzees and recent adaptation in human populations

Undoubtedly, a set of genetic changes constituted the adaptations that made us humans. We tried to identify rapidly evolving genes in the human lineage and asked whether they were still evolving rapidly in different human populations, or, on the contrary, whether their involvement in defining humans froze their speed of change. Specifically, we compared as many human genes with their orthologs in chimpanzee, mouse, rat and dog as possible and applied a branch-site likelihood method to test for positive selection on the human lineage. Significant cases were then further characterized for signatures of recent positive selection on the 39 worldwide human populations from the HGDP Diversity panel through population differentiation, allele frequency threshold analyses, and by exploring the maintenance of long unbroken haplotypes using SNP data.

2. Approximation to the bases of human adaptation: detection of natural selection on functionally related genes

The availability of SNP genotyping data comprising all the genome on different human populations has allowed different genome-wide scans of natural selection in humans. From these scans of selection we have identified candidate regions, which are functionally related to traits that have putatively been selected during human evolution such as those involved in nutrition, metabolism, disease and pathogen interaction. We use next-generation sequencing techniques to determine the complete unbiased allele frequency spectrum of these candidate regions in different populations. In those cases where the imprint of selection is confirmed we aim to determine the molecular bases of the functional adaptation. In the case of nutrition, we hypothesize that some genes related to the metabolism of micronutrients may have been under natural selection, possibly as an adaptation to changes in the diet of human populations or as a response of the immune system to new pathogens.

We are currently working on the identification of functionally relevant variants by investigating molecular phenotypes at different levels such as mRNA expression, enzyme activity, micronutrient levels or receptor function.

PUBLICATIONS 2009

- Berniell-Lee, G., Calafell, F., Bosch, E., Heyer, E., Sica, L., Mouguiama-Daouda, P., Van der Veen, L., Hombert, J-M., Quintana-Murci, L., Comas, D. 2009. Genetic and demographic implications of the Bantu expansion: insights from human paternal lineages. *Molecular Biology and Evolution* 26: 1581-1589.
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- Castellano, S., M. Andrés A., Bosch, E., Bayes, M., Guigó, R., G. Clark, A. 2009. Low exchangeability of selenocysteine, the 21st amino acid, in vertebrate proteins. *Molecular Biology and Evolution* 26: 9:2031-2040.
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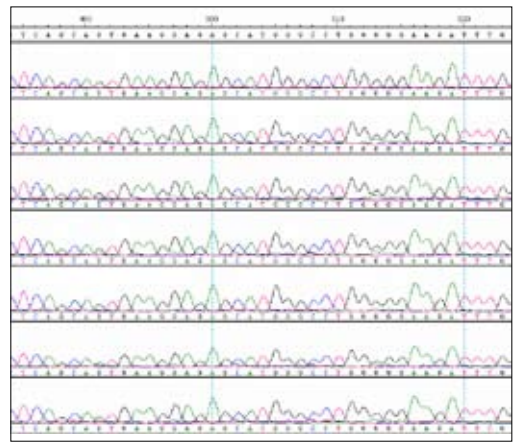
FUNDED PROJECTS

Project Title: *Detección de la selección natural en genes candidatos: aproximación a las bases de la adaptación humana*
Financed by: *Subdirección General de Proyectos de Investigación (Ref. BFU2008-01046)*
Years: *2009-2011*
PI: *Elena Bosch*

Project Title: *Grup de Recerca Consolidat-SGR*
Financed by: *Generalitat de Catalunya (2009 SGR-1101)*
Years: *2009-2013*
PI: *Jaume Bertranpetit*



GROUP

HUMAN GENOME DIVERSITY LAB

GROUP MEMBERS

David Comas, Group Leader

| Professor, UPF

Begoña Martínez-Cruz, Post-doc | UPF Contract

David Soria, Post-doc | UPF Contract

Karla Sandoval, PhD Student | CONACYT Scholarship

Isabel Mendizabal, PhD Student | Basque Country Scholarship

Laura Rodríguez-Botigué, PhD Student | FI Scholarship

Paula Sanz, Technician | UPF Contract

RESEARCH OUTLINE

Our group's research is focused on the understanding of the current genomic diversity in human populations in order to establish the mechanisms, causes and consequences of this genetic variation. Concerning population processes, the research of our group has focused on the analysis of uniparental markers (Y-chromosome and mitochondrial DNA) as well as autosomal markers to answer several questions about the origins of human populations. Within this framework we have addressed questions about the population history of Central African groups, the peopling of the Americas, or the diversity within North African populations. Concerning genomic processes, our research has focused on the analysis of the diversity of genes involved in complex diseases in order to describe the standard diversity in healthy individuals and to unravel its implications in disease, such as psychiatric and immunological disorders.

RESEARCH SUBLINES

1. The Genographic Project

This is a project launched by the National Geographic and IBM which aims to unravel the migration history of the human species through genetic markers. We are involved in the analysis of uniparental genomes in Western and Central Europe.

2. Genetic history of north African and American human populations

We try to establish the evolutionary processes (demography and adaptation) that have modeled the genetic diversity of human populations in these geographical areas.

3. Genetic variants associated to phenotypes in human populations

Our goal is to describe those genetic variants related to distinct phenotypes, such as height and skin color, taking certain human populations as a model.

PUBLICATIONS 2009

- Berniell-Lee, G., Calafell, F., Bosch, E., Heyer, E., Sica, L., Mouguiama-Daouda, P., Van der Veen, L., Hombert, J-M., Quintana-Murci, L., Comas, D. 2009. Genetic and demographic implications of the Bantu expansion: insights from human paternal lineages. *Molecular Biology and Evolution* 26: 1581-1589.
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FUNDED PROJECTS

Project Title: *Análisis de la diversidad genética humana en poblaciones nativas del continente americano (A/7694/07)*
Financed by: *Programa de Cooperación Interuniversitaria e Investigación Científica (AECI): Spain – Mexico*
Years: *2008-2009*
PI: *David Comas*

Project Title: *Analyse génétique des isolats berbères du sud Tunisien et leur relation avec les populations de la péninsule Ibérique (A/8394/07)*
Financed by: *Programa de Cooperación Interuniversitaria e Investigación Científica (AECI): Spain – Tunisia*
Years: *2008-2009*
PI: *David Comas*

Project Title: *Diversidad genética en poblaciones humanas de África Central: implicaciones demográficas, lingüísticas y culturales (CGL2007-61016/BOS)*
Financed by: *Dirección General de Investigación Científica y Técnica*
Years: *2007-2010*
PI: *David Comas*

Project Title: *Grup de Recerca en Biologia Evolutiva (2009SGR1101)*
Financed by: *Direcció General de Recerca, Comissionat per a Universitats i Recerca, Generalitat de Catalunya*
Years: *2009-2012*
PI: *Jaume Bertranpetit*

Project Title: *The Genographic project: Western/Central Europe region*
Financed by: *National Geographic and IBM*
Years: *2006-2010*
PIs: *Jaume Bertranpetit and David Comas*

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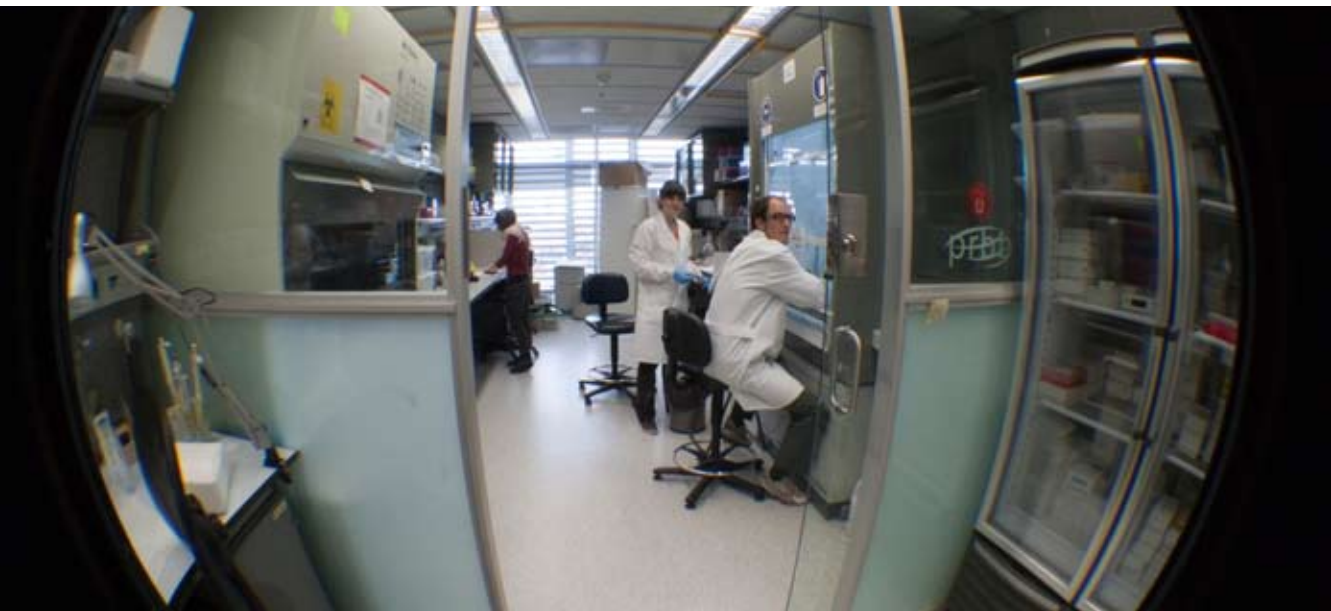


IBE HIGHLIGTED PAPERS

NEW KEYS IN THE REGULATION OF INSECT METAMORPHOSIS

Bellés, X., Gómez-Orte, E. MicroRNA-dependent metamorphosis in hemimetabolan insects. *PNAS*, Dec. 2009.

Through their biological cycle, insects go through a number of life stages that can be quite diverse each other from a morphological and physiological point of view. Look for example at the differences between the caterpillar and the adult of the same lepidopteran species. Until now, entomology manuals described that the regulation of insect metamorphosis is based on hormones, like ecdysteroids, which induce the successive molts, and juvenile hormones, which maintain the juvenile character of them, so repressing metamorphosis. Only when juvenile hormones are absent the insect is able to molt into the adult stage. In addition, a number of transcription factors have been reported as mediators of the above hormones, as well as a number of effector genes that codify for proteins giving the characteristic shape and behaviour of a juvenile or an adult stage, and whose expression depends on the aforementioned hormones and transcription factors.

The work of Xavier Bellés and Eva Gómez reports the occurrence of a new level in the regulation of insect metamorphosis, which is governed by microRNAs, RNAs of some 22 nucleotides which, in general, play a repressing action on mRNA stability and translation. Using the RNA interference as a methodological approach, and working on the German cockroach, *Blattella germanica,* as an experimental model, the above authors silenced the expression of the enzyme dicer-1, which is essential in the process of microRNA formation from the respective precursors. When dicer-1 expression was silenced in the last nymphal instar of the cockroach, the production of microRNAs was impaired and the experimental insects, instead of molting to the adult stage as controls did, they transformed into giant supernumerary nymphs. This demonstrated that microRNAs are essential for correct metamorphosis.

The hypothesis emerging form these experiments is that in the molt to adult, particular microRNAs would repress the expression of genes giving nymphal characters, that is, they would refine the shift from the nymphal to the adult genetic program. Further work by Xavier Bellés group should focus on elucidating which particular microRNAs are involved in such process and which are their respective target mRNAs.

LOW GENETIC DIVERSITY AMONG NEANDERTAL MITOCHONDRIAL GENOMES

Briggs, A.W., M. Good, J., E. Green, R., Krause, J., Maricic, T., Stenzel, U., Lalueza-Fox, C., Rudan, P., Brajkovic, D., Kucan, Z., Gusic, I., Schmitz, R., Doronichev, V.B., Golovanova, L.V., de la Rasilla, M., Fortea, J., Rosas, A., Pääbo, S. 2009. Targeted retrieval and analysis of five Neandertal mtDNA genomes. *Science* 325:318-321.

Neandertals were a human group with a distinct physical appearance that lived in Eurasia from about 400,000 until their extinction 28,000 years ago, after the arrival of modern humans to Europe, about 40,000 years ago. In 1997, mitochondrial DNA was extracted for first time from a Neandertal skeleton. The sequences were different to those found in modern humans and supported the view that Neandertals didn't contribute to our mitochondrial gene pool. In 2008, scientists at the Max Planck Institute for Evolutionary Anthropology were able to retrieve the complete mitogenome (mitochondrial genome) of a Neandertal individual (labelled Vi33.16) from the Croatian site of Vindija. The mitogenome was obtained by piecing together 8,341 sequences, generated after 37 full runs of 454 pyrosequencing (Life Sciences, Roche). But this unspecific approach is clearly untenable in most Neandertal samples, in which endogenous sequences are well below 1%.

Now, a more efficient and accurate method of sampling ancient DNA has been developed by a team led also by Max Planck Institute researchers. The method, named Primer Extension Capture (PEC), combines the specificity of the primers, that allows the isolation of the endogenous DNA from all the bacterial, junk DNA accumulated in the fossils, with the high throughput of the new massively parallel sequencing technologies. The new approach has allowed the retrieval of five complete new mitogenomes representing most of the Neandertals' geographic range: one from Spain (El Sidrón 1253), one from Russia (Mezmaiskaya 1), two from Germany (Feldhofer 1 and 2) and another one from Croatia (Vindija 33.25). The efficiency of the PEC method has dramatically

increased the endogenous sequence ratios. In the Iberian sample, for instance, the original retrieval ratio was 0.05%, and increased to 40.2% after the PEC capture.

The level of genetic diversity among the six Neandertal mitogenomes is extremely low, less than that seen in current modern humans and similar to the genetic diversity of modern Europeans. For instance, two of the samples, coming from Croatia and Germany, and separated by 850 km, have exactly the same mitogenome. This can only happen at a reasonable probability if the population was very small (and consequently, its mitochondrial diversity).

Using population genetics methods, the researchers estimate the effective population size in only about 3,500 Neandertal females (that is, maybe 10,000 Neandertals in a particular moment in Eurasia).

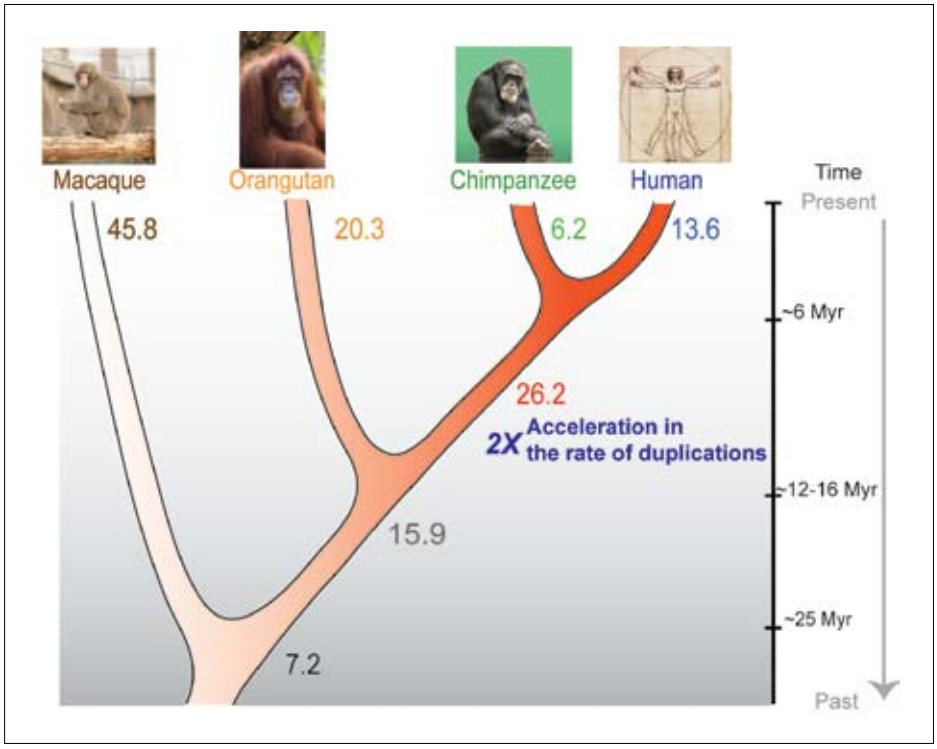
In addition to, their mitochondrial protein-coding genes show a faster evolutionary rate than those from chimpanzees and modern humans. This pattern suggests that Neandertals always had a low population density, because purifying selection is less effective at purging weakly deleterious mutations on these genes in small populations. This demographic pattern was probably a factor contributing to their extinction in the face of competition for resources with modern humans.

A BURST OF SEGMENTAL DUPLICATIONS IN THE GENOME OF THE AFRICAN GREAT APE ANCESTOR

Marquès-Bonet, T., M. Kidd, J., Ventura, M., A. Graves, T., Cheng, C., Hillier, L.W., Jiang, Z. et al. 2009. A burst of segmental duplications in the genome of the African great ape ancestor. *Nature* 457: 877-881.

A figure of 1% genomic differences between humans and chimpanzees had emerged after a decade of genetic studies that culminated in 2005 with the publication of the chimpanzee genome. That paper included what was considered, at the time, a comprehensive comparative study between the genome of our closest living relatives and our own.

However, a new study published in *Nature* on 12th February, the 200th anniversary of Charles Darwin's birthday, and co-authored by IBE researchers, shows not only that the quantity of differences are much larger than 1%, but that they are of a quite different quality than previously thought. The new study shows large differences in the genomes of humans and great apes within large duplicated genome segments. These differences amount to up to 10% of the genomes humans and chimpanzees. Moreover, these segments are such that they may contain full genes and other functional elements that may be present in one species and absent in others. Indeed, these duplicated regions are so complex that they had not been studied with detail so far. Scientists had focused in single-copy genome regions, that can be readily compared and that are 99% identical between humans and chimpanzees. Hence the difference between previous and current results.



Most of these differences detected now occurred at a time just prior to the speciation of chimpanzees, gorillas, and humans. That is, the common ancestor of humans, chimpanzees and gorillas had an unusual activity of duplication. The causes of this unusual amount of genomic activity are still unknown, just as the functions of most of the genes that were affected by these processes. Interestingly, the acceleration in sequence duplication occurred in an era when other types of mutations had slowed within the hominid (human-like) lineage. These results suggest that evolutionary properties of copy-number mutations, such as repeated segments, differ from other forms of mutations.

To understand the pattern and rate of genomic duplication during evolution, the researchers constructed a map of segmental duplications for four primate genomes: macaque, orangutan, chimpanzee, and human. They then compared the patterns across the four species. They characterized a duplication as shared if it occurred in two or more of the four species and lineage-specific if it was found in just one species. A small fraction of the duplicated content was human-specific, while the majority of the content was shared with the other species. In addition, the research effort unveiled striking examples of recurrent duplications of DNA segments that happened independently in different lineages. Most of the shared duplications were already present in the chimp-human common ancestor, but these are highly variable in copy number between and within human and great ape species.

Determining why humans and chimpanzees differ so much at a physical and behavioral level but are genetically so similar has been, and still is, a great challenge. Non-duplicated regions of the genome, including single-copy genes, are only 1% different between the two species; their proteins are virtually identical; and there are very few rearrangements that distinguish ape-human chromosomes. In contrast, Marquès-Bonet et al (2009) noted that the duplicated sequences show much more variation than the other portions of the genetic code.

Of course, there is still no final answer as to why chimpanzees and humans are different. Maybe segmental duplications that are specific to humans are another layer to explore, or maybe the distinction between human and chimpanzees is not to be found in these genetic differences.

What is certain is that genetic differences contribute significantly to what makes us human, and we know that these regions of our genetic code are changing much more rapidly than most others. The next challenge will be making sense of all these differences and the genes that are affected by them.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OTHER SCIENTIFIC ACTIVITIES

DISSEMINATION OF SCIENCE

The year 2009 has been the bicentennial of Darwin's birthday, and sesquicentennial of publication of his book *The Origin of Species*. Thus, during 2009, the IBE has been especially busy in all aspects related to science dissemination around Darwin, including specialized seminars, conferences given in a variety of contexts (from academic to lay associations), scientific exhibitions, as well as numerous written contributions in journals of science dissemination and newspapers. The detailed description of such activities is available on request.

DOCTORAL THESES DEFENDED

PhD Student:	Andrés Moreno-Estrada
Title:	*Analysis of Human Genetic Variation in Candidate Genes under Positive Selection on the Human Lineage*
Thesis Director:	Elena Bosch
Institution & Date:	Universitat Pompeu Fabra. April 2009

PhD Student:	Anna Ferrer-Admetlla
Title:	*Human Genetic diversity in Genes Related to Host-pathogen Interaction*
Thesis Director:	Jaume Bertranpetit
Institution & Date:	Universitat Pompeu Fabra. July 2009

PARTICIPATION IN MASTERS AND POSTGRADUATE COURSES

Course	Type	Organized by	Researcher
Epigenetic regulation of Drosophila telomeres: Control of telomeric retrotransposons. Master in develpmental Biology and genetics	Master	Universitat de Barcelona (UB)	Elena Casacuberta
Mobile elements and evolution of the Genome. Master in Bioinformatics	Master	Universitat Pompeu Fabra (UPF)	
Mobile elements and genome evolution	Master in develpmental Biology and genetics	Universitat de Barcelona (UB)	
Ovogènese em insectos	Postgraduate course	Universidad de Sao Paulo, Faculdade de Filosofia, Ciencias e Letras de Tibeirao Preto	M. Dolors Piulachs
Fisiologia i Endocrinologia Comparades	Postgraduate course	Universitat de Barcelona (UB)	Xavier Bellés
Biomedical Research: Genomes and Systems	Master	Universitat Pompeu Fabra (UPF)	Francesc Calafell
Bioinformatics for Health Science: Biomedical Informatics	Master	Universitat Pompeu Fabra (UPF)	
Biologia Humana: Antropología Forense	Master	UAB-UB	
Biología Humana: avances metodológicos en el estudio de interacciones gen-ambiente	Master	UAB-UB	
Filogenias y Genealogías de DNA: Reconstrucción y Aplicaciones	Postgraduate course	Universidad de Barcelona (UB)	José Castresana
Máster en Biología del Desarrollo y Genética	Master	Universidad de Barcelona (UB)	
Curso: Fundamentos de Antropología Forense. Master de Antropología Biológica	Master	UAB-UB	Carles Lalueza-Fox

Course	Type	Organized by	Researcher
Master en Comunicación Científica, Médica y Ambiental	Master	UPF-IDEC	Carles Lalueza-Fox
Genetic Epidemiology Master: MSc Public Health	Master	Universitat Pompeu Fabra (UPF)	David Comas
Principles in Biology and Biomedicine	Master	Universitat Pompeu Fabra (UPF)	
"Biomedical Research: Genomes and Systems"	Master	Universitat Pompeu Fabra (UPF)	
Master en Recerca Biomèdica (BIOMED): "Genomas y Sistemas"	Master	Universitat Pompeu Fabra (UPF)	Elena Bosch
Biomedical Research: Genomes and Systems	Master	Universitat Pompeu Fabra (UPF)	Arcadi Navarro
Bioinformatics for Health Science: Biomedical Informatics	Master	Universitat Pompeu Fabra (UPF)	
Bioinformatics for Health Science: Biomedical Data Analysis	Master	Universitat Pompeu Fabra (UPF)	
Biología Humana: grandes procesos evolutivos	Specialisation: grade	Universitat Pompeu Fabra (UPF)	
Monitorización de Ensayos Clínicos	Master	Universitat de Barcelona (UB)	
Bioinformatics for Genomic Variability	Master	Universidad Complutense de Madrid	
The gentic Architechture of Complex Disease	Specialisation	Instituto Gulbenkian de Ciência (Oeiras, Portugal)	
Master in Biodiversidad	Master	Universitat de Barcelona (UB)	Salvador Carranza

RETREAT CHRONICLE

Finally, on the 14th and 15th December, the members of IBE convened at the Monastery of Bellpuig de les Avellanes (close to Balaguer and 161 Km from Barcelona) for their Annual Retreat. This meeting provides a unique opportunity for all members of the IBE to network, share their scientific experiences, and acquire a detailed overview of the scientific activities at the IBE. The formal scientific program included six lectures and 49 posters. One PI per IBE program was invited to lecture on the research at their group: Xavier Franch (member of the Functional Evolution in Insects program, who spoke on "Morphogenesis: a window to look at evolution"), Ricard Solé (Complex Systems, "Computation, multicellularity and evolution: from theory to synthetic biology"), Arcadi Navarro (Computational and Comparative Genomics, "Evolutionary Novelties in Primate Genomes"), Salvador Carranza (Animal Phylogeny and Systematics, "Systematics, biogeography and evolution of reptiles and amphibians"), and David Comas (Population Genetics, "Insights to the genetic structure of human populations in Central Africa"). Additionally, Carles Lalueza-Fox (Computational and Comparative Genomics) was asked to present a more general and popularized overview of his research field, namely ancient DNA, in a talk whose title, "Some things to do once you are dead" gives a measure of Carles' brand of humor.

Post-docs and graduate students were required to summarize their research in a poster format; some time was devoted to viewing and discussing posters, with subjects and approaches that covered the breadth of IBE: from field work to in silico approaches, through molecular genetics, in areas such as insect and reptile phylogeography, human population genetics, insect reproductive physiology, primate comparative genomics, and the genomics of mobile elements, to name a few. A prize for the best poster was granted by popular vote to graduate student Elisenda López-Panadés.

The isolated, calm atmosphere at the monastery fostered a lively exchange of ideas, both in the formal scientific program and in the social activities. Those included a tour of the monastery, which was founded in 1166 by the Order of Canons Regular of Prémontré. It served as a center of higher learning, until the community disbanded in 1835. Since then, the compound has been a Salesian school, a home of retirement for Salesian brothers, and part of it is open now to the public as a hotel. Other social activities were a hike in the surrounding hills, and a nocturnal and lengthy informal discussion in the underground cellar.

The Annual Retreat succeeded in creating a venue in which communication flowed freely and the IBE fully functioned as a cohesive unit.


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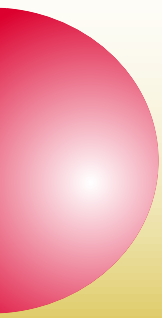

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