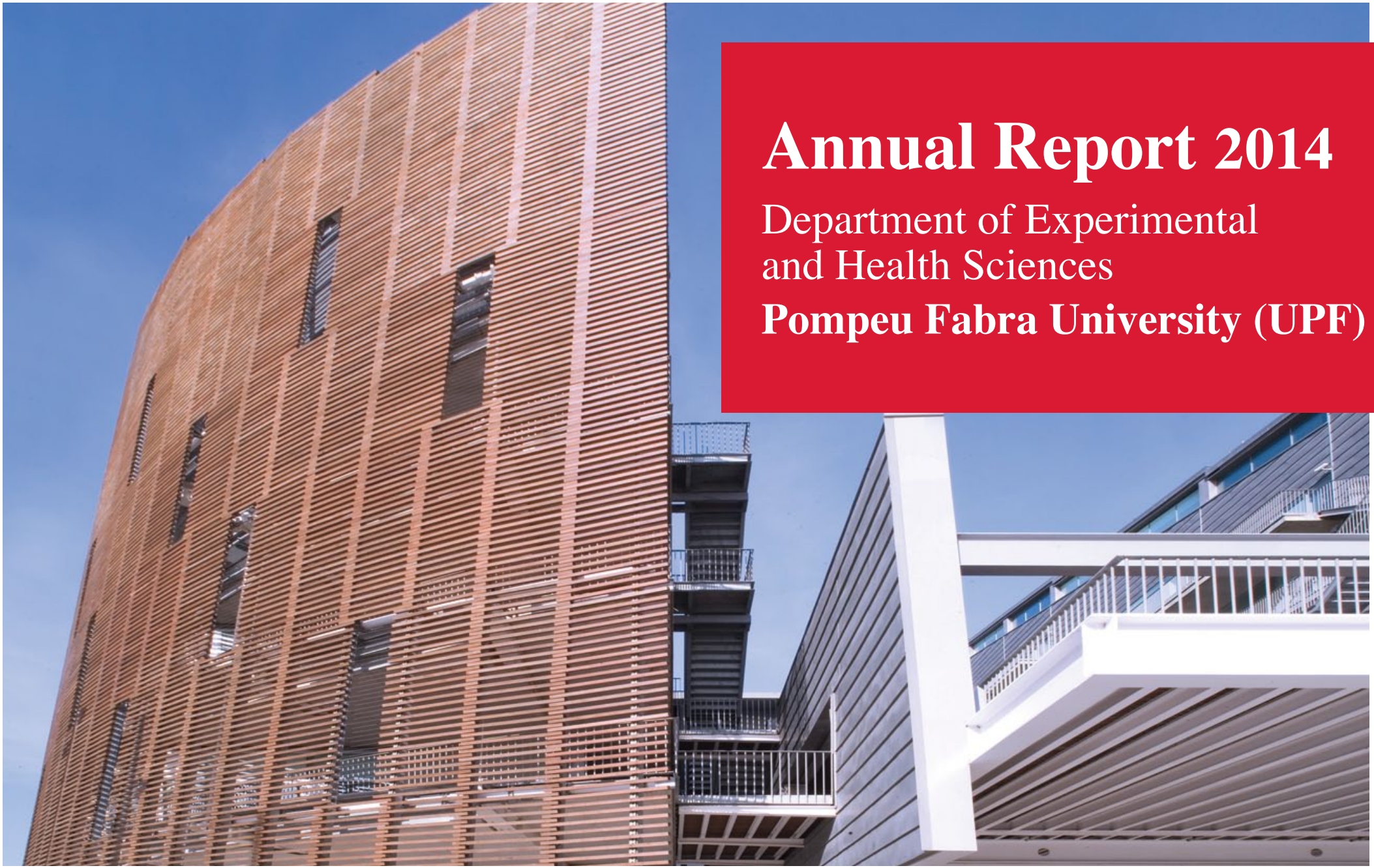

Annual Report 2014

Department of Experimental and Health Sciences

Pompeu Fabra University (UPF)

upf. Universitat Pompeu Fabra Barcelona

Department of Experimental and Health Sciences

Main menu

Foreword of the Director

There are few jobs more enjoyably frustrating than doing Science. This is due, in part, to the nature of Science itself, since, as George Bernard Shaw noted, *Science never solves a problem without creating ten more*. But it is also built-in the personality of scientists: we quickly forget what we have achieved and eagerly look for new challenges. As Maria Sklodowska-Curie famously said: *One never notices what has been done; one can only see what remains to be done*. We are always happy, always dissatisfied, always on the move. At the DCEXS, every day brings new opportunities of noticing what remains to be done; be it in our labs, performing complex experiments, or in front of our computers, developing new algorithms, or in the classroom, talking to new generations that have yet to yet taste the glorious mixture of feelings that is to do Science. It is quite natural that we should feel delighted at the privilege.

Yet another challenging year has gone by, with no signs of improvement in the country's economic situation, but again we have managed to keep up the hard work and, in doing so, we have been rewarded. For instance, 2014 saw an enormous 60% increase in our competitive funding relative to 2013, with grants from an impressive range of bodies, including European, USA and Spanish funding agencies. Also in 2014, our researchers published 65% of their papers in journals of the first decile and our university became 13th best university in the world among those under 50 years (Times Higher Education Ranking, 2014), and the 1st Spanish university in productivity in teaching and research (U-Ranking BBVA Foundation and Ivie, 2014) as well as in quality of scientific production (Ranking Scimago, 2014). In a sense, all this is business as usual, but it is not idle to remind ourselves that, even if a lot remains to be done, we have achieved much under dire circumstances.

Beyond our usual performance, we have had also our first times. The best example is the award of a *Honoris Causa* Doctorate to Professor Sydney Brenner on April the 3rd 2014. We should be happy that we had the chance to pay homage to one of the towering figures in the history of biology an indeed of science at large. Let me be clear: professor Brenner is so great, so unique, that this is one of the rare cases in which the awardee honors the awarding institution by accepting the Doctorate rather than the other way around. Professor Brenner agreed to honor us and perhaps this was the highest point of our institutional life last year.

Another first time was the extension of the retreat of our Scientific Committee to include part of the faculty. The retreat took place in Món Sant Benet on September the 15th and 16th 2014. The aim of the retreat was bringing together scientists, heads of the core facilities and key staff from our administration, offering opportunities to get to know each other's work, to potentiate collaborations, and to discuss the best strategies for the DCEXS. In addition to a session of the Scientific Committee there were talks by PIs from all Research Programmes, who presented their latest results; and a very, very interesting after-dinner Master Class (ask around, if you will).

Our teaching and communication work was also quite satisfying with the new Medicine degree already in place and the consolidation of an even newer degree in Biomedical Engineering, which will see its first graduates next year 2015. Indeed, we are quite excited about 2015 in several respects. First, our first cohort of Medicine graduates will take the statewide qualifying exams for clinical residents, MIR. The MIR results are a very good indicator for ranking the academic proficiency of Medical Schools, and we certainly have high expectations about our students' capabilities. Then, after having run for several years with remarkable success in terms of students' satisfaction and employment rates, our Human Biology degree and several of our Master degrees are now being evaluated by independent external accreditation agencies. While we can only wish for a very positive outcome of this accrediation next year, we can already express our pride in the commitment, professionalism, and sense of community shown throughout this process by our faculty, administrative personnel, and of course the main protagonists, our students. As for outreaching activities, our yearly Symposium was devoted this year to New Insights in Genetics and Neuroscience Research. The increasing success of our DCEXS Symposia is quite encouraging for us, stimulating new ideas for future editions and spurring other initiatives aimed not only to professional scientists but also to the general public.

In summary, last year was better than the previous one and it is clear that we keep improving, so we can say with full confidence that 2015 will be even better. Thanks to all of you for making it possible.

Arcadi Navarro,
DCEXS Director

"One never notices what has been done; one can only see what remains to be done"

Maria Sklodowska-Curie
Scientist, Science advocate and Hero

The DCEXS

The Department of Experimental and Health Sciences (DCEXS) was founded in 1998 by the Pompeu Fabra University (UPF), a young, public and modern university born in 1990 and called to become one of the leading European universities. Within this framework, the great challenge of the DCEXS has been to successfully develop a project where research and teaching are firmly integrated.

Together with the UPF's Faculty of Health and Life Sciences, the DCEXS is responsible for three undergraduate degrees: Human Biology (since 1998), Medicine (2008) and Biomedical Engineering (2011). The Department also runs Master's degrees in the fields of biomedicine, pharmaceutical and biotechnology industries, clinical laboratory sciences, and public health, and PhD Programmes in Biomedicine, fully taught in English and recognized by independent agencies. Scientific research is perceived by the students, both undergraduates and postgraduates, as an essential tool in their studies.

The DCEXS is strategically located within the Barcelona's Biomedical Research Park (PRBB), a large scientific infrastructure that gathers together several public research centres and is physically connected to Barcelona's Hospital del Mar, thus being one of the largest hubs of biomedical research in southern Europe. This close contact has allowed DCEXS to establish strategic alliances with surrounding research institutes affiliated to the UPF such as the Centre for Research in Environmental Epidemiology (CREAL), the Centre for Genomic Regulation (CRG) or the Hospital del Mar Medical Research Institute (IMIM).

Over the last few years, the DCEXS has achieved a remarkable presence in different research fields and a growing research output and impact. DCEXS researchers have published 179 research articles in 2014, with 85% in journals that fall in the first quartile, and 64% in the first decile.

Regarding participation in international projects, a remarkable example is the FP7 European project *NeuroPain*. Coordinated by Rafael Maldonado, head of the Neuropharmacology Laboratory at the DCEXS, *NeuroPain* started in January 2014. Neuropathic pain can be the result of a traumatic injury but it can also be caused by the degeneration of nerve structures in the absence of injury. This pain is difficult to alleviate with conventional therapies and may become severe and disabling. Basic research of new analgesics is extremely difficult especially because of the low predictive validity of animal models available for chronic pain, and therefore this condition is very difficult to treat; *NeuroPain* aims to overcome these obstacles by means of an interdisciplinary collaboration between basic research scientists, clinicians and leading private companies.

Another example of successful results in European calls is Iñaki Ruiz-Trillo, a researcher at the joint UPF-CSIC Institute of Evolutionary Biology (IBE), who was awarded an ERC Consolidator Grant. The aim of this project is to understand one of the most important evolutionary transitions

in the history of life: the origin of multicellular animals from their unicellular ancestors. In particular, Ruiz-Trillo and his team will try to address how genes involved in multicellularity were co-opted at the onset of animals and whether gene regulation played an important role into the origin of the complex metazoan bodyplans. To this end, they will take profit of two non-model systems recently developed by the lab in two different unicellular lineages closely related to animals: the filasterean Capsaspora owczarzaki and the ichthyosporean Creolimax fragrantissima. Finally, they plan to use single-cell genomics to understand the ecology, distribution and adaptation of uncultured unicellular linages that are close relatives to animals.

In recognition of the excellence of the department, in 2014 DCEXS researchers Jordi García Ojalvo and María Cristina López Rodríguez received the ICREA Academia Award. Also in 2014, Arnau Busquets' thesis entitled "Targeting the endocannabinoid system for Therapeutic Purposes", supervised by DCEXS professors Andrés Ozaita and Rafael Maldonado, was awarded the Prize of the Spanish Royal Academy of Doctors in the Life and Health Sciences category.

Direction

Director:
Arcadi Navarro

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José Aramburu
Francisco J. Muñoz

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Baldo Oliva

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Carlos López Otín (U. Oviedo)

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José Luis López Barneo (Instituto de Biomedicina de Sevilla)
Fernando Rodríguez Artalejo (U. Autónoma Madrid)
Francisco Sánchez Madrid (CNIC)
Alfonso Valencia (CNIO)

Teaching

The Department of Experimental and Health Sciences is committed to the teaching quality as well as the educative objectives of the Faculty of Health and Life Sciences. This Faculty was born on the premises of a common and innovative project which was initiated by the Dean under the support of a technical unit. This project has been very successful in achieving an excellent teaching of generic and specific competences of the Faculty graduates. The teaching of Department members has been repeatedly recognized by several prizes awarded by the Generalitat de Catalunya (four Vicens Vives awards in 2002, 2005, 2007 and 2013) as well as the Spanish Government (Prize to the Teaching Innovation in 2006).

The degree in Human Biology began in 1998 with an innovative teaching methodology. Small size classes, problem-based learning, student tutoring, high content of practical skills and continued evaluation were combined for a high quality education. DCEXS study programmes became the reference at UPF because of the implementation of European Higher Education Area (EHEA) methodology.

According to the U-Ranking 2015 (Fundación BBVA-Ivie, which integrates indicators in teaching, research and technological innovation), the UPF is the first choice for Medicine and Human Biology studies. The first cohort of Medicine students graduated in 2014 and all of them passed the qualifying state exam for clinical specialisation (MIR), with 90% of our students having obtained positions in major hospitals and clinical centres.

Bachelor Degrees

- **Human Biology**
  The degree in Human Biology is especially designed to enable graduates to work professionally in three major fields: the pharmaceutical and biotechnological industry, clinical laboratories and biomedical research.
- **Medicine (UPF-UAB)**
  The Faculty's MD studies are characterized by the strong relationship between biomedical research and clinical practice.
- **Biomedical Engineering**
  An interdisciplinary degree that provides with education in the fields of biomedicine, technology and biomedical computational modelling.

Master's programmes

- **Bioinformatics for Health Sciences**
  The Master's programme in Bioinformatics for Health Sciences is designed to provide professionals and researchers with skills and abilities geared towards the development of new computational strategies and IT systems for their use in biomedical research.
- **Pharmaceutical Industry and Biotechnology**
  The primary aim of this Master's programme is to train students in the area of companies dedicated to the research of drugs and biotechnology products to prevent and treat human diseases.
- **Biomedical Research**
  The Master's degree in Biomedical Research focuses on the study of the molecular, cellular, physiological and evolutionary bases of biological processes and their pathological or adaptive alterations, and is mainly aimed at students who wish to obtain a PhD in different fields of Biomedicine.

Teaching

- **Clinical Analysis Laboratory**
  The Master's programme in Clinical Analysis Laboratory focuses on the application of laboratory techniques for clinical diagnosis and presymptomatic and predisposition testing. It includes aspects related to clinical and environmental microbiology, biochemistry, immunology, clinical and multifactorial genetics, molecular genetics applied to forensic diagnostics, genetic counselling and assisted reproduction techniques, as well as clinical assessment and interpretation of results obtained with laboratory techniques.
- **Public Health**
  The mission of the Master's programme in Public Health is to train students to understand the processes of health/disease and its determinants from the population perspective, and to address health problems through collective interventions for the promotion, protection and restoration of health.
- **Pre-service Science Teacher Training**
  The aim of this Master's is to train students to develop the basic skills to become a professional school science teacher. Students learn the fundamentals of science education, logics of designing curricula in natural science, pedagogical contents needed to educate adolescents and the key elements to innovate in school science.
- **Genetic Counselling**
  This is the only course in Spain officially accredited by the European Board of Medical Genetics to train professional genetic consultants. The Master's in Genetic Counselling provides professionals to inform patients about genetic diseases and advise them on family planning issues related to them (understand their heritage, know the risk of transmission to offspring, etc.).

In addition, DCEXS Faculty coordinates participates in different courses in several Master's coordinated by other universities: Neurosciences (UB), Clinical and Biomedical Research (UB), and Workplace Health and Safety (UPC).

PhD

- **PhD in Biomedical Sciences**
  The PhD in Biomedicine is a training programme that aims to encourage scientists to develop innovative research projects in the field of Health and Life Sciences to complete a doctoral thesis. It provides all necessary (analytical, experimental, and theoretical) tools to develop this research project and a scientific career. The PhD programme is an international programme attended by a large number of foreign students. The PhD has been verified by ANECA (National Agency for the Evaluation, Quality, and Accreditation). In October 2011, the doctoral programme in Biomedicine was awarded the newly created "Mention towards Excellence" (MEE2011-0323) by the Spanish Ministry of Education.

Bringing Science to young students Programme

The DCEXS, in collaboration with PRBB, has the Bringing Science to young students Programme, which aims at encouraging scientific vocations and encompasses several scientific dissemination activities addressed to school children. The main actions are:

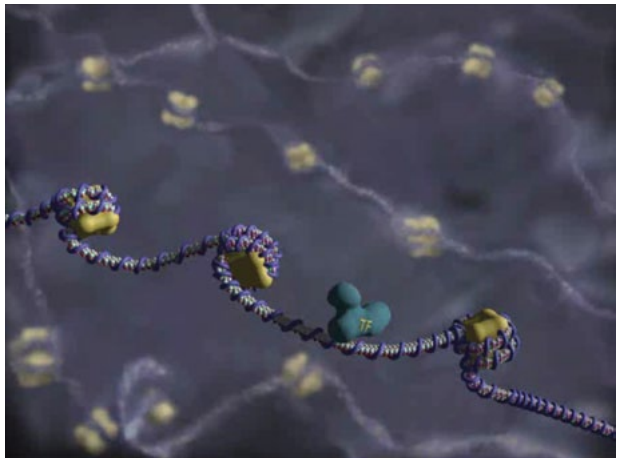
- **PRBB Award** for high school research projects, celebrated yearly since 2005 (http://premi.prbb.org/).
- **Escolab activities:** visits to labs are organised for high school students since 2008 (http://escolab.bcn.cat/).
- **Play Decide Debates:** role play in which high school students debate about socio-scientific topics.
- **Scientific talks for high school students in the PRBB auditorium:** more than 350 students per year attend scientific talks about topics such as genomics, evolution or neuropharmacology.
- **UPF Junior Campus:** a course on molecular biology addressed to high school students took place in 2013 and 2014.

Scientific Highlights 2014

Nadal-Ribelles M, Solé C, Xu Z, Steinmetz LM, de Nadal E, Posas F (2014) Control of CDC28 CDK1 by a stress-induced lncRNA. Mol Cell 53:1-13.

Osmotic stress triggers cell adaptation through gene expression regulation

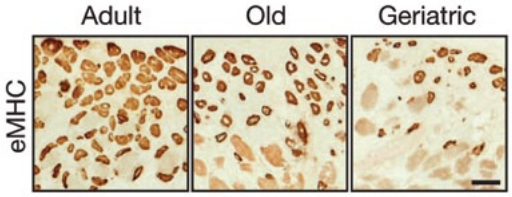
The analysis of gene expression in yeast using 'tiling arrays' has helped us to define the limits, structure and quantity of coding and non-coding transcripts throughout the genome. We have seen that Hog1 induces a set of non-coding RNAs (lncRNAs) under stress. One of the genes expressing a Hog1-dependent lncRNA in antisense orientation is CDC28, the cyclin-dependent kinase 1 (CDK1) that controls the cell cycle in yeast. Cdc28 lncRNA mediates the induction of CDC28 expression, which results in cells able to reenter the cell cycle more efficiently after stress. This may represent a general mechanism to prime expression of genes needed after stresses are alleviated.

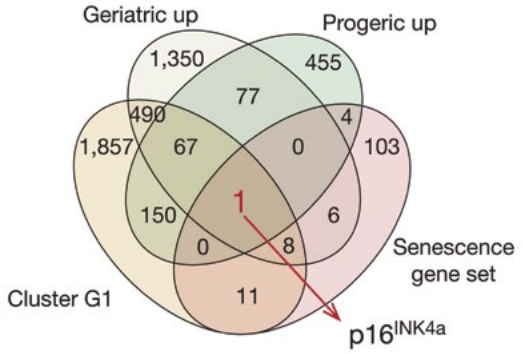


Sousa-Victor P, Gutarra S, García-Prat L, Rodriguez-Ubreva J, Ortet L, Ruiz-Bonilla V, Jardí M, Ballestar E, González S, Serrano AL, Perdiguero E, Muñoz-Cánoves P (2014) Geriatric muscle stem cells switch reversible quiescence into senescence. Nature 506(7488):316-21.

Understanding age-related tissue degeneration

This work explains the irreversible decline of muscle regenerative capacity during aging.
In mammals, muscle stem cells are in a dormant quiescent state and, in response to injury, they activate and support regeneration. This paper shows that during geriatric age in mice, these stem cells cannot activate and regeneration in impaired, and this defect is caused by a mechanism involving p16INK4a derepression specifically at this advanced age. As the same signaling pathway is dysregulated in human geriatric cells, the findings may provide a basis for attenuating loss of muscle regenerative capacity in very old humans.





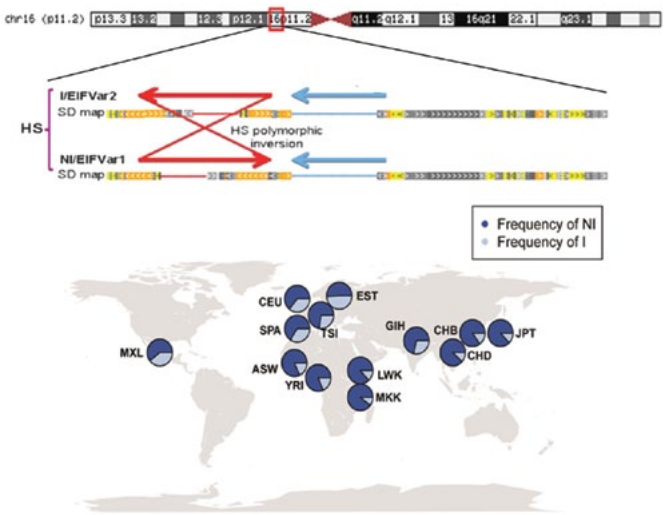
Muscle stem cell reversible quiescence is impaired at geriatric age and in progeria. Venn diagram of the overlap among significantly upregulated genes in adult, old, geriatric and progeric, compared to young, muscle stem cells pointed p16INK4a.

Scientific Highlights 2014

González JR, Càceres A, Esko T, Cuscó I, Puig M, Esnaola M, Reina J, Siroux V, Bouzigon E, Nadif R, Reinmaa E, Milani L, Bustamante M, Jarvi D, Antó JM, Sunyer J, Demenais F, Kogevinas M, Metspalu A, Càceres M, Pérez- Jurado LA (2014) A Common 16p11.2 Inversió Underlies the Joint Susceptibility to Asthma and Obesity. Am J Hum Genet 94(3):361-72.

Joint susceptibility to asthma and obesity relies on a variation in a chromosomal region

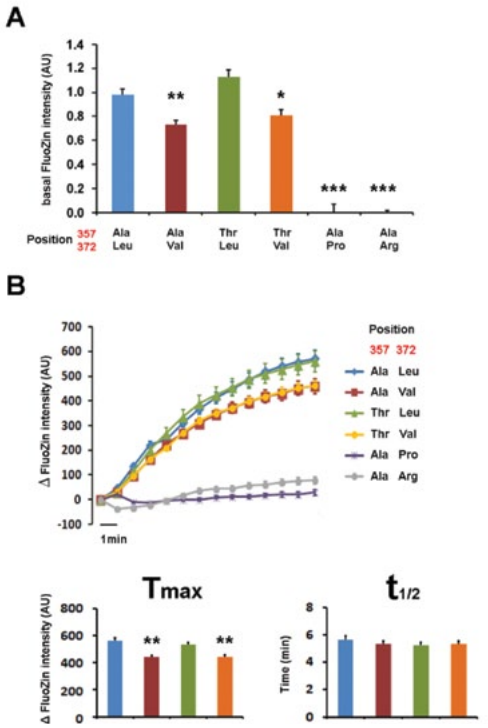
For a long time, epidemiological studies have shown that obese individuals are more likely to develop asthma than non obese subjects. This paper provides the first genetic evidence that sustains the joint susceptibility to both diseases. Researchers carried out a genetic study of 5.800 human samples, finding a chromosomal variable region that can provide either protection or susceptibility. The different variants of this region show a geographic distribution, suggesting an evolutionary adaptive mechanism.



Engelken J, Carnero-Montoro E, Pybus M, Andrews K, Lalueza-Fox C, Comas D, Sekler I, de la Rasilla M, Rosas A, Stoneking M, Valverde MA, Vicente R, Bosch E (2014) Extreme Population Differences in the Human Zinc Transporter ZIP4 (SLC39A4) Are Explained by Positive Selection in Sub-Saharan Africa. PLoS Genet 10(2):e1004128.

A common change of a zinc transporter in African populations is due to positive selection

Zinc is critically important for human health since it is involved in many functions in our body and in severe illnesses. This research has found out that a variation in a gene encoding for a zinc transporter in the intestine (ZIP4) has an extremely marked geographical distribution, limited to Sub-Saharan populations. The change in ZIP4 entails a less effective absorption of zinc, and the research team hypothesizes about a protective mechanism against pathogens that need zinc, being the first time that the marked distribution of this mutation is proven to be consequence of positive selection.

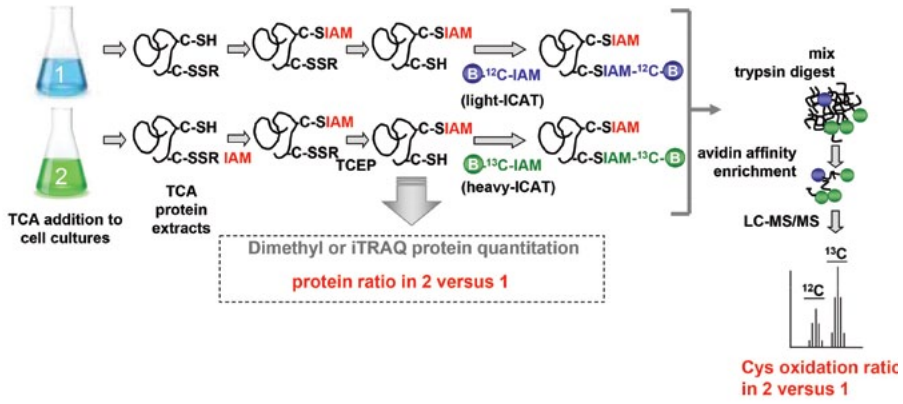


Scientific Highlights 2014

García-Santamarina S, Boronat S, Domènech A, Ayté J, Molina H, Hidalgo E (2014) Monitoring in vivo reversible cysteine oxidation in proteins using ICAT and mass spectrometry. Nat Protoc 9:1131-45.

A proteomic approach to measure reversible cysteine oxidation

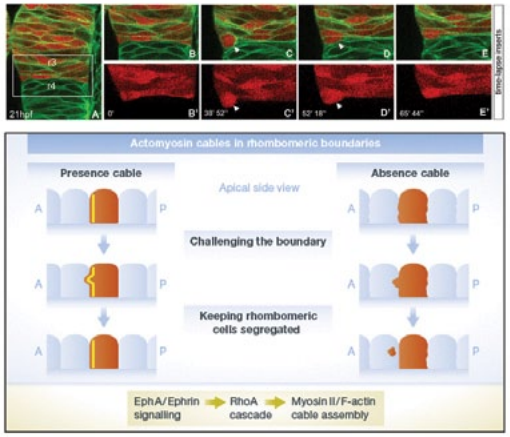
It is widely accepted the importance of cysteine oxidation in the catalytic activities of many proteins, in the toxicity associated to oxidative stress, and in the activation of reactive oxygen species-responding signalling cascades. The wide role of reversible cysteine oxidation in physio- and pathological conditions has prompted many researchers to develop techniques to characterize the oxidized thiol proteomes of cells grown under different environmental and genetic conditions. Within this manuscript, we describe a gel-free approach, based on the labelling of oxidized thiols in acidic extracts with iodoacetamide-based isotope-coded affinity tag (ICAT) reagents, followed by mass spectrometry analysis, which overcomes all the defects of previous methods and constitutes a friendly, easy-to-apply, cheap and not time consuming methodology for standard laboratories and proteomic facilities.



Calzolari S, Terriente J, Pujades C (2014) Cell segregation in the vertebrate hindbrain relies on actomyosin cables located at the interhombomeric boundaries. EMBO J 33(7):686-701.

Proper embryonic development of the brain depends on cell segregation

This paper reveals the importance of cell segregation for the development of the central nervous system (CNS) in zebrafish. During embryonic development, groups of cells with different functions are separated in compartments. The research focuses on the development of the hindbrain, the posterior brain, and how cells from different compartments are segregated by physical barriers based on actomyosin cables. If the formation of the actomyosin barrier is compromised, cell mixing can occur, leading to serious problems in the future brain. Defects in the formation of the interface between cellular populations play an important role in tumor progression and metastasis.

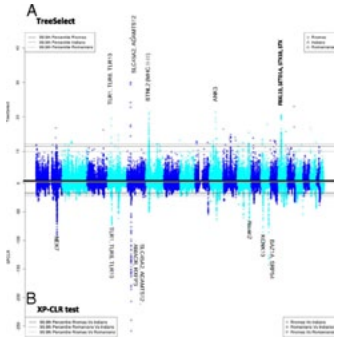


Scientific Highlights 2014

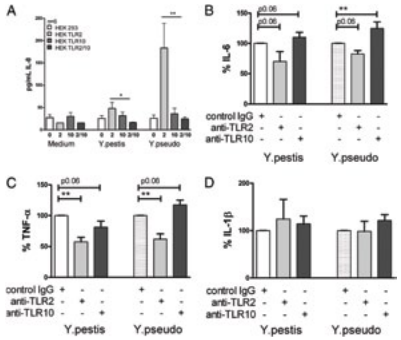
Laayouni H, Oosting M, Luisi P, Ioana M, Alonso S, Ricaño-Ponce I, Trynka G, Zhernakova A, Plantinga T, Cheng S, van der Meer JMW, BK T, Popp R, Sood A, Wijmenga C, Joosten LAB, Bertranpetit B, Netea MG (2014) The common evolutionary history of European and Roma populations identifies convergent evolution exerted by plague on TLR1/TLR6/TLR10 pattern recognition system. PNAS 111(7):2668-73.

Our genome: a time warp into the era of Black Death

This article gives a unique perspective on the impact of evolution on the immune system under pressure by infections, using two populations with different genetic ancestry, Europeans and Rroma (Gypsies), which have lived in the same geographic area and have been exposed to similar environmental infections. We identified several genes under evolutionary pressure in European and Gipsy populations, but not in a Northwest Indian population, the geographic origin of the Gipsy population. Three Toll-like receptor genes showed a strong signal of adaptive selection and their gene products are functional receptors for *Yersinia pestis*, the agent of plague. Thus, we identified immune system genes as being shaped by convergent evolution in two populations with different origins under the same infectious environment.



Manhattan plot of results of selection tests in Rroma, Romanians, and Indians using TreeSelect statistic (A) and XP-CLR statistic (B). Chromosomes ordered from chromosome 1 to chromosome 22.

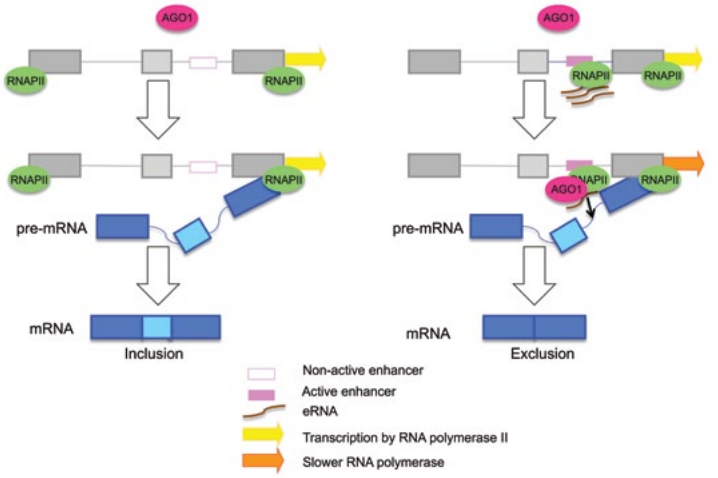


*The role of TLR10 for the recognition of Y. pestis and Y. pseudotuberculosis. (A) HEK293 transiently transfected with TLR2, TLR10, or TLR2/10, and stimulated with 1 × 105 heat-inactivated Y. pestis or Y. pseudotuberculosis, respectively. Bars represent the means ± SEM of at least three separate experiments. (B) PBMCs stimulated with Y. pestis or Y. pseudotuberculosis per mL. n = 6; means ± SEM; *P = 0.05, **P = 0.01. (C) TNF-α production after PBMCs stimulated with Y. pestis or Y. pseudotuberculosis in the presence or absence of 10 μg/mL antibody. (D) IL-1β production after 24 h of stimulation. Means ± SEM; *P = 0.05, **P = 0.01. The data shown are from three independent experiments each performed in duplicate.*

Alló M, Agirre E, Bessonov S, Bertucci P, Gómez Acuña L, Buggiano V, Bellora N, Singh B, Petrillo E, Blaustein M, Miñana B, Dujardin G, Pozzi B, Pelisch F, Bechara E, Agafonov DE, Srebrow A, Lührmann R, Valcárcel J, Eyras E, Kornblihtt AR (2014) Argonaute-1 binds transcriptional enhancers and controls constitutive and alternative splicing in human cells. PNAS 111(44):15622-9.

The new voyage of the Argonautes

Argonaute proteins are well characterized factors in post-transcriptional gene silencing, the process by which small RNAs trigger mRNA degradation or inhibit translation in the cytoplasm. We report that Argonaute proteins also play important roles in the nucleus. Our genome-wide analysis reveals that Argonaute- 1 (AGO-1) binds preferentially to active transcriptional enhancers and that this association is mediated by the RNAs that are transcribed from these enhancers (eRNAs). Moreover, the interaction of AGO-1 with enhancers does not seem to regulate transcription of the neighboring genes but of alternative and constitutive splicing. These results contribute to the understanding of the complex regulation of gene expression in eukaryotic cells.



Third Symposium of the DCEXS

The Third Symposium of the DCEXS, entitled "New insights in Genetics and Neuroscience research" took place on the 26th of November 2014 at the Barcelona Biomedical Research Park (PRBB). It was organized by the Genetics and Neurosciences Programme and it brought together leading researchers in the fields of Neurosciences, Developmental Biology, and Genetics.

The programme included the following talks:

- Milk in development- good or bad for behaviour and the brain?
  Ian Kitchen (University of Surrey, UK)
- Alzheimer Disease Pathogenesis: insights from neural development.
  Paola Bovolenta (Centro de Biología Molecular "Severo Ochoa", Spain)
- A taste of development and regeneration.
  Linda Barlow (University of Colorado, School of Medicine, USA)
- Recessive ataxia by partial loss of function: a common theme.
  Michel Koenig (INSERM- IURC, France)
- Cell Reprogramming-based Modeling of Neurodevelopmental Disorders: Insights into Transcriptional and Epigenetic Dysregulation.
  Giuseppe Testa (IFOM-IEO, Italy)
- Role of Reelin in adult brain plasticity and in Alzheimer's Disease pathogenesis.
  Eduardo Soriano (Universitat de Barcelona, Spain)

One of the main aims of the symposiums is to promote the education of young scientists, therefore students are actively invited to participate and encouraged to present their data in the poster session. Over 300 people registered for the symposium, and 20 PhD and Master's students participated in the poster competition. The poster entitled "Modelling eating-addiction in mice" by Samantha Mancino won the first prize –an iPad–, and the poster entitled "Neuronal architecture abnormalities and synaptic activity impairment in mice heterozygous for different deletions of the Williams-Beuren syndrome locus" by Cristina Borralleras won the second prize –a copy of the 4th edition of Fundamental Neu-Wroscience by Squire and Berg–. Both prizes were sponsored by Elsevier and presented by Arcadi Navarro, Director of the DCEXS, and Carlos Rodríguez, Elsevier representative.

Honoris causa award to Professor Sidney Brenner

Sydney Brenner, Nobel Prize laureate in physiology or medicine and considered one of the architects of modern biology, was awarded a doctorate *honoris causa* by UPF on April the 3rd 2014. He was the first scientist to receive this honour from the University, in recognition of his brilliant career in teaching and research in the field of molecular biology, which has made him one of the world's leading names in the field.

Arcadi Navarro, the DCEXS Director, was the sponsor of the ceremony and accompanied Sydney Brenner throughout the event. The doctoral encomium was given by lecturers Miguel Beato, researcher at the Centre for Genomic Regulation (CRG), Fernando Giráldez and Jaume Bertranpetit, professors at the DCEXS. The three encomia referred to Brenner's main contributions to molecular biology, developmental biology and evolutionary biology, respectively.

DCEXS Research groups

- Cell and Molecular Biology Programme
- Molecular Medicine Programme
- Evolutionary Biology and Complex Systems Programme
- Biomedical Informatics Programme
- Genetics and Neurosciences Programme
- Transversal Programme: Public Health and Education in Health Sciences

Cell and Molecular Biology Programme

Coordinator: Miguel Valverde

Research focuses on molecules within cells, their interactions and their roles in the function of individual cells and living organisms. The programme covers a broad range of disciplines including cell and molecular biology, physiology, genomics, microbiology and pathology. The main research activities of the programme are divided in three areas: cell signaling, genomic regulation and pathophysiology. The integration of these three disciplines provides a depth insight on intracellular mechanisms in response to different stimuli including stress or harmful molecules and viruses. One of the main aims of this programme is to elucidate the molecular basis of human diseases.

- **Cell Biology Group**
  Pura Muñoz-Cánoves
- **Cell Signalling Research Group**
  Francesc Posas and Eulàlia de Nadal
- **Ageing Brain Research Group**
  Francisco J. Muñoz
- **Molecular Physiology and Channelopathies**
  Miguel Ángel Valverde and José Manuel Fernández-Fernández
- **Molecular Virology**
  Juana Díez
- **Infection Biology Group**
  Andreas Meyerhans

Cell Biology Group

Pura Muñoz-Cánoves

www.upf.edu/cellbiology

Research Outline

Our research aims to understand the mechanisms regulating stem cell homeostasis and regenerative functions: how stem cells maintain quiescence, are activated, proliferate and differentiate, and finally self-renew, and how they interact with the external inflammatory environment. Research has been specially focused on stem cells of skeletal muscle. In particular, we want to shed light on: **1)** the age-associated muscle decline and wasting (sarcopenia) and loss of stem-cell regenerative functions with aging; and **2)** the physiopathology of muscular dystrophies, with a specific interest in the contribution of inflammation and fibrosis to dystrophy progression. These studies are relevant for regenerative medicine.

Current Projects / Research lines

- **Understanding the relevance of inflammation and fibrosis in muscle regeneration and dystrphy progression.**
  We investigate the Implication of the inflammatory infiltrate in dystrophic muscle and how it promotes collagen deposition (fibrosis) and Duchenne muscular dystrophy progression.
- **Understanding the role of the cytokine IL-6 in skeletal muscle regeneration and growth.**
  We investigate how the cytokine IL-6 controls the cross-talk of satellite cells and inflammatory cells during the process of muscle repair after damage.
- **Understanding the function and mechanism of action of p38 MAPK signaling in myogenesis.**
  We investigate how the p38 signaling pathway regulates controls satellite cell activation from quiescence, proliferation, differentiation and return to the quiescent state (self renewal).
- **Understanding the mechanisms underlying muscle stem cell regenerative decline in aging.**
  We investigate why muscle stem cells lose their homeostatic and regenerative functions during the aging of an organism.

Selected publications 2014

- **Sousa-Victor P, Gutarra S, García-Prat L, Rodriguez-Ubreva J, Ortet L, Ruiz-Bonilla V, Jardí M, Ballestar E, González S, Serrano AL, Perdiguero E, Muñoz-Cánoves P (2014)** Geriatric muscle stem cells switch reversible quiescence into senescence. *Nature 506:316-21.*
- **Segalés J, Perdiguero E, Muñoz-Cánoves P (2014)** Epigenetic control of adult skeletal muscle stem cell functions. *FEBS J doi: 10.1111/febs.13065.*
- **Pessina P, Cabrera D, Morales MW, Riquelme CA, Gutiérrez J, Serrano AL, Brandan E, Muñoz-Cánoves P (2014)** Novel and optimized strategies for inducing fibrosis in vivo: focus on Duchenne Muscular Dystrophy. *Skelet Muscle doi: 10.1186/2044-5040-4-7.*
- **Kharraz Y, Guerra J, Pessina P, Serrano AL, Muñoz-Cánoves P (2014)** Understanding the process of fibrosis in Duchenne muscular dystrophy. *Biomed Res Int doi: 10.1155/2014/965631.*
- **Sousa-Victor P, Perdiguero E, Muñoz-Cánoves P (2014)** Geroconversion of aged muscle stem cells under regenerative pressure. *Cell Cycle 13(20):3183-90.*

Other relevant publications from last 10 years

- **Serrano AL, Baeza-Raja B, Perdiguero E, Jardí M, Muñoz-Cánoves P (2008)** Interleukin-6 is an essential regulator of satellite cell-mediated skeletal muscle hypertrophy. *Cell Metab 7:33-44.*
- **Vidal B, Serrano AL, Tjwa M, Suelves M, Ardite E, De Mori R, Baeza B, Martínez de Lagrán M, Ruiz-Bonilla V, Jardí M, Gherardi R; Degen J, Christov C, Dierssen M, Dewerchin M, Carmeliet P, Muñoz-Cánoves P (2008)** Fibrinogen drives dystrophic muscle fibrosis via a TGFb/alternative macrophage activation pathway. *Genes Dev 22:1747-52.*
- **Perdiguero E, Sousa-Victor P, Ruiz-Bonilla V, Jardí M, Caelles C, Serrano A.L, Muñoz-Cánoves P (2011)** p38/MKP-1-regulated AKT coordinates macrophage transitions and resolution of inflammation during tissue repair. *J Cell Biol 195:307-22.*

Other PI: *Antonio L. Serrano and Eusebio Perdiguero.*

Postdocs: *Yacine Kharraz, Patrizia Pessina, Jessica Segalés and Mònica Zamora.*

PhD students: *Laura García-Prat, Joana Guerra, Diana Mesquita, Beatriz de Lucas and Pedro Maseres (sharing with the Cell Signalling Research Group of Drs. Posas and de Nadal).*

Technicians: *Vanessa Ruíz, Laura Ortet, Mercè Jardí, Susana Gutarra, Vera Lukesova and Begoña Ampudia.*

Project Manager: *Marina Raya.*

Cell Signalling Research Group

Francesc Posas and Eulàlia de Nadal

www.upf.edu/cellsignaling

Research Outline

Our group studies how cells detect and respond to environmental changes. We focus in the characterization of stress-responsive signal transduction pathways, especially those controlled by MAP kinases of the Hog1/p38 family. Using the S. *cerevisiae* yeast and higher eukaryotic cells as model organisms, we study the molecular mechanisms required to respond to changes in the extracellular environment and which are the adaptive responses required for cell survival. Proper adaptation involves the modulation of several basic aspects, such as the control of cell cycle and regulation of gene expression. We also analyze the basic signaling properties of the HOG pathway. We have demonstrated that cellular communication using complex engineered networks can be implemented to perform *in vivo* cellular computation.

Current Projects / Research lines

- **Function and regulation of SAPK signaling pathways in eukaryotic cells.**
  Study of the signaling properties of the p38/Hog1 SAPK pathway in response to cellular stress.
- **Identification and characterization of proteins under the control of the yeast Hog1 MAPK.**
  Definition of the substrates regulated by Hog1 and dissection of the cellular processes involved in stress adaptation.
- **Chromatin dynamics of transcriptional stress response in yeast.**
  Characterization of the regulatory mechanisms required for modulation of gene expression in response to stress by the yeast Hog1 SAPK.
- **Cell cycle control by Hog1 MAPK in yeast.**
  Characterization of the role of Hog1 in the regulation of cell cycle progression in response to stress.
- **Molecular basis to stress-adaptation by p38 MAPK in mammalian cells.**
  Unraveling whether the functions of the yeast Hog1 are also carried out by MAP kinases of the SAPK family, such as p38 and JNK, in mammalian cells.
- **Distributed Biological Computation.**
  In collaboration with Dr. Ricard Solé group (UPF) we aim at comprehensive understanding and implementation of biological computation.

Selected publications 2014

- **Nadal-Ribelles M&, Solé C&, Xu Z, Steinmetz LM, de Nadal E*, Posas F* (2014)** Control of Cdc28 CDK1 by a stress-induced lncRNA. *Mol Cell 53(4):549-61.*
- **Pauls E, Ruiz A, Badia R, Permanyer M, Gubern A, Riveira-Muñoz E, Torres-Torronteras J, Alvarez M, Mothe B, Brander C, Crespo M, Menéndez-Arias L, Clotet B, Keppler OT, Martí R, Posas F, Ballana E, Esté JA (2014)** Cell Cycle Control and HIV-1 Susceptibility Are Linked by CDK6-Dependent CDK2 Phosphorylation of SAMHD1 in Myeloid and Lymphoid Cells. *J Immunol 193(4):1988-97.*
- **Solé C&, Nadal-Ribelles M&, de Nadal E*, Posas F* (2014)** A novel role for lncRNAs in cell cycle control during stress adaptation. *Curr Genet PMID:25262381.*

*& Authors contributed equally to the work; * Corresponding Author*

Other relevant publications from last 10 years

- **de Nadal E, Zapater M, Alepuz PM, Sumoy L, Mas G, Posas F* (2004)** The MAPK Hog1 recruits Rpd3 histone deacetylase to activate osmoresponsive genes. *Nature 427(6972):370-4.*
- **Regot S&, Macia J&, Conde N, Furukawa K, Kjellén J, Peeters T, Hohmann S, de Nadal E, Posas F*, Solé RV* (2011)** Distributed Biological Computation with Multicellular Engineered Networks. *Nature 469:207-11.*
- **Duch A, Felipe-Abrio I, Barroso S, Yaakov G, García-Rubio M, Aguilera A, Nadal E, Posas F* (2013)** Coordinated control of replication and transcription by a SAPK protects genomic integrity. *Nature 493(7430):116-9.*

*& Authors contributed equally to the work; * Corresponding Author*

Postdocs: *Alba Duch, Albert Gubern, Romilde Manzoni, Mariona Nadal, Arnau Ulsamer, Gerhard Seisenbacher, Matteo Viganò, Andrea Silva, Silvia Velázquez, Ramon Amat, Jorge Pérez and Silvia Tognetti.*

PhD students: *Caterina Carbonell, Arturo Urrios, Berta Canal and Pedro Maseres.*

Technicians: *Santiago Cavero, Laia Subirana and Aída Fernández.*

Project Manager: *Montse Morillas.*

Ageing Brain Research Group

Francisco J. Muñoz

www.upf.edu/fisio

Research Outline

Free radicals production generated by fibrillar aggregates of Aß leads to neuronal death in Alzheimer's Disease (AD). Aß activates NO production which reacts to form peroxynitrite that nitrotyrosine proteins, mainly the triose phosphate isomerase (TPI) producing the toxic methylglyoxal (MG). We have demonstrated that MG is the major intracellular effector of neuronal apoptosis in AD through the activation of caspase-3 and bax, and the decrease of bcl-2 and mitochondrial potential. We have also found that albumin, an extracellular protein, is also significantly nitrotyrosinated in brain, cerebrospinal fluid and plasma of AD patients contributing to the progression of the disease.

Current Projects / Research lines

- **The effect of the ß-galactosidase decrease and the consequent increase in the ganglioside GM1 in neurons on the production and aggregation of the amyloid ß-peptide: APP could be localized in GM1 clusters preventing its processing by α-secretase.**
  Moreover GM1 clusters could be promoting BACE1 amiloydogenic activity. An increase of the concentration of Aβ in neuron extracellular matrix will favour Aβ oligomerization by the interaction with GM1 especially in the asialyzated state.
- **The role of nitro-oxidative stress in the formation of Aß oligomers and fibers and their toxicity in skeletal muscle in Inclusion Body Miopathy type 2: The Aß binding to GM1 is regulated by sialic acid.**
  Interestingly GNE (Bifunctional UDP-N-acetylglucosamine 2-epimerase / N-acetylmannosamine kinase) myopathy (GNE-m) is a degenerative disease that affects to skeletal muscle due to unusual intracellular aggregation of Aß. The mutation in GNE impairs protein syalization in cells.

Selected publications 2014

- **Tajes M, Eraso-Pichot A, Rubio-Moscardó F, Guivernau B, Ramos-Fernández E, Bosch-Morató M, Guix FX, Clarimón J, Miscione GP, Boada M, Gil-Gómez G, Suzuki T, Molina H, Villà-Freixa J, Vicente R, Muñoz FJ (2014)** Methylglyoxal produced by amyloid-β peptide-induced nitrotyrosination of triosephosphate isomerase triggers neuronal death in Alzheimer's disease. *J Alzheimers Dis 41(1):273-88.*
- **Ramos-Fernández E, Tajes M, Palomer E, Ill-Raga G, Bosch-Morató M, Guivernau B, Román-Dégano I, Eraso-Pichot A, Alcolea D, Fortea J, Nuñez L, Paez A, Alameda F, Fernández-Busquets X, Lleó A, Elosúa R, Boada M, Valverde MA, Muñoz FJ (2014)** Posttranslational nitro-glycative modifications of albumin in Alzheimer's disease: implications in cytotoxicity and amyloid-β peptide aggregation. *J Alzheimers Dis 40(3):643-57.*
- **Muñoz FJ, Godoy JA, Cerpa W, Poblete IM, Huidobro-Toro JP, Inestrosa NC (2014)** Wnt-5a increases NO and modulates NMDA receptor in rat hippocampal neurons. *Biochem Biophys Res Commun 444(2):189-94.*
- **Tajes M, Eraso-Pichot A, Rubio-Moscardó F, Guivernau B, Bosch-Morató M, Valls-Comamala V, Muñoz FJ (2014)** Methylglyoxal reduces mitochondrial potential and activates Bax and caspase-3 in neurons: Implications for Alzheimer's disease. *Neurosci Lett 580:78-82.*
- **Bellot A, Guivernau B, Tajes M, Bosch-Morató M, Valls-Comamala V, Muñoz FJ (2014)** The structure and function of actin cytoskeleton in mature glutamatergic dendritic spines. *Brain Res1573:1-16.*

Other relevant publications from last 10 years

- **Guix FX, Ill-Raga G, Bravo R, Nakaya T, de Fabritiis G, Coma M, Miscione GP, Villà-Freixa J, Suzuki T, Fernàndez-Busquets X, Valverde MA, de Strooper B, Muñoz FJ (2009)** Amyloid-dependent triosephosphate isomerase nitrotyrosination induces glycation and tau fibrillation. *Brain 132(Pt 5):1335-45.*
- **Coma M, Guix FX, Ill-Raga G, Uribesalgo I, Alameda F, Valverde MA, Muñoz FJ (2008)** Oxidative stress triggers the amyloidogenic pathway in human vascular smooth muscle cells. *Neurobiol Aging 29(7):969-80.*
- **Coma M, Guix FX, Uribesalgo I, Espuña G, Solé M, Andreu D, Muñoz FJ (2005)** Lack of oestrogen protection in amyloid-mediated endothelial damage due to protein nitrotyrosination. *Brain 128(Pt 7):1613-21.*

Postdocs: *Marta Tajes.*

PhD students: *Mònica Bosch-Morató, Biuse Guivernau and Victòria Valls-Comamala.*

Molecular Physiology and Channelopathies

Miguel Ángel Valverde
and José Manuel Fernández-Fernández

www.upf.edu/fisio

Research Outline

The research interest of our laboratory is focused on the study of ion channels and regulatory proteins involved in the generation of intracellular calcium signals, with special interest in those participating in mechano-osmotic responses, the control of vascular tone, airways physiology and neurotransmission.

Current Projects / Research lines

- **Molecular determinants of TRPV4 channel activity and regulation.**
  We analyze the molecular mechanisms relevant to channel gating by osmotic stimuli, particularly the role of the N-terminus tail.
- **TRP channels and calcium signaling in health and disease.**
  The main goal of the project is to tackle aspects that are still poorly defined regarding the structural domains relevant to the generation of TRP-mediated Ca2+ signals, the mechano-osmotransduction in both epithelia and joints and the identification of genetic defects in TRP channels ("channelopathies") and other Ca2+ transport mechanisms that may occur in the context of ciliated epithelia and joint pathology.
- **Identification of new molecular determinants controlling the function of voltage-gated Ca2+ and K+ channels in physiology and pathology.**
  From the analysis of missense mutations in the CaV2.1 (P/Q) channel associated to familial hemiplegic migraine or episodic ataxia type 2, we aim to identify the role of different domains both in the gating of voltage-operated Ca2+ (CaV) channels and in their functional interaction with presynaptic exocytotic (SNARE) proteins. Also we search for new modulators of K+ channels controlling the arterial tone.

Selected publications 2014

- **Fernández-Mariño AI, Valverde MA, Fernández-Fernández JM (2014)** BK channel activation by tungstate requires the β1-subunit extracellular loop residues essential to modulate voltage sensor function and channel gating. *Pflugers Arch 466(7):1365-75.*
- **Engelken J, Carnero-Montoro E, Pybus M, Andrews GK, Lalueza-Fox C, Comas D, Sekler I, de la Rasilla M, Rosas A, Stoneking M, Valverde MA, Vicente R, Bosch E. (2014)** Extreme Population Differences in the Human Zinc Transporter ZIP4 (SLC39A4) Are Explained by Positive Selection in Sub-Saharan Africa. *PLoS Genet 10(2):e1004128.*
- **Grau C, Arató, K, Fernández-Fernández JM, Valderrama A, Sindreu C, Fillat C, Ferrer I, de la Luna S, Altafaj X (2014)** DYRK1A-mediated phosphorylation of GluN2A at Ser1048 regulates the surface expression and channel activity of GluN1/GluN2A receptors. *Front Cell Neurosci 331 doi: 10.3389/fncel.2014.00331.*
- **Vila-Pueyo M, Gené GG, Flotats-Bastardes M, Elorza X, Sintas C, Valverde MA, Cormand B, Fernández-Fernández JM, Macaya A (2014)** A loss-of-function CACNA1A mutation causing benign paroxysmal torticollis of infancy. *Eur J Paediatr Neurol 18(3):430-433.*
- **Ramos-Fernández E, Tajes M, Palomer E, Ill-Raga G, Bosch-Morató M, Guivernau B, Román-Dégano I, Eraso A, Alcolea D, Fortea J, Nuñez L, Paez A, Alameda F, Fernàndez-Busquets X, Lleó A, Elosúa R, Boada M, Valverde MA, Muñoz FJ (2014)** Posttranslational Nitro-Glycative Modifications of Albumin in Alzheimer's Disease: Implications in Cytotoxicity and Amyloid ß-Peptide Aggregation. *J Alzh Dis 40(3):643-57.*

Other relevant publications from last 10 years

- **Fernández-Fernández JM, Tomás M, Vázquez E, Orio P, Latorre R, Sentí M, Marrugat J, Valverde MA (2004)** Gain-of-function mutation in the calcium-activated potassium channel β1 subunit associated with low prevalence of diastolic hypertension. *J Clin Invest 113:1032-9.*
- **Fernandes J, Lorenzo IM, Andrade YN, Garcia-Elias A, Serra SA, Fernández-Fernández JM, Valverde MA (2008)** IP3 sensitizes TRPV4 channel to the mechado- and osmotransducing Messenger 5'-6'-epoxyeicosatrienoic acid. *J Cell Biol 181(1):143-55.*
- **Serra SA, Cuenca-León E, Llobet A, Rubio-Moscardo F, Plata C, Carreño O, Fernàndez-Castillo N, Corominas R, Valverde MA, Macaya A, Cormand B, Fernández-Fernández JM (2010)** A mutation in the first intracellular loop of CACNA1A preventes P/Q channel modulation by SNARE proteins and lowers exocytosis. *PNAS 107(4):1672-7.*

Other PI: *Rubén Vicente.*

Postdocs: *Carole Jung, Francisca Rubio, Anna Garcia-Elias and Maria Isabel Bahamonde.*

PhD students: *Amado Carreras-Sureda, Sanela Mrkonjic, Gerard Cantero-Recasens, Kerstin Kiefer, Carlos Pardo and Roberto Garcia.*

Technicians: *Cristina Plata.*

Molecular Virology

Juana Díez

www.upf.edu/virologyunit

Research Outline

Viruses are obligatory intracellular parasites. Because of their limited coding capacity, they completely depend on the cellular machinery for expansion. Studies on the interaction of viruses with their host cells are thus essential to understand how viruses multiply and to design novel strategies for therapeutic interventions. In addition, such studies might uncover novel mechanisms used not only by viruses but also by the host to regulate gene expression.

Current Projects / Research lines

- **Definition of viral and cellular translation landscapes.**
  Translation control plays a major role in positive-strand RNA virus infections. This viral group includes major human pathogens such as hepatitis C virus and emerging viruses. The specialized networks of translationally-controlled mRNAs are predicted to direct initiation and progression of infection. However, an in depth analyses of these networks is lacking. We are using system approaches to address this key issue in infection biology.
- **Development of broad-spectrum antivirals.**
  Our laboratory has previously demonstrated that multiple RNA viruses utilize common host cell factors for their multiplication. By targeting such host factors it would be possible to develop drugs that target multiple viruses. This is of great interest to simplify co-infection treatments and to control novel pathogens by reducing further transmission. Moreover, such antivirals are predicted to show a high barrier to resistance due to the genetic stability of the host genome.

Selected publications 2014

- **Pérez-Vilaró G, Fernández-Carrillo C, Mensa L, Miquel R, Sanjuan X, Forns X, Pérez-Del-Pulgar S, Díez J (2014)** Hepatitis C virus infection inhibits P-body granule formation in human livers. *J Hepatol 62(4):785-90*.
- **Fleta-Soriano E, Matinez JP, Hinkleman B, Gerth K, Washausen P, Díez J, Frank R, Sasse F, Meyerhans A (2014)** The myxobacterial metabolite ratjadone A inhibits HIV infection by blocking the Rev/CRM1-mediated nuclear export pathway. *Microb Cell Fact 13:17*.
- **Latorre I, Saludes V, Díez J, Meyerhans A (2014)** Nucleic Acids as Molecular Diagnostics (Chapter: Techniques of nucleic acid-based diagnosis in the management of bacterial and viral infectious diseases). *Editorial: E. M. A. Keller, Wiley-VCH Verlag GmbH & Co*.
- **Saludes V, Latorre I, Meyerhans A, Díez J (2014)** Nucleic Acids as Molecular Diagnostics (Chapter: MicroRNAs in human microbial infections and disease outcomes). *Editorial: E. M. A. Keller, Wiley-VCH Verlag GmbH & Co*.

Other relevant publications from last 10 years

- **Scheller N, Mina LB, Galão RP, Chari A, Giménez-Barcons M, Noueiry A, Fischer U, Meyerhans A, Díez J (2009)** Translation and replication of hepatitis C virus genomic RNA depends on ancient cellular proteins that control mRNA fates. *PNAS;106(32):13517-22*.
- **Galao RP, Chari A, Alves-Rodriguez I, Mas A, Kambach C, Fischer U, Diez J (2010)** LSm1-7 complex binds to specific sites in viral RNA genomes and regulate their translation and replication. *RNA 16(4):817-22*.
- **Pérez-Vilaró G, Scheller N, Saludes V, Díez J (2012)** Hepatitis C virus infection alters P-body composition but is independent of P-body granules. *J Virol 86(16):8740- 9*.

Postdocs: *Georgios Koutsoudakis*.

PhD students: *Jennifer Jungfleisch, Bernat Blasco Moreno and Rowaedh Bawaked*.

Project Manager: *Gemma Pérez Vilaró*.

Infection Biology Group

Andreas Meyerhans

www.upf.edu/virologyunit

Research Outline

The main aims of the Infection Biology Laboratory are (i) to understand the factors that regulate the decision between an acute versus a persistent infection course, (ii) to define the factors that control the dynamic balance of virus expansion and immune control in persistent infections and (iii) to identify small chemical compounds with broad-spectrum antiviral activities

Current Projects / Research lines

- **American Foundation for AIDS Research: "Enhanced premature self-activation of HIV-1 protease to induce apoptosis".**
  The aim of this project is to define in silico novel compounds that induce premature HIV protease dimerization within infected cells and thereby induce cell apoptosis.
- **Ministerio de Economía y Competitividad (SAF2013-46077-R): "Facing persistent viral infections: on fate decisions & therapeutic approaches".**
  The aim of this project is to (1) identify mechanisms that determine infection outcomes, (2) gain detailed insights into infection control mechanisms, and (3) set the basis for the development of new antiviral drugs.
- **European COST Action CM1407: "Challenging organic syntheses inspired by nature - from natural products chemistry to drug discovery"; PI: Prof. Dr. Bruno Botta, Rome, Italy; (http://www.cost.eu/COST_Actions/cmst/Actions/CM1407).**
  The aim of this COST Action is to combine synthetic chemistry, computational chemistry, chemical biology, and pharmacology to find new lead structures of pharmaceutical relevance.

Selected publications 2014

- **Banks HT, Kapraun DF, Link KG, Thompson WC, Peligero C, Argilaguet J, Meyerhans A (2014)** Analysis of variability in estimates of cell proliferation parameters for cyton-based models using CFSE-based flow cytometry data. *J Inverse III-Posed Probl. DOI: 10.1515/jiip-2013-0065.*
- **Fleta-Soriano E, Martinez JP, Hinkelmann B, Gerth K, Washausen P, Diez J, Frank R, Sasse F, Meyerhans A (2014)** The myxobacterial metabolite ratjadone A inhibits HIV infection by blocking the Rev/CRM1-mediated nuclear export pathway. *Microb Cell Fact 13:17.*
- **Latorre I, Saludes V, Díez J, Meyerhans A (2014)** Techniques of nucleic acid-based diagnosis in the management of bacterial and viral infectious diseases. *Pages 201 - 216 in Nucleic Acids as Molecular Diagnostics, Editors, E. Meese & A. Keller, Wiley-VCH Verlag GmbH & Co.*
- **Saludes V, Latorre I, Meyerhans A, Díez J (2014)** MicroRNAs in human microbial infections and disease outcomes. *Pages 217 - 240 in Nucleic Acids as Molecular Diagnostics, Editors, E. Meese & A. Keller, Wiley-VCH Verlag GmbH & Co.*

Other relevant publications from last 10 years

- **Martinez JP, Sasse F, Brönstrup M, Diez J, Meyerhans A (2015)** Antiviral drug discovery: broad-spectrum drugs from nature. *Nat Prod Rep 32:29-48.*
- **Martinez JP, Hinkelmann B, Fleta-Soriano E, Steinmetz H, Jansen R, Diez J, Frank R, Sasse F, Meyerhans A (2013)** Identification of Myxobacteria-derived HIV inhibitors by a high-throughput two-step infectivity assay. *Microb Cell Fact 12:85.*
- ***Reiter J, *Pérez-Vilaró G, *Scheller N, Mina LB, Díez J, Meyerhans A (2011)** Hepatitis C virus RNA recombination in cell culture. *J Hepatol 55:777-83.*

Postdocs / Researchers: *Jordi Argilaguet, Javier Pablo Martínez, Kashif Sadiq, Irene Latorre and Yasuko Yokota (visiting Professor from Tokyo University).*

PhD students: *Cristina Peligero and Eric Fleta.*

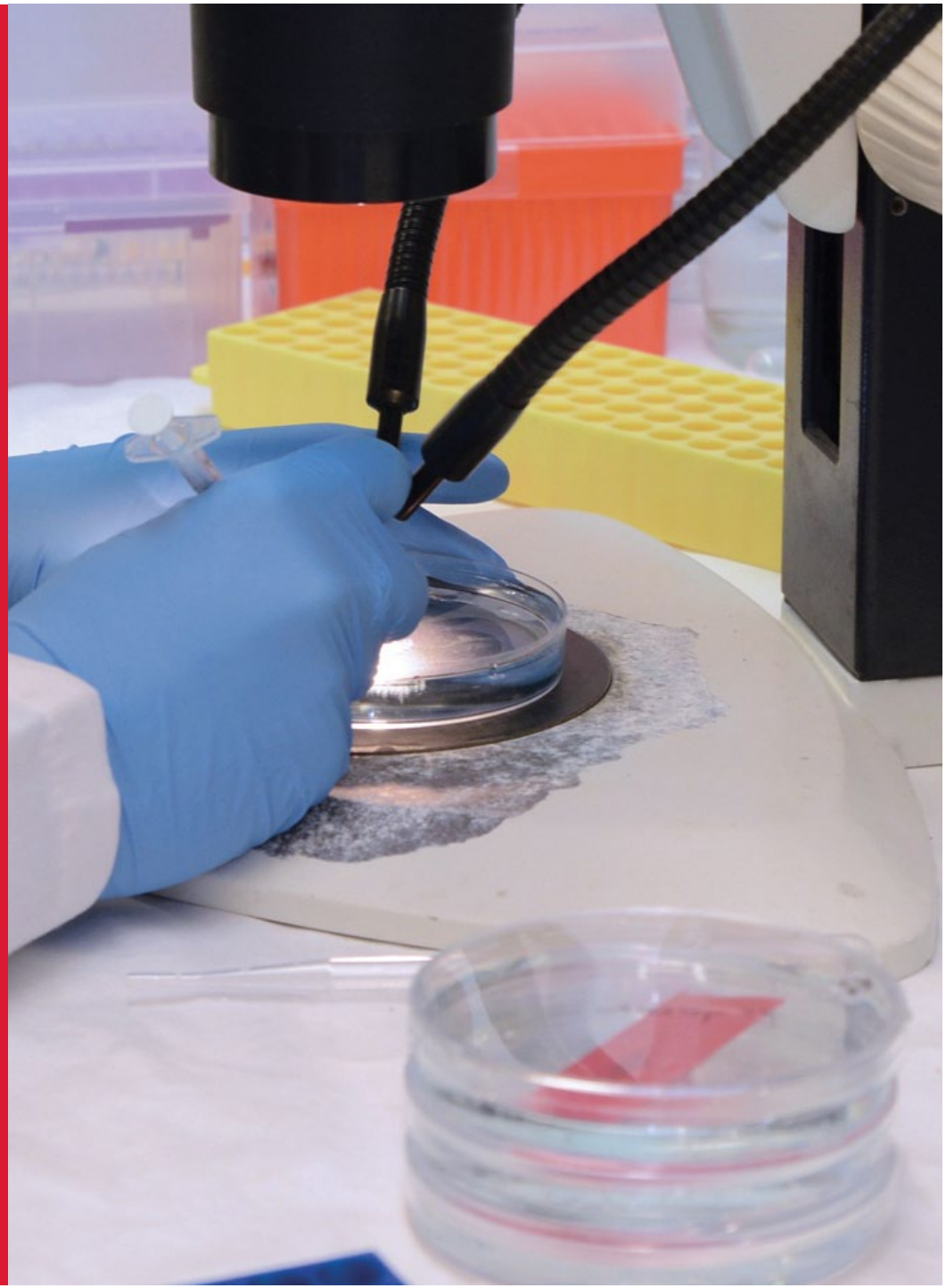
Molecular Medicine Programme

Coordinator: José Ayté

The Molecular Medicine Programme integrates several research groups with diverse, but overlapping scientific interests aiming to decipher the molecular mechanisms that underlie physiological processes and the diseases associated with them. Normal and pathological processes are studied from different disciplines (molecular biology, immunology, biochemistry, proteomics, and neurobiology) using unicellular and pluricellular model organisms. This enriched and diverse scientific environment together with a superb spectrum of state-of-the-art methodologies makes the Molecular Medicine Programme an exceptional training ground, for undergraduate students, graduate students and postdoctoral fellows, who in turn also contribute to the high vitality of the Programme.

During 2014, all the PIs have been able to renew all the national grants and several PIs participate in EU funded projects. We also welcomed a new ICREA Academia member.

- **Oxidative Stress and Cell Cycle Group**
  Elena Hidalgo and José Ayté
- **Immunopathology**
  Miguel López-Botet
- **NFAT proteins and immune response**
  Cristina López-Rodríguez and José Aramburu
- **Proteomics and Protein Chemistry**
  David Andreu
- **Neurobiology of Behavior Research Group (GReNeC)**
  Olga Valverde



Oxidative Stress and Cell Cycle Group

Elena Hidalgo and José Ayté

www.upf.edu/osccg/articles

Research Outline

Using the fission yeast as a model system, our group is interested in studying the components and molecular mechanisms which regulate the responses to oxidative stress and the mitotic and meiotic cell cycle, using cutting edge approaches in molecular biology, proteomics/mass spectrometry and live cell imaging, as well as traditional genetics.

Current Projects / Research lines

- **Reactivity of H2O2 with proteins – toxicity and signaling**
  - **a.** We are studying the **Sty1 MAP kinase -Atf1 transcription factor** cascade, and performing screens to identify all genes affecting the stress response.
  - **b.** We want to know what makes **Pap1** a transcription factor so sensitive to H2O2.
  - **c.** We are analyzing the homeostasis of **protein carbonyls and protein aggregation**, to decipher the bases of the aging process and of **neurodegenerative** diseases.
- **How cell cycle regulates gene expression and how alterations of gene expression can also modulate cell cycle progression?**
  - **d.** We are analyzing how **MBF** (the functional homolog of mammalian RB/E2F) is **regulated in an unperturbed cell cycle**, and isolating and characterizing **new components of the MBF complex**.
  - **e.** Several fission yeast genes have a specific splicing programme during meiosis. We are dissecting the splicing regulation during meiosis, characterizing the role of several spliceosome components.

Selected publications 2014

- **García P, Paulo E, Gao J, Wahls W, Ayté J, Lowy E, Hidalgo E (2014)** Binding of the transcription factor Atf1 to promoters serves as a barrier to phase nucleosome arrays and avoid cryptic transcription. *Nucleic Acids Res 42:10351-9.*
- **García-Santamarina S, Boronat S, Hidalgo E (2014)** Reversible cysteine oxidation in hydrogen peroxide sensing and signal transduction. *Biochemistry 53:2560-80.*
- **Paulo E, García-Santamarina S, Calvo IA, Carmona M, Boronat S, Domènech A, Ayté J, Hidalgo E (2014)** A genetic approach to study H2O2 scavenging in fission yeast - distinct roles of peroxiredoxin and catalase. *Mol Microbiol 92:246-57.*
- **García-Santamarina S, Boronat S, Domènech A, Ayté J, Molina H, Hidalgo E (2014)** Monitoring in vivo reversible cysteine oxidation in proteins using ICAT and mass spectrometry. *Nat Protoc 9:1131-45.*
- **Boronat S, Domènech A, Paulo E, Calvo IA, García-Santamarina S, García P, Encinar del Dedo J, Barcons A, Serrano E, Carmona M, Hidalgo E (2014)** Thiol-based H2O2 signalling in microbial systems. *Redox Biol 2:395-9.*

Other relevant publications from last 10 years

- **Calvo IA, Boronat S, Domènech A, García-Santamarina S, Ayté J, Hidalgo E (2013)** Dissection of a redox relay: H2O2-dependent activation of the transcription factor Pap1 through the peroxidatic Tpx1-thioredoxin cycle. *Cell Reports 5:1413-24.*
- **Zuin A, Carmona M, Morales-Ivorra I, Gabrielli N, Vivancos AP, Ayté J, Hidalgo E (2010)** Life-span extension by calorie restriction relies on the Sty1 MAP kinase stress pathway. *EMBO J 29:981-91.*
- **Moldón A, Malapeira J, Gabrielli N, Gogol M, Gómez-Escoda B, Ivanova T, Seidel C, Ayté J (2008)** Promoter-driven splicing regulation in fission yeast. *Nature 455:997-1000.*

Postdocs: *Susanna Boronat, Isabel Alves, Patricia García, Javier Encinar and Stefan Hummer.*

PhD students: *Esther Paulo, Iva Knezevic, Alba Domenech and Alberto González.*

Technicians: *Mercè Carmona.*

Immunopathology

Miguel López-Botet

www.upf.edu/immuno

Research Outline

Our research has focused for over 20 years on human Natural Killer (NK) cell inhibitory and activating receptors (NKR) which control their response against viral infections and tumors. The characterization of CD94/NKG2 and ILT2 (LILRB1) receptors which interact with HLA class I molecules represent our most relevant past contributions. We currently study the role of NKR in the response to human cytomegalovirus (HCMV). This herpes virus which establishes a prevalent and life-long persistent infection may cause severe congenital disorders and represents a common complication in immuno-compromised patients, potentially contributing to the pathogenesis of chronic inflammatory disorders.

Current Projects / Research lines

- **NK cell-mediated response to HCMV infection in health and disease.**
  We originally reported that HCMV promotes in healthy individuals and under pathological conditions a variable and persistent reconfiguration of the human NK cell compartment, whose hallmark is the expansion of an NK subset expressing the CD94/NKG2C activating receptor specific for HLA-E. In this context, we currently explore the: a) nature of the underlying molecular and cellular mechanisms; b) role in the antiviral defense; c) regulation by Killer Immunoglobulin-like Receptors (KIR); d) implications in different clinical settings (e.g. organ and hematopoietic transplantation, Multiple Sclerosis…); d) putative impact in the response to other pathogens and tumors; e) relation with the adaptive antiviral response. These issues are being addressed at the experimental level in our laboratory, as well as through suitable collaborations with different clinical teams.

Selected publications 2014

- **López-Botet M, Muntasell A, Vilches C.** The CD94/NKG2C+ NK-cell subset on the edge of innate and adaptive immunity to human cytomegalovirus infection. *Semin Immunol. 2014 26:145-51.*
- **Sansoni P, Vescovini R, Fagnoni FF, Akbar A, Arens R, Chiu YL, Cičin-Šain L, Dechanet-Merville J, Derhovanessian E, Ferrando-Martinez S, Franceschi C, Frasca D, Fulöp T, Furman D, Gkrania-Klotsas E, Goodrum F, Grubeck-Loebenstein B, Hurme M, Kern F, Lilleri D, López-Botet M, Maier AB, Marandu T, Marchant A, Matheï C,Moss P, Muntasell A, Remmerswaal EB, Riddell NE, Rothe K, Sauce D, Shin EC, Simanek AM, Smithey MJ, Söderberg-Nauclér C, Solana R, Thomas PG, van Lier R,Pawelec G, Nikolich-Zugich J.** New advances in CMV and immunosenescence. *Exp Gerontol. 2014 55:54-62.*
- **Noyola DE, Alarcón A, Noguera-Julian A, Muntasell A, Muñoz-Almagro C, García J, Mur A, Fortuny C, López-Botet M.** Dynamics of the NK-cell subset redistribution induced by cytomegalovirus infection in preterm infants. *Hum Immunol. (in press)*

Other relevant publications from last 10 years

- **Gumá M, Angulo A, Vilches C, Gómez-Lozano N, Malats N, López-Botet M (2004)** Imprint of human cytomegalovirus infection on the NK cell receptor repertoire. *Blood 104: 3664.*
- **Gumá M, Budt M, Sáez A, Brckalo T, Hengel H, Angulo A, López-Botet M (2006)** Expansion of CD94/NKG2C+ NK cells in response to human cytomegalovirus-infected fibroblasts. *Blood 107:3624.*
- **Magri G, Muntasell A, Romo N, Sáez-Borderías A, Pende D, Geraghty DE, Hengel H, Angulo A, Moretta A, López-Botet M (2011)** NKp46 and DNAM-1 NK cell receptors drive the response to human cytomegalovirus infected myeloid dendritic cells overcoming viral immune evasion strategies. *Blood 117:848.*

Postdocs: *Aura Muntasell Castellví (IMIM Researcher) and Jordi Pou Sánchez (IMIM).*

PhD students: *María López Montañés, Marcel Costa García and Aldi Pupuleku.*

Technicians: *Gemma Heredia Diaz and Andrea Vera Barrón.*

NFAT proteins and immune response

Cristina López and Jose Aramburu

www.upf.edu/immuno/description/nfat_desc
www.upf.edu/immuno/description/regulation_desc

Research Outline

The immune system plays an essential role in the organism, both in the defense against pathogens and tumors as in regulating the function of multiple tissues. Immune cells continuously sense a wide variety of inputs from other cells and their environment, and use transcription factors and chromatin regulatory mechanisms to integrate this information into specific gene expression patterns that shape their activity and functional specialization. In our group we are broadly interested in understanding gene expression regulatory mechanisms that allow immune cells to respond to stimuli such as pathogens and differentiation cues and to maintain functional competence under stress.

Current Projects / Research lines

- **Regulation of macrophage and T lymphocyte functions by the transcription factor NFAT5.** NFAT5 belongs to the Rel family of transcription factors, which comprises the NF-kappaB and the calcineurin-dependent NFAT proteins. These factors regulate a wide variety of processes in immune cells, as well as in other tissues and organs. We have shown that NFAT5 regulates T cell activation and survival under osmotic stress in vitro and in vivo, and identified osmostress-independent roles of NFAT5 in thymocyte development and anti-pathogen responses mediated by macrophages. We are currently investigating the involvement of NFAT5 in a wider range of immune functions.
- **Stress adaptation mechanisms in T lymphocytes and macrophages.** Accurate immune responses require that leukocytes are able to respond appropriately to specific signals such as cytokines and maintain this capability under a variety of stress conditions. We are investigating diverse mechanisms that allow immune cells to maintain their functionality under stress.

Selected publications 2014

- **Aramburu J, Ortells MC, Tejedor S, Buxadé M, López-Rodríguez C (2014)** Transcriptional regulation of the stress response by mTOR. *Sci Signal Vol 7, re2.*
- **Aramburu J, López-Rodriguez C (2014)** Nuclear Factor of Activated T cells (NFAT). *Encyclopedia of Medical Immunology. 1 - 2, pp. 824 - 833. Springer Science + Business Media. LLC23, Spring Street, New York, NY 10013-1578. Mackay I, Rose NR, Diamond B, Davidson A (Eds.). Book chapter.*

Other relevant publications from last 10 years

- **Berga-Bolaños R, Alberdi M, Buxadé M, Aramburu J, López-Rodríguez C (2013)** NFAT5 induction by the pre-T-cell receptor serves as a selective survival signal in T-lymphocyte development. *PNAS 110:16091-6.*
- **Ortells MC, Morancho B, Drews-Elger K, Viollet B, Laderoute KR, López-Rodríguez C, Aramburu J (2012)** Transcriptional regulation of gene expression during osmotic stress responses by the mammalian target of rapamycin (mTOR). *Nucleic Acids Res 40:4368-84*
- **Buxadé M, Lunazzi G, Minguillón J, Iborra S, del Val M, Aramburu J, López-Rodríguez C (2012)** Gene expression induced by Toll-like receptors in macrophages requires the transcription factor NFAT5. *J Exp Med 209:379-93.*

Postdocs: *Maria Buxadé.*

PhD students: *Maria Alberdi, Mónica Tellechea, Sonia Tejedor, Hector Huerga, Sara Santana and Arnau García.*

Technicians: *Valeria Sirenko.*

Proteomics and Protein Chemistry

David Andreu

www.upf.edu/uprot

Research Outline

We use both synthetic and analytical tools to understand or reproduce the role of proteins in various biological processes. For instance, we make extensive use of synthetic peptides as vaccines against animal viral diseases such as classical swine fever or foot-and-mouth disease. We also design and develop peptides as antimicrobial agents and as shuttles for intracellular delivery of otherwise poorly absorbed drugs. In proteomics, we have used mass spectrometry to identify proteins involved in oocyte fertilization and we are developing smart hydrogel nanoparticles to enrich low-abundance proteins in blood samples prior to analysis.

Current Projects / Research lines

- **Peptide-based vaccines against foot-and-mouth disease virus (FMDV) and classical swine fever virus (CSFV).**
  We have developed novel scaffolds for displaying clinically relevant B- and T-cell epitopes of FMDV, which causes the economically most devastating animal disease worldwide. Our candidate induces 100% protection in both swine and cattle, is versatile –readily adaptable to new outbreaks– and can be efficiently and rapidly produced. We look forward to extensive field trials and commercial application in Asia. A similar approach is applied for CSFV.
- **Antimicrobial peptides (AMPs).**
  Work focuses on (i) bioinformatic tools for predicting AMP regions in proteins; (ii) evolutionary pathways for the transition from aggregating to membrane-active AMPs; (iii) discovery of new AMP and antitumor motifs from snake venoms; (iv) refining AMP pharmacophores to develop better-than-native versions.
- **Cell-penetrating peptides.**
  We use CPPs to deliver poorly absorbed drugs into parasites and/or macrophages, thus defeating drug resistance and making new inroads for trypanosome chemotherapy. We also investigate uptake mechanisms of a new CPP class recently developed in our laboratory.

Selected publications 2014

- **Defaus S, Gupta P, Andreu D, Gutiérrez-Gallego R (2014)** Protein glycosylation – structure versus function. *Analyst 139:2944-67*.
- **De la Torre BG, Hornillos V, Luque-Ortega JR, Abengózar MA, Amat-Guerri F, Acuña AU, Rivas L, Andreu D (2014)** A BODIPY-embedding miltefosine analog linked to cell-penetrating Tat(48-60) peptide favors intracellular delivery and visualization of the antiparasitic drug. *Amino Acids 46:1047-58*.
- **José A, Rovira-Rigau M, Luna J, Giménez-Alejandre M, Vaquero E, Andreu D, Alemany R, Fillat C (2014)** A genetic fiber modification to achieve matrix-metalloprotease-activated infectivity of oncolytic adenovirus. *J Control Release 192C:148-56*.
- **Falcao CB, de la Torre BG, Pérez-Peinado C, Barron AE, Andreu D, Rádis-Baptista G (2014)** Vipericidins, novel cathelicidin-related peptides from the venom gland of South American pit vipers. *Amino Acids 46:2561-71*.
- **Freire J, Veiga AS, Rego de Figueiredo I, de la Torre BG, Santos NC, Andreu D, da Poian A, Castanho M (2014)** Nucleic acid delivery by cell penetrating peptides derived from dengue virus capsid protein. Design and mechanism of action. *FEBS J 281:191-215*.

Other relevant publications from last 10 years

- **Torrent M, Valle J, Nogués MV, Boix E, Andreu D (2011)** The generation of antimicrobial peptide activity: a trade-off between charge and aggregation? Angew. *Chemie 50:10686-9*.
- **Fernández-Reyes M, Rodríguez-Falcón M, Chiva C, Pachón J, Rivas L, Andreu D (2009)** The cost of resistance to colistin in Acinetobacter baumannii: a proteomic perspective. *Proteomics 9:1632-45*.
- **Cubillos C, de la Torre BG, Jakab A, Clementi G, Borràs E, Bárcena J, Andreu D, Sobrino F, Blanco E (2008)** Enhanced mucosal IgA response and solid protection against foot-and-mouth disease virus challenge induced by a novel dendrimeric peptide. *J Virol 82:7223-30*.

Senior researcher: *Beatriz G. de la Torre.*
Senior associate: *Ricardo Gutiérrez-Gallego.*
Postdocs: *Sira Defaus and Gerard Such.*
PhD students: *Sira Defaus and Clara Pérez-Peinado.*
Visiting PhD students: *Laura Höh, Carol Sidrim and Maria Gallo.*
Technicians: *Javier Valle, Yolanda Tor and Mariona López.*

Neurobiology of Behavior Research Group (GReNeC)

Olga Valverde

www.upf.edu/grenec

Research Outline

The research of our team is devoted to identify the neurobiological basis underlying several psychiatric disorders, in particular drug addiction, affective disorders, cognitive impairments, chronic pain and neurotoxicity. We employ behavioral models using mice combined with neurochemical, immunohistochemical and molecular tools. We are interested in the influence of specific targets related to the above mentioned pathologies like the adenosine A2a receptors, the endocannabinoid system and the orphan G protein coupled receptor GPR3. More recently, we are using new approaches including proteomics techniques and biocomputational analysis in collaboration with other research teams for better understanding our neurobehavioral outputs. Our integrative strategy helps us to identify appropriate biomarkers and to propose new preventives strategies and therapeutical applications for mental health.

Current Projects / Research lines

- **The neurobiological substrate involved in drug addiction.**
  We have contributed to characterize the role of endocannabinoids in the processes associated to drug addiction. The CB1 cannabinoid receptors allow the transition from the acute rewarding effect to the development of a compulsive disorder that characterize the addictive phenomenon
- **The neurobiology of depressive disorders.**
  Our studies also revealed that endocannabinoids modulate monoaminergic system through CB1 receptors. Therefore, endocannabinoid system is crucial for the maintenance of mood, allowing us to propose that CB1 KO mice could be considered as an animal model of depression.
- **Co-morbidity between drug addiction and depression.**
  We have participated in the characterization of different models of psychiatric co-morbidity (drug addiction and depression) using different approximations. Therefore we investigated early-life adverse events, like maternal deprivation and early-drug consumption in the later development of mood and anxiety disorders. We further assess whether mod disorders could affect drugs self-administration behaviour. Our findings demonstrated that depressive states can impair the motivation for psychostimulants and alcohol consumption in adolescent using animal models.

Selected publications 2014

- **Martini M, Pinto AX, Valverde O (2014)** Estrous cycle and sex affect cocaine-induced behavioural changes in CD1 mice. *Psychopharmacology 231:2647-59*.
- **Segura-Puimedon M, Sahún I, Velot E, Dubus P, Borralleras C, Rodrigues AJ, Valero MC, Valverde O, Sousa N, Herault Y, Dierssen M, Pérez-Jurado LA, Campuzano V (2014)** Heterozygous deletion of the Williams-Beuren syndrome critical interval in mice recapitulates most features of the human disorder. *Hum Mol Genet 23(24):6481-94*.
- **García AM, Brea J, Morales-García JA, Perez DI, González A, Alonso-Gil S, Gracia-Rubio I, Ros-Simó C, Conde S, Cadavid MI, Loza MI, Perez-Castillo A, Valverde O, Martinez A, Gil C (2014)** Modulation of cAMP-specific PDE without emetogenic activity: new sulfide-like PDE7 inhibitors. *J Med Chem 57(20):8590-607, 2014*.
- **Batalla A, Crippa JA, Busatto GF, Guimaraes FS, Zuardi AW, Valverde O, Atakan Z, McGuire PK, Bhattacharyya S, Martín-Santos R (2014)** Neuroimaging studies of acute effects of THC and CBD in humans and animals: a systematic review. *Curr Pharm Des 20(13):2168-85*.

Other relevant publications from last 10 years

- **Tourino C, Valjent E, Ruiz-Medina J, Herve D, Ledent C, Valverde O (2012)** The orphan receptor GPR3 modulates the early phases of cocaine reinforcement. *Br J Pharmacol 167(4):892-904*.
- **Touriño C, Ledent C, Maldonado R, Valverde O (2008)** CB1 cannabinoid receptor modulates 3,4-methylenedioxymethamphetamine acute responses and reinforcement. *Biol Psychiatry 63(11):1030-8*.
- **Laurent P, Becker JA, Valverde O, Ledent C, de Kerchove d'Exaerde A, Schiffmann SN, Maldonado R, Vassart G, Parmentier M (2005)** The prolactin-releasing peptide antagonizes the opioid system through its receptor GPR10. *Nat Neurosci 8: 1735-41*.

Postdocs: *Marta Portero Treserra*.

PhD students: *Irene Gracia Rubio, Lidia Cantacorps and María Moscoso Castro*.

Technicians: *Neus Toro Ortz*.

Visiting students: *Miguel Angel Lujan and Laia Castells*.

Evolutionary Biology and Complex Systems Programme

Coordinator: David Comas

The Evolutionary Biology and Complex Systems Programme is composed by inter-disciplinary groups whose main research interest focuses on the analysis of processes and mechanisms generating diversity in biological and artificial entities including their organization and interactions. The entities under study cover a wide range of natural and artificial elements from single molecules, cells, genomes and organisms to whole ecosystems.

The research challenges on this programme require both theoretical and experimental approaches with a remarkable computational input. Several disciplines are also required to achieve our scientific goals, such as genomics, physics, statistical and computational genetics, network theory, molecular and cell biology, linguistics, among others.

- **Evolutionary systems biology**
  Jaume Bertranpetit
- **Human Genome Diversity Group**
  David Comas
- **Genomics of individuality**
  Francesc Calafell
- **Evolutionary Population Genetics**
  Elena Bosch
- **Evolutionary Genomics**
  Arcadi Navarro
- **Comparative Genomics**
  Tomas Marquès-Bonet
- **Complex Systems Lab**
  Ricard Solé
- **Language Evolution**
  Luc Steels
- **Dynamical Systems Biology**
  Jordi García-Ojalvo
- **Single Cell Behavior**
  Lucas Carey

Evolutionary systems biology

Jaume Bertranpetit

http://biologiaevolutiva.org/jbertranpetit
Publications 2014: http://biologiaevolutiva.org/jbertranpetit/scientific-publications/?y=2014

Research Outline

We are a group of biologists interested in evolution using genomics as a tool. Our goal is to approach our own evolutionary history and to understand the basic mechanisms having been acting in shaping our past. A main interest is to understand adaptation though the detection of positive (adaptive) selection in the genomes. We are applying tools of network theory and systems biology to unravel the genetic bases of complex adaptations.

Current Projects / Research lines

- Our research focuses on the understanding of natural selection and adaptation in humans and in primates through the comparative analysis of genomes. Our purpose is the understanding of complex adaptations by genome wide analyses of the footprints that natural selection has left in the genomes after its action. The different forms of selection (purifying, balancing and positive) are analyzed both among human populations in order to detect population-specific adaptations, and among primates in order to recognize species-specific adaptive selection and to measure the strength of purifying selection. The action of selection is measured and understood integrated in molecular physiological pathways or networks to understand the basis of complex adaptations and how networks have been shaped by natural selection. In humans we try to identify population specific adaptations and in primates the places in the genome with human specificities. We have ongoing work in reconstructing population history through genome diversity in India and in Africa.

Selected publications 2014

- **Colombo M, Laayouni H, Invergo BM, Bertranpetit J, Montanucci L (2014)** Metabolic flux is a determinant of the evolutionary rates of enzyme-encoding genes. *Evolution 68(2):605-13. PMID: 24102646*
- **Pybus M+, Dall'Olio GM+, Luisi P+, Uzkudun M+, Carreño-Torres A, Pavlidis P, Laayouni H, Bertranpetit J *, Engelken J* (2014)** 1000 Genomes Selection Browser 1.0: a genome browser dedicated to signatures of natural selection in modern humans. *Nucleic Acid Res 42(1): D903-9. PMID 24275494.*
- **Laayouni H, Oosting M, Luisi P, Ioana M, Alonso S, Ricaño-Ponce I, Trynka G, Zhernakova A, Plantinga T, Cheng S, van der Meer JMW, BK T, Popp R, Sood A, Wijmenga C, Joosten LAB, Bertranpetit B*, Netea MG (2014)** The common evolutionary history of European and Rroma populations identifies convergent evolution exerted by plague on TLR1/TLR6/TLR10 pattern recognition system. *PNAS 111(7):2668-73. PMID: 24550294*
- **Invergo BM, Montanucci L, Koch KW, Dell'Orco D, Bertranpetit J (2014)** A comprehensive model of light adaptation in mammalian rod cells. *Mol BioSyst 10(6):1481-9. PMID: 24675755*
- **Yamamoto F, Cid E, Yamamoto M, Saitou N, Bertranpetit J, Blancher A (2014)** An integrative evolution theory of histo-blood group ABO and related genes. *Sci Rep doi: 10.1038/srep06601. PMID: 25307962*

Other relevant publications from last 10 years

- **Bosch E, Laayouni H, Morcillo-Suarez 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(1):338.*
- **Montanucci L, Laayouni H, Dall'Olio GM and Bertranpetit J (2011)** Molecular evolution and network-level analysis of the N-Glycosylation metabolic pathway across primates. *Mol Biol Evol 28(1):813-23.*
- **Casals F, Sikora M, Laayouni H, Montanucci L, Muntasell A, Lazarus R, Calafell F, Awadalla P, Netea MG, Bertranpetit J (2011)** Genetic adaptation of the antibacterial human innate immunity network. *BMC Evol Biol 11(1):202.*

Postdocs: *Hafid Laayouni and Ludovica Montanucci.*

PhD students: *Giovanni dall'Olio, Pierre Luisi, Brandon Invergo, Marc Pybus and Mayukh Mondal.*

Human Genome Diversity Group

David Comas

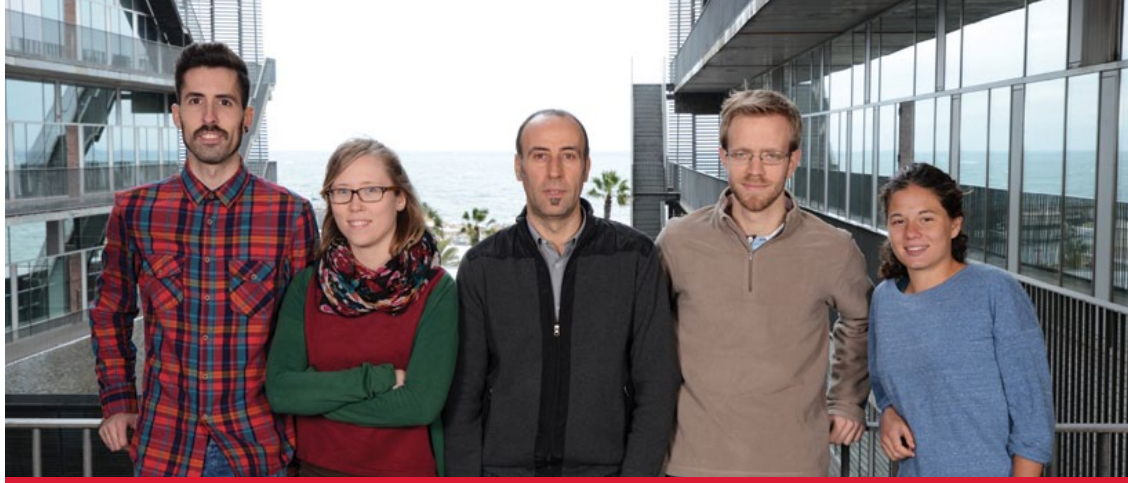
http://biologiaevolutiva.org/dcomas

Research Outline

The research of the group is focused on the human genome diversity analysis in order to infer the (genomic and population) processes responsible for this diversity and try to establish the (population, adaptive, and epidemiological) consequences of the human genetic variability. Thus, the main research lines of the group are focused on aspects of human genome diversity, population genetics, genome variation and disease susceptibility, and genome evolution and disease.

Current Projects / Research lines

- **The population structure of human North African populations.**
  The present research line aims to analyze the genetic diversity of human North African populations in order to establish their population structure and determine the impact of several cultural and historical migrations into the gene pool of the extant North African groups. Several human populations are been analyzed using high resolution **uniparental markers** (mitochondrial DNA and Y-chromosome) in order to define maternally- and paternally-inherited lineages, and **whole genome autosomal markers** (SNPs) and **copy number variants** (CNV).
- **The Roma: the population history of European Gypsies.**
  The aim of the present research line is to unravel, through the analysis of uniparental and whole genome autosomal markers, the **geographic origin** of the Roma, their **migration routes** to Europe, their settlement in Europe, the **admixture** with host populations and the **sexual asymmetry** of the admixture.



Selected publications 2014

- **Engelken J, Carnero-Montoro E, Pybus M, Andrews GK, Lalueza-Fox C, Comas D, Sekler I, de la Rasilla M, Rosas A, Stoneking M, Valverde MA, Vicente R, Bosch E (2014)** Extreme population differences in the human zinc transporter ZIP4(SLC39A4) are explained by positive selection in sub-Saharan Africa. *PLoS Genetics 10(2) e1004128*.
- **Elhaik E, Tatarinova T, Chebotarev D, Piras IS, Calo CM, De Montis A, Atzori M, Marini M, Tofanelli S, Francalacci P, Pagani L, Tyler-Smith C, Xue Y, Cucca F, Schurr TG, Gaieski JB, Melendez C, Vilar MG, Owings AC, Gomez R, Fujita R, Santos FR, Comas D, Balanovsky O, Balanovska E, Zalloua P, Soodyall H, Pitchappan R, ArunKuma GP, Hammer M, Matisoo-Smith L, Wells SR, The Genographic Consortium (2014)** Geographic Population Structure of worldwide human populations infers biogeographical origin. *Nat Commun 5:3513*.
- **Solé-Morata N, Bertranpetit J, Comas D, Calafell F (2014)** Recent radiation of R-M269 and high Y-STR haplotype resemblance confirmed. *Ann Hum Genet 78:253-254*.
- **Ballantyne KN, et al (2014)** Towards male individualization with rapidly mutating Y-chromosomal STRs. *Hum Mutat 35(8):1021-32*.
- **Lazaridis I, et al (2014)** Ancient human genomes suggest three ancestral populations for present-day Europeans. *Nature 513:409-413*.

Other relevant publications from last 10 years

- **Henn BM, Botigué LR, Gravel S,Wang W, Brisbin A, Byrnes JK, Fadhlaoui-Zid K, Zalloua PA, Moreno-Estrada A, Bertranpetit J, Bustamante CD, Comas D (2012)** Genomic Ancestry of North Africans Supports Back-to-Africa Migrations. *PLoS Genetics 8(1)e1002397*.
- **Mendizabal I, Lao O, Marigorta UM, Wollstein A, Gusmão L, Ferak V, Ioana M, Jordanova A, Kaneva R, Kouvatsi A, Kučinskas V, Makukh H, Metspalu A, Netea MG, de Pablo R, Pamjav H, Radojkovic D, Rolleston SJ, Sertic J, Macek M Jr, Comas D*, Kayser M* (2012)** Reconstructing population history of European Romani from genome-wide data. *Current Biology 22:2342-9*.
- **Botigué LR, Henn BM, Gravel S, Maples BK, Gignoux CR, Corona E, Atzmon G, Burns E, Ostrer H, Flores C, Bertranpetit J, Comas D*, Bustamante CD* (2013)** Gene flow from North Africa contributes to differential human genetic diversity in Southern Europe. *PNAS 110:11791-6*.

Postdocs: *Lara Rubio-Araúna, Neus Solé-Morata, Gerard Serra and Àlex Mas.*

Technicians: *Mònica Vallés.*

Genomics of individuality

Francesc Calafell

http://biologiaevolutiva.org/fcalafell

Research Outline

The general topics that interest us revolve around the genomics of individuality: what is there in our genomes that make 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)? We have applied this frame to a wider scope that views the individual as part of a genealogy, sharing lineages with individuals that are related to them. We focus on the Y chromosome, which marks paternal lineages, and to another (cultural) marker of the same lineages: the surname.

Current Projects / Research lines

- **A genetic atlas of Catalan surnames.**
  We selected a list of 50 Catalan surnames and gathered ~50 men for each of those surnames, for a total sample of 2,550. We typed 17 Y-chromosome STRs and 68 SNPs in those samples, and we addressed questions related to the structure of the surname distribution, surname history, and possible forensic applications. This project is in collaboration with David Comas and Jaume Bertranpetit (IBE), and is mostly undertaken by Neus Solé. See http://cognoms.upf.edu.
- **Phylogeography of the Y chromosome in the Iberian Peninsula.**
  In collaboration with Marian Martínez de Pancorbo (Basque Country University, Vitoria), we are studying the R1b-DF27 branch of the Y chromosome phylogeny in Western European populations, where it accounts for >40% of all Y chromosomes. We are genotyping STRs and recently discovered SNPs in W. European populations to trace the origin and history of this main branch of the Y chromosome diversity.

Selected publications 2014

- **Garcia-Etxebarria K, Garcia-Garcerà M, Calafell F (2014)** Consistency of metagenomic assignment programs in simulated and real data. *BMC Bioinformatics 15:90*.
- **Solé-Morata N, Bertranpetit J, Comas D, Calafell F (2014)** Recent Radiation of R-M269 and High Y-STR Haplotype Resemblance Confirmed. *Ann Hum Genet 78:253-254*.
- **Džunková M, Garcia-Garcerà M, Martínez-Priego L, D'Auria G, Calafell F, Moya A (2014)** Direct sequencing from the minimal number of DNA molecules needed to fill a 454 picotiterplate. *PLoS One 9(6):e97379*.

Other relevant publications from last 10 years

- **Calafell F, Almasy L, Sabater-Lleal M, Buil A, Mordillo C, Ramírez-Soriano A, Sikora M, Souto JC, Blangero J, Fontcuberta J, Soria JM (2010)** Sequence variation and genetic evolution at the human F12 locus: mapping quantitive trait nucleotides that influence FXII plasma levels. *Hum Mol Genet 19:517-25*.
- **Javed A, Melé M, Pybus M, Zalloua P, Haber M, Comas D, Netea MG, Balanovsky O, Balanovska E, Jin L, Yang Y, Pitchappan R, ArunKumar G, Bertranpetit J, Calafell F*, Parida L; The Genographic Consortium (2012)** Recombination Networks as Genetic Markers in A Human Variation Study of the Old World. *Hum Genet 131:601-13*.
- **Garcia-Garcerà M, Coscollà M, Garcia-Etxebarria K, Martín-Caballero J, González-Candelas F, Latorre A and Calafell F (2012)** Staphylococcus prevails in the skin microbiota of long-term immunodeficient mice. *Environ Microbiol 14:2087-98*.

Postdocs: *Neus Solé*.

Evolutionary Population Genetics

Elena Bosch

http://biologiaevolutiva.org/ebosch

Research Outline

Our research focuses on investigating different aspects of human genetic diversity. In particular, we are interested in: (i) human adaptation, that is, in identifying traits that have undergone positive selection during human evolution in order to understand the adaptive events that have shaped our genomes; and (ii) the architecture of the genetic predisposition to complex disease. The search for genetic signatures of selection is pursued at different levels using comparative data and exploring intraspecific diversity patterns. As for complex disease, we believe that the application of population genetic models can help in unraveling the genetic contribution to them.

Current Projects / Research lines

- **Human adaptation: immune system and nutrition.**
  Beyond the detection of the footprint of natural selection, we experimentally investigate the phenotypical functional consequences of the genetic variants suspected under natural selection.
- **Role of selection in coding and non-coding regions of the genome.**
  We are analyzing sequence data at both intraspecific and interespecific levels in order to investigate the role of natural selection in all coding and regulatory elements of particular gene pathways.
- **Rare variants and the etiology of complex diseases.**
  Using an evolutionary approach and resequencing data in candidate genes we attempt to evaluate whether rare variants contribute to Parkinson's disease.
- **Natural selection on disease genes.**
  By analyzing human sequence data, divergence and network properties, we hope to characterize the selective pressures acting on genes associated to Mendelian and complex diseases in order to understand differences on penetrance, age of onset, and risk allele frequencies.

Selected publications 2014

- **Engelken J, Carnero-Montoro E, Pybus M, Andrews GK, Lalueza-Fox C, Comas D, Sekler I, de la Rasilla M, Rosas A, Stoneking M, Valverde MA, Vicente R, Bosch E (2014)** Extreme Population Differences in the Human Zinc Transporter ZIP4 (SLC39A4) are Explained by Positive Selection in Sub-Saharan Africa. *PLOS Genetics 10(2): e1004128.*
- **Cenit MC, Martínez-Florensa M, Consuegra M, Bonet L, Carnero-Montoro E, Armiger N, Caballero-Baños M, Arias MT, Benitez D, Ortego-Centeno N, de Ramón E, Sabio JM, Garcia-Hernádez FJ, Tolosa C, Suárez A, González-Gay MA, Bosch E, Martín J, Lozano F (2014).** Analysis of Ancestral and Functionally Relevant CD5 Variants in Systemic Lupus Erythematosus Patients. *PLoS ONE 9(11): e113090.*

Other relevant publications from last 10 years

- **Carnero-Montoro E, Bonet L, Engelken J, Bielig T, Martínez-Florensa M, Lozano F, Bosch E (2012)** Evolutionary and functional evidence for positive selection at the human CD5 immune receptor gene. *Mol Biol Evol 29(2): 811–23.*
- **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. *Mol Biol Evol 26(10): 2285- 97.*
- **Moreno-Estrada A, Casals F, Ramírez-Soriano A, Oliva B, Calafell F, Bertranpetit J, Bosch E (2008)** Signatures of selection in the human olfactory receptor OR5I1 gene. *Mol Biol Evol 25(1):144-54.*

PhD students: *Nino Spataro and Juan Antonio Rodriguez.*

Technicians: *Mònica Vallés.*

Project Manager: *Judit Sainz.*

Evolutionary Genomics

Arcadi Navarro

http://biologiaevolutiva.org/anavarro

Research Outline

Life in our planet 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 even 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 people to disease. All this knowledge empowers us to control our future but, above all, it is fun to obtain.

Current Projects / Research lines

- **Molecular evolution of Segmental Duplications.**
  Our genomes present many Segmental Duplications (SDs), sequences with high identity that can vary in copy number and that are fundamental for the creation of novel genes. We use both experimental and computational techniques to understand patterns of molecular evolution within SDs.
- **Positive selection in the human lineage.**
  We study the signature of adaptive changes out the usual paradigm of new mutations that arise in single-copy protein-coding regions. Recently, we have been focusing on how natural selection influences regulatory regions within gene networks.
- **Temporal and spatial distribution of human disease variants.**
  We study alleles linked to disease susceptibility to ascertain, for instance, what are the evolutionary causes of senescence.
- **Evolution of Herpesviridae and their relationship with complex disease.**
  Herpesviridae are associated to many complex diseases, including cancers and Multiple Sclerosis. We study full viral sequences and link them with human variability.
- **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.

Selected publications 2014

- **Rodriguez JA, Marigorta UM, Navarro A (2014)** Integrating genomics into evolutionary medicine. *Curr Op Gen Dev 29:97–102. (doi:10.1016/j.gde.2014.08.009)*
- **Hartasánchez DA, Vallès-Codina O, Brasó-Vives M, Navarro A (2014)** Interplay of interlocus gene conversion and crossover in segmental duplications under a neutral scenario. *G3 4:1479-89. (doi:10.1534/g3.114.012435)*
- **Santpere G, Darre F, Blanco S, Alcami A, Villoslada P, Albà MM, Navarro A (2014)** Genome-wide analysis of wild-type Epstein-Barr virus genomes derived from healthy individuals of the 1000 Genomes Project. *Genome Biol Evol (doi:10.1093/gbe/evu).*
- **Faria R, Navarro A (2014)** Pool and conquer: new tricks for (c)old problems. *Mol Ecol 23:1653–5. doi:10.1111/mec.12685.*
- **Olalde I, Allentof ME, Sánchez-Quinto F, Santpere G, Chiang CWK, DeGiorgio M, Prado-Martínez J, Rodríguez JA, Rasmussen S, Quilez J, Ramírez O, Fernández M, Prada ME, Vidal-Encinas JM, Nielsen R, Netea MG, Novembre J, Sturm RA, Sabeti P, Marquès-Bonet T, Navarro A, Willerslev E, Lalueza-Fox C (2014)** Derived Immune and Ancestral Pigmentation Alleles in a 7,000-Year-old Mesolithic European. *Nature 507:225-8.*

Other relevant publications from last 10 years

- **Morcillo-Suarez C, Alegre J, Sangros R, Gazave E, de Cid R, Milne R, Amigo J, Ferrer-Admetlla A, Moreno-Estrada A, Gardner M, Casals F, Pérez-Lezaun A, Comas D, Bosch E, Calafell F, Bertranpetit J, Navarro A (2008)** SNP Analysis To Results (SNPator): a web-based environment oriented to statistical genomics analyses upon SNP data. *Bioinformatics 24(14):1643-4.*
- **Faria R, Navarro A (2010)** Chromosomal speciation: rearranging theory with pieces of evidence. *Trends Ecol Evol 25:660-9.*
- **The Orangutan Genome Consortium (Including A Navarro and 6 other members of my team) (2011)** Comparative and demographic analysis of orang-utangenomes. *Nature 469: 529–33.*

Postdocs: *David Allen Hughes, Rui Faria, Carlos Morcillo, Gerard Muntané and Gabriel Santpere.*

PhD students: *Marina Brasó Vives, Diego Hartasánchez, Txema Heredia, Rajendra Mandaje, Juan Antonio Rodríguez and Marco Telford.*

Technicians: *Xavier Farré and Juan Manuel Fuentes.*

Project Manager: *Judit Sainz.*

Comparative Genomics

Tomas Marquès-Bonet

http://biologiaevolutiva.org/tmarques

Research Outline

Our main line of research is centered in the discovery of the extent of all kinds of genome variation within different phenotypically genomes. Specifically, we study genome variation (centered on CNVs), gene expression and epigenetic differences in the human species in the context of great ape evolution and other mammalian genomes such as canids. The goal is to create an integrated view of genome evolution by studying changes in the composition, frequency, size and location at every major branchpoint of recent human evolution.

Current Projects / Research lines

- **Genomic variation in humans and great apes.**
  Despite international efforts to characterize thousands of human genomes, primates have somehow been forgotten. Our goal is to understand the origins of genomic variants and phenotypical differences among species and model variation within species to provide a proper perspective to human diversity.
- **Epigenetics and transcriptomics of non-human primates.**
  The recognition of post-genomic modifications with high biological impact is a focus of research in model and non-model organisms in the last years. In this line of research, I use integrative analyses of genomic variants, with gene expression and epigenetics in non-human primates to explore the relationship of these three layers of complexity.
- **Canid evolution.**
  The domestic dog has been recognized as an important organism for studying the relationship between selection, genome variation, and phenotypic diversity. In this line of research I do explore structural variation related to the process of domestication.

Selected publications 2014

- **Olalde I, Allentof ME, Sánchez-Quinto F, Santpere G, Chiang CWK, DeGiorgio M, Prado-Martínez J, Rodríguez JA, Rasmussen S, Quilez J, Ramírez O, Fernández M, Prada ME, Vidal-Encinas JM, Nielsen R, Netea MG, Novembre J, Sturm RA, Sabeti P, Marquès-Bonet T, Navarro A, Willerslev E, Lalueza-Fox C (2014)** Derived Immune and Ancestral Pigmentation Alleles in a 7,000-Year-old Mesolithic European. *Nature 507:225-8*.
- **Worley KC et al. (Marmoset genome Consortium including B. Lorente-Galdos and T. Marques-Bonet) (2014)** The Genome of the Common Marmoset: A Comparative Analysis of an Extraordinary South American Primate". *Nat Genet 46(8):850-7. doi: 10.1038/ng.3042*.
- **Venkatesh B, Lee AP, Ravi V, Lian MM, Maurya AK, Swann JB, Ohta Y, Flajnik MF, Sutoh Y, Kasahara M, Hoon S, Gangu V, Roy SW, Irimia M, Korzh V, Kondrychyn I, Tay BH, Tohari S, Lim ZW, Kong KW, Ho S, Lorente-Galdos B, Quilez J, Marques-Bonet T, Raney BJ, Ingham PW, Tay A, Hillier LW, Minx P, Boehm T, Wilson RK, Brenner S, Warren WC (2014)** The elephant shark genome provides unique insights into gnathostome evolution. *Nature 505(7482):174-9. doi: 10.1038/nature12826*.
- **Carbone L et al (Gibbon Genome Consortium including B. Lorente-Galdos and Tomas Marques-Bonet) (2014)** The gibbon genome provides a novel perspective on the accelerated karyotype evolution of small apes. *Nature 513(7517):195-201. doi: 10.1038/nature13679*.
- **Ramirez O, Olalde I, Berglund J, Lorente-Galdos B, Webster MT, Wayne RK, Lalueza-Fox C, Vilà C, Marques-Bonet T (2014)** Analysis of structural diversity in wolf-like canids reveals post-domestication variants. *BMC genomics 15:465. doi: 10.1186/1471-2164-15-465*.

Other relevant publications from last 10 years

- **Hernando-Herraez I, Prado-Martinez J, Garg P, Fernandez-Callejo M, Heyn H, Hvilsom C, Navarro A, Esteller M, Sharp AJ, Marques-Bonet T (2013)** Dynamics of DNA Methylation in Recent Human and Great Apes Evolution. *PLOS Genetics 9(9):e1003763*.
- **Prado-Martinez J et al Tomas Marques-Bonet (2013)** Great ape genetic diversity and population history. *Nature 499(7459):471-5*.
- **Lorente-Galdos B, Bleyhl J, Santpere G, Vives L, Ramirez O, Hernandez J, Anglada R, Copper GM, Navarro A, Eichler E, Marques-Bonet T (2013)** Fast exon evolution in duplicated regions in hominids. *Genome Biol doi: 10.1186/gb-2013-14-1-r9*.

Postdocs: *Belén Lorente.*

PhD students: *Javier Prado, Irene Hernando, Tiago Carvalho and Raquel Garcia.*

Technicians: *Marcos Fernández.*

Complex Systems Lab

Ricard Solé

http://complex.upf.edu/publications

Research Outline

The Complex Systems Lab is an interdisciplinary research team exploring the evolution of complex systems, both natural and artificial, searching for their common laws of organization. Our research spans a broad range of systems, with special attention to major synthetic transitions, evolutionary bioengineering and network biology.

Current Projects / Research lines

- **Evolutionary innovations**
  We use both theoretical and experimental approaches to the origins of evolutionary innovations and major transitions in biological and artificial systems.
- **Multicellularity: origins, maintenance and decay**
  We want to develop a general theoretical framework for the origins and development of complex multicellular systems, including early emergence through evolution (evo-devo) and the boundaries of synthetic multicellularity.
- **Open-ended Emergence of evolving systems**
  We develop a theory of emergence of complexity through evolutionary dynamics and the conditions for open-endedness in living and artificial systems.
- **Biological computation**
  We study the nature, origins and evolution of living computational systems, both natural and synthetic.

Selected publications 2014

- **Solé RV, Valverde S, Rodríguez-Caso C, Sardanyés J (2014)** Can a minimal replicating construct be identified as the embodiment of cancer? *Bioessays 36(5):503-12* .
- **Macía J, Solé RV (2014)** How to Make a Synthetic Multicellular Computer. *PLoS one 9(2): e81248*.
- **Koenigsberger AA, Goñi J, Solé RV, Sporns O (2014)** Network morphospaces. *J R Soc Interface, 12: 08812*.
- **Corominas-Murtra B, Fortuny J, Solé RV (2014)** Towards a mathematical theory of meaningful communication. *Nature Sci Rep 4:4587*.
- **Azzurro E, Tuset VM, Lombarte A, Maynou F, Simberloff D, Rodríguez-Pérez A, Solé RV (2014)** External morphology explains the success of biological invasions. *Ecol Lett 17:1455–63*.

Other relevant publications from last 10 years

- **Corominas-Murtra B, Goñi J, Solé RV, Rodríguez-Caso C (2013)** On the origins of hierarchy in complex networks. *PNAS 110(33):13316-21*.
- **Regot S, Macia J, Conde N, Furukawa K, Kjellén J, Peeters T, Hohmann S, de Nadal E, Posas F, Solé RV (2011)** Distributed Biological Computation with Multicellular Engineered Networks. *Nature 469:207-11*.
- **Montoya JM, Pimm S, Solé RV (2006)** Ecological networks and their fragility. *Nature 442, 259-64*.

Other PIs: *Javier Macía, Carlos Rodríguez-Caso and Sergi Valverde.*

Postdocs: *Josep Sardanyés, Dani Rodríguez-Amor and Raúl Montañez.*

PhD students: *Adriano Bonforti, Max Carbonell, Núria Conde, Salvador Durán, Luis Seoane and Ben Shirt-Ediss.*

Technicians: *Eva García Ramallo.*

Project Manager: *Jesús González.*

Language Evolution

Luc Steels

http://biologiaevolutiva.es/lsteels

Research Outline

The goal of our research is to develop a theory for the origins and evolution of language. Such a theory necessarily involves three aspects: social, cultural, and biological. The social aspect should give us answers to the question 'Why did humans start to talk?'. The cultural aspect should answer how new language forms arise in language and keep on changing over time. The biological aspect addresses how the biological foundations for language may have arisen. We focus mostly on the cultural aspect, developing and testing agent-based models explaining how features of language, such as agreement systems, arise and culturally evolve.

Current Projects / Research lines

- **Origins and evolution of grammatical structures**
  There is virtually no theory of the fundamental processes underlying the evolution of language. We try to understand the cognitive mechanisms, interaction patterns, and collective dynamics that could explain how grammatical structures arise by building agent-based models and using the hypothesis that self-organization and (linguistic) selection are the primary driving forces.
- **Fluid Construction Grammar (FCG)**
  In order to conduct agent-based experiments in language evolution it is necessary to have a computational formalism that is capable to handle variation, flexibility, and change. The formalism takes a construction grammar viewpoint and it consists of data structures for representing linguistic knowledge and mechanisms for parsing, production, and language learning (www.fcg-net.org).
- **Neural implementations of FCG**
  To bridge the gap between computational models and neurobiology, we are investigating how a replicator dynamics model of the brain could potentially be used to implement the highly complex operations that FCG demands.

Selected publications 2014

- **Steels L (2014)** Robot Tutoring. *In: Anthony G. Cohn, Bernd Neumann, Alessandro Saffiotti, and Markus Vincze. Dagstuhl Reports. 1 ed. Schloss Dagstuhl--Leibniz-Zentrum fuer Informatik.*
- **Garcia E, Steels L (2014)** Strategies for the emergence of first-order constituent structure. *Proceedings of Evolang X, Vienna.*
- **Gangemi, A., Hafner, V. V, Kuhn, W., Scheider, S., Steels, L., & Kuhn, W. (2014).** Spatial reference in the Semantic Web and in Robotics. *Dagstuhl Reports, 4(3), 181–201. doi:10.4230/DagRep.4.3.181*
- **Spranger, M., & Steels, L. (2014).** Discovering communication through ontogenetic ritualisation. *In 4th International Conference on Development and Learning and on Epigenetic Robotics (pp. 14–19). IEEE. doi:10.1109/DEVLRN.2014.6982948*
- **Steels, L. (2014).** Breaking down false barriers to understanding. *In D. Dor, C. Knight, & J. Lewis (Eds.), The Social Origins of Language. Oxford Scholarship Online. doi:/10.1093/acprof:oso/9780199665327.003.0024*

Other relevant publications from last 10 years

- **Beuls K, Steels L (2013)** Agent-Based Models of Strategies for the Emergence and Evolution of Grammatical Agreement. *PLoS ONE 8(3): 5896*
- **Van Trijp R, Steels L (2012)** Multilevel alignment maintains language systematicity. *Advances in Complex Systems 15(3-4): 1250039-0.*
- **Steels L (2011)** Modeling the cultural evolution of language. *Physics of Life Reviews, 8 (4), pp-. 339-356.*

PhD students: *Emília Garcia Casademont.*

Project Manager: *Maria Ferrer Bonet.*

Technician: *Jorge Diz Pico.*

Dynamical Systems Biology

Jordi García Ojalvo

http://dsb.upf.edu

Research Outline

Our lab is interested in the dynamics of living systems, from unicellular organisms to human beings. We use dynamical phenomena to identify the molecular mechanisms of cellular processes, such as decision making in bacteria, signaling in the immune system, and pluripotency and tissue homeostasis in stem cells. Using a combination of theoretical modeling and experimental tools such as time-lapse fluorescence microscopy and microfluidics, we investigate dynamical phenomena like biochemical pulses and oscillations, and study how these processes coexist inside the cell in a coordinated way. We also study the emergence of collective rhythms in cortical and brain networks.

Current Projects / Research lines

- **Dynamics of gene regulation in bacteria.**
  We study the dynamics of gene expression in bacteria by time-lapse fluorescence microscopy, together with theoretical modeling. The goal is to unravel the molecular mechanisms of cellular functions at the single-cell level.
- **Dynamics of cellular signaling.**
  We study how cells respond to external signals, and how information is integrated by signaling networks. In particular we study the oscillatory response of immune system cells to cytokine stimulation, to understand the response to therapy in immune diseases.
- **Mesoscopic brain dynamics.**
  We aim to relate functional measures of brain activity, obtained from fMRI and EEG, with the underlying connectivity structure of the brain. Our models allow us to search for dynamical correlates of neurodegenerative diseases.
- **Collective neuronal oscillations.**
  We investigate how the dynamical properties of individual neurons affect cortical oscillations, and how these oscillations are used to communicate information efficiently across distant brain areas.

Selected publications 2014

- **Sancristobal B, Vicente R, Garcia-Ojalvo J (2014)** Role of frequency mismatch in neuronal communication through coherence. *J Comput Neurosci 37:193-208*.
- **Barardi A, Malagarriga D, Sancristobal B, Garcia-Ojalvo J, Pons AJ (2014)** Probing scale interaction in brain dynamics through synchronization. *Philos Trans R Soc 369, 20130533*.
- **Barardi A, Sancristobal B, Garcia-Ojalvo J (2014)** Phase-coherence transitions and communication in the gamma range between delay-coupled neuronal populations. *PLoS Comput Biol 10, e1003723*.
- **Balenzuela P, Rue P, Boccaletti S, Garcia-Ojalvo J (2014)** Collective stochastic coherence and synchronizability in weighted scale-free networks. *New J Phys 16, 013036*.

Other relevant publications from last 10 years

- **Süel GM, Garcia-Ojalvo J, Liberman LM, Elowitz MB (2006)** An excitable gene regulatory circuit induces transient cellular differentiation. *Nature 440:545-50*.
- **Cagatay T, Turcotte M, Elowitz MB, Garcia-Ojalvo J, Suel GM (2009)** Architecture-dependent noise discriminates functionally analogous differentiation circuits. *Cell 139:512-22*.
- **Espinar L, Dies M, Cagatay T, Süel GM, Garcia-Ojalvo J (2013)** Circuit-level input integration in bacterial gene regulation. *PNAS 110:7091-6*.

Postdocs: *Elena Abad Adán.*

PhD students: *Alessandro Barardi, Marta Dies Miracle, Lara Sofía Escuaín de Poole, Marçal Gabaldà Sagarra, Letícia Galera Laporta, Maciej Jedynak and Rosa Martínez Corral.*

Single Cell Behavior

Lucas Carey

www.upf.edu/scb

Research Outline

Many global health problems, such as the resistance of tumors to chemotherapy and of microbes to antibiotics, are caused not by differences in the genome, but by stochastic (random) variability between cells. Individual cells in an isogenic population express different genes, grow differently, and respond differently to stimuli and stress. However, the mechanisms that determine why genetically identical individuals differ are not well understood. We combine mathematical modeling with high-throughput quantitative single cell measurements to understand, from a stochastic point of view, the molecular mechanisms that underlie gene expression and cell growth and division.

Current Projects / Research lines

- **The causes and consequences of stochastic variation in cellular fitness.**
  We have developed a novel method to characterize the intracellular state of cells that differ only by stochastic differences in their rate of growth and division. In addition, we are characterizing the genetic and environmental factors that result in changes in the single-cell fitness distribution.
- **Fundamental biological questions through large libraries.**
  Many fundamental questions in biology can only be answered by exploring large sequence spaces. We can construct and measure diverse libraries with >250,000 unique sequences, and are doing so in order to better understand evolution, epistasis and gene expression.

Selected publications 2014

- **Van Dijk D, Manor O, Carey LB (2014)** A quantitative analysis of publication metrics and success on the academic job market. *Curr Biol doi: 10.1016/j.cub.2014.04.039*.
- **Fernández-Sainz IJ, Largo E, Gladue DP, Fletcher P, O'Donnell V, Holinka LG, Carey LB, Lu X, Nieva JL, Borca MV (2014)** Effect of specific amino acid substitutions in the putative fusion peptide of structural glycoprotein E2 on Classical Swine Fever Virus replication. *Virology 456-457:121-30*.

Other relevant publications from last 10 years

- **Carey LB, van Dijk D, Sloot PMA, Kaandorp JA, Segal E (2013)** Promoter sequence determines the relationship between expression level and noise. *PLoS Biology e1001528*.
- **Rest JS, Morales CM, Waldron JB, Opulente DA, Fisher J, Moon S, Bullaughey K, Carey LB, Dedousis D (2012)** Nonlinear fitness consequences of variation in expression level of a eukaryotic gene. *Mol Biol Evol 2:448-56*.
- **Wang* H, Carey* LB, Cai Y, Wijnen H, Futcher B (2009)** Recruitment of Cln3 cyclin to promoters controls cell cycle entry via histone deacetylase and other targets. *PLoS Biology e1000189*.

Postdocs: *Lorena Espinar.*

PhD students: *Alsu Missarova.*

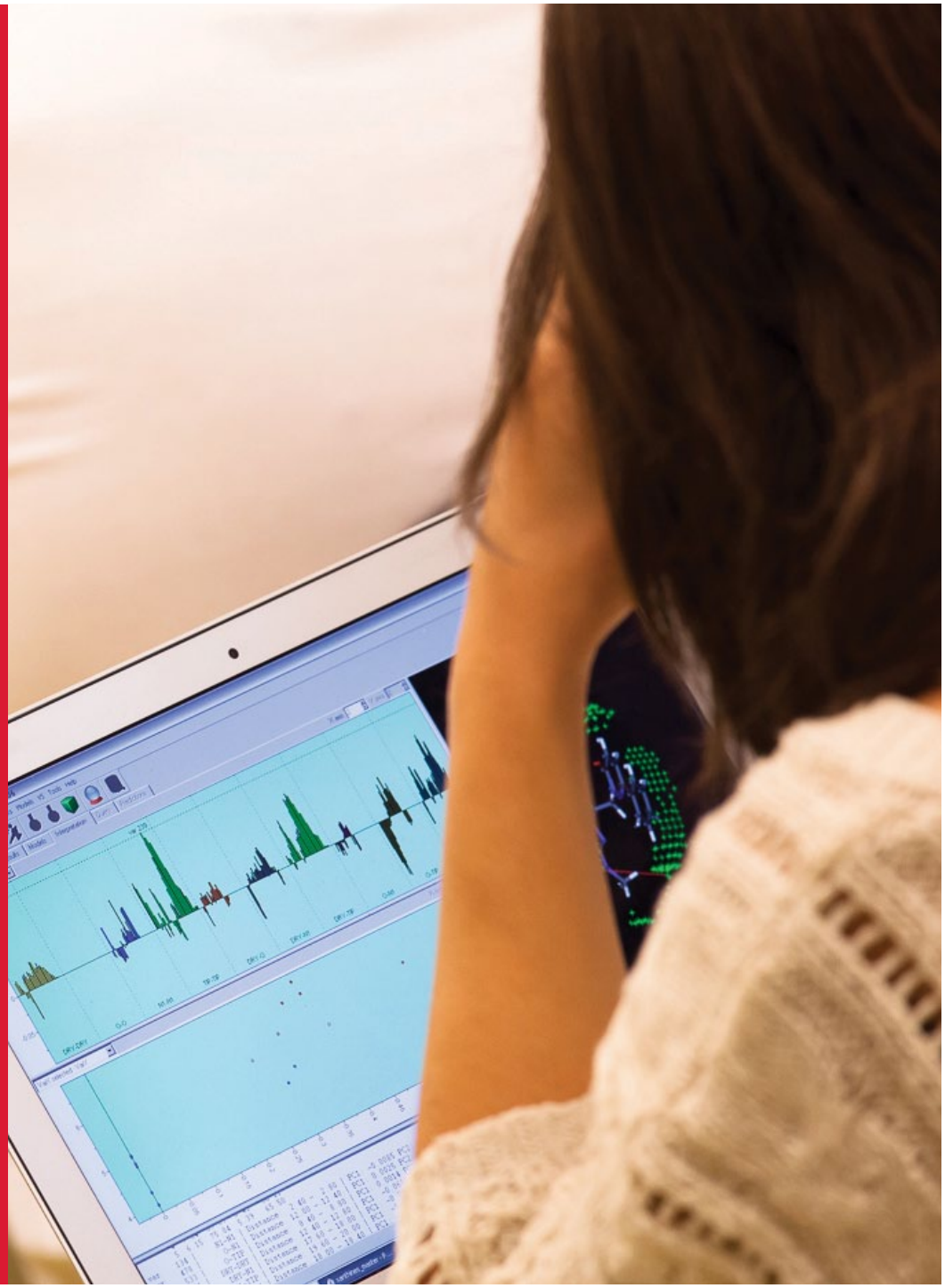
Master's students: *Julia Domingo and Carlos Toscano Ochoa.*

Biomedical Informatics Programme

Coordinator: Ferran Sanz

The Research Programme on Biomedical Informatics (GRIB) is a joint research programme of the Department of Experimental and Health Sciences of the UPF and the Hospital del Mar Medical Research Institute (IMIM). The GRIB is organized into nine in silico labs: Biomedical Genomics (UPF), Computational Biophysics (UPF), Computational Genomics (UPF), Evolutionary Genomics (IMIM), Functional Genomics (UPF), Integrative Biomedical Informatics (IMIM-UPF), PharmacoInformatics (IMIM-UPF), Structural Bioinformatics (UPF) and Systems Pharmacology (IMIM). Ferran Sanz, head of the IBI group is also the coordinator of GRIB. The GRIB mission is to develop and apply computational methods and information technologies for a better understanding and prediction of biological phenomena, giving especial emphasis to those related to the human diseases, their prevention, diagnosis and pharmacological treatment. GRIB faculty members have wide experience in the participation and coordination of research projects funded by the European Commission. Some of the ongoing EC-funded projects are: eTOX, on the in silico prediction of drug toxicities; Open Phacts, about the computational extraction, integration and exploitation of open source knowledge to support drug discovery; EMIF to develop an efficient international framework for the research reuse of patient-level data, and RNPnet about the RNP structure, function and mechanism of action. Two additional EU-funded projects will start in 2015: IPiE, about the in silico assessment of pharmaceuticals in the environment, and MedBioinformatics, on the creation of medically-driven integrative bioinformatics applications focused on oncology, CNS disorders and their comorbidities.

- **Biomedical Genomics Group**
  Núria López-Bigas
- **Computational Biophysics Group**
  Gianni de Fabritiis
- **Computational Genomics**
  Eduardo Eyras
- **Functional genomics Group**
  Robert Castelo
- **Integrative Biomedical Informatics Group**
  Ferran Sanz
- **PharmacoInformatics Group**
  Manuel Pastor
- **Structural Bioinformatics Group**
  Baldo Oliva



Biomedical Genomics Group

Núria López-Bigas

http://bg.upf.edu/group/index.php

Research Outline

Our group is focused on the study of cancer from a genomics perspective. Specifically, our group is interested in the development of computational approaches to analyse cancer genomes to identify mutations, genes and pathways driving tumorigenesis and the identification of their therapeutic targeting opportunities.

Current Projects / Research lines

- **Noncoding drivers.**
  Although the coding part of the human genome has been now largely explored in the search for cancer driver mutations, the extent of involvement of noncoding mutations in cancer development remains still a mystery. We are now analysing the pattern of somatic mutations across tumours in noncoding regions to identify signals of positive selection, these signals are an indication that mutations in the region have been positively selected during tumour evolution and are thus directly involved in the tumour phenotype.
- **In silico Drug prescription.**
  We have developed an In silico drug prescription algorithm, which makes use of the knowledge acumulated in IntOGen.org, in particular cancer drivers across tumor types and their targeted therapeutic options, to identify the driver mutations in a tumor sample and in silico prescribe approved and experimental targeted drugs that may benefit the patient. We aim to consolidate this knowledge into a useful tool for clinical use. Toward this direction we are working in close collaboration with clinical partners who are interested in the technology and help us to improve it and adapt it for its use in a clinical and research setting.

Selected publications 2014

- **Hoadley KA, Yau C, Wolf DM, Cherniack AD, Tamborero D, Ng S, Leiserson MD, Niu B, McLellan MD, Uzunangelov V, Zhang J, Kandoth C, Akbani R, Shen H, Omberg L, Chu A, Margolin AA, Van't Veer LJ, Lopez-Bigas N, Laird PW, Raphael BJ, Ding L, Robertson AG, Byers LA, Mills GB, Weinstein JN, Van Waes C, Chen Z, Collisson EA (2014)** Cancer Genome Atlas Research Network, Benz CC, Perou CM, Stuart JM. Multiplatform Analysis of 12 Cancer Types Reveals Molecular Classification within and across Tissues of Origin. *Cell 158(4):929-44.*
- **Schroeder MP, Rubio-Perez C, Tamborero D, Gonzalez-Perez A, Lopez-Bigas N (2014)** OncodriveROLE classifies cancer driver genes in loss of function and activating mode of action. *Bioinformatics 30(17):i549-55.*
- **Deu-Pons J, Schroeder MP, Lopez-Bigas N (2014)** jHeatmap: an interactive heatmap viewer for the web. *Bioinformatics 30(12): 1757-8.*
- **Truscott M, Islam ABMMK, Lightfoot J, Lopez-Bigas N, Frolov MV (2014)** An Intronic microRNA Links Rb/E2F and EGFR Signaling. *Plos Genet 10(7):e1004493*

Other relevant publications from last 10 years

- **Gonzalez-Perez A, Perez-Llamas C, Deu-Pons J, Tamborero D, Schroeder MP, Jene-Sanz A, Santos A, Lopez-Bigas N (2013)** IntOGen-mutations identifies cancer drivers across tumor types. *Nat Methods (11):1081-2.*
- **Gonzalez-Perez A, Lopez-Bigas N (2011)** Improving the assessment of the outcome of non-synonymous SNVs with a Consensus deleteriousness score (Condel). *Am J Hum Genet 88(4):440-9.*

Postdocs: *David Tamborero, Loris Mularoni, Michael Schroeder and Sabarinathan Radhakrishnan.*

Other PI: *Abel González-Pérez.*

PhD students: *Joan Frigola, Carlota Rubio and Davide Polizzi.*

Technicians: *Jordi Deu-Pons and Fernando Benito.*

Computational Biophysics Group

Gianni de Fabritiis

www.multiscalelab.org

Research Outline

Our group research interests are at the interface between computation and biology, with an application focus on biomedicine. Specifically, we develop new computational physics methods and apply them to understand biological problems mainly at the level of protein folding and binding. This knowledge is then used to design molecules with therapeutic applications in mind.
We study macromolecule dynamics and energetics using mainly accelerated processors (Graphics processing units (GPUs) http://www.gpugrid.net) and the accelerated molecular dynamics program ACEMD. The simulation of proteins can directly increase our knowledge on the molecular mechanisms of a biological activity and help experimental scientists to understand an experiment from a molecular, more fundamental point of view.

Current Projects / Research lines

- **Biomedicine.**
  We search new molecules to alter protein behavior with possible therapeutic implications, using new simulation-based methods for drug discovery. We develop in-silico fragment based drug discovery methods to explore the binding chemical space of a target and simulate drug-like binding events for the determination of kinetics, affinities and poses. New small molecules and peptides developed are then tested experimentally.
- **Computational physics.**
  We develop new codes for molecular dynamics simulations (ACEMD) running on special hardware to maximize the data throughput and extend the window of exploration of biological phenomena by simulations. We also work on distributed, volunteer computing where we perform most of our calculations with the help of people worldwide donating their computer time (GPUGRID).
- **Protein folding and binding.**
  We computationally investigate biological systems to understand the mechanisms of biological processes at the atomistic level. The goal is to be able to create solid, quantitative hypothesis of how proteins behaves, how chemical modifications alter binding and folding, discover hidden order in intrinsically disordered proteins and understand molecular recognition pathways between molecules.

Selected publications 2014

- **Stanley N, Esteban S, De Fabritiis G (2014)** Kinetic modulation of a disordered protein domain by phosphorylation. *Nat Commun 5:5272*.
- **Doerr S, De Fabritiis G (2014)** On-the-fly learning and sampling of ligand binding by high-throughput molecular simulations. *J Chem Theory Comput 10(5):2064–9*.
- **Dainese E, De Fabritiis G, Sabatucci A, Oddi S, Angelucci C, Di Pancrazio C, Giorgino T, Stanley N, Cravatt B, Maccarrone M (2014)** Membrane lipids are key-modulators of the endocannabinoid-hydrolase FAAH. *Biochem J 457(3):463-72*.

Other relevant publications from last 10 years

- **Sadiq K, Noe F, De Fabritiis G (2012)** Kinetic characterization of the critical step in HIV-1 protease maturation. *PNAS 109(50):20449-54*.
- **Buch I, Giorgino T, De Fabritiis G (2011)** Complete reconstruction of an enzyme-inhibitor binding process by molecular dynamics simulations. *PNAS 108:10184-9*.

PhD students: *Noelia Ferruz, Stefan Doerr, Gerard Martínez and Nathaniel Stanley.*

Computational Genomics

Eduardo Eyras

http://regulatorygenomics.upf.edu

Research Outline

We focus on the role of RNA processing in cancer. In particular, we are addressing the following questions: 1) What are the RNA processing alterations that take place in cancer? 2) What is the functional impact of RNA processing alterations and how they contribute to cancer? 3) Is there a potential role for RNA processing alterations in prognosis and therapy? We are developing the necessary tools to tackle these questions and to contribute to the addition of RNA processing information into current approaches of cancer precision medicine.

Current Projects / Research lines

- **"Elucidating the network of breast cancer".**
  Sandra Ibarra Cancer Foundation.
  We study the alterations in alternative splicing in different cancer types and how these alterations impact the network of protein-protein interactions to uncover novel mechanisms of tumorigenesis.
- **"Predictive models of RNA regulation – applications to splicing and cancer".**
  MICINN (Plan Nacional)
  We apply Machine Learning methods to find novel RNA-based signatures in cancer to find novel prognostic and therapeutic targets.
- **"An integrated approach to post-transcriptional regulation of gene expression and its role in human disease". MICINN (Consolider)**
  We investigate role of RNA binding proteins and RNA processing mechanisms in tumors.
- **"RNPnet – RNP structure, function and mechanism of action" ITN EU.**
  We study the relation between chromatin and splicing.
- **"Epigenetic modulation of alternative splicing in breast cancer".**
  Sandra Ibarra Cancer Foundation
  We study the role of epigenetic modifications in breast cancer and how these affect splicing.

Selected publications 2014

- **Alló M, Agirre E, Bessonov S, Bertucci P, Gómez Acuña L, Buggiano V, Bellora N, Singh B, Petrillo E, Blaustein M, Miñana B, Dujardin G, Pozzi B, Pelisch F, Bechara E, Agafonov DE, Srebrow A, Lührmann R, Valcárcel J, Eyras E*, Kornblihtt AR (2014)** Argonaute-1 binds transcriptional enhancers and controls constitutive and alternative splicing in human cells. *PNAS 111(44):15622-9. (* co-corresponding author).*
- **Alamancos GP, Agirre E, Eyras E (2014)** Methods to study splicing from high-throughput RNA sequencing data. *Methods Mol Biol 1126:357-97.*
- **Plass M, Eyras E (2014)** Approaches to link RNA secondary structures with splicing regulation. *Methods Mol Biol 1126:341-56.*
- **Raj B, Irimia M, Braunschweig U, Sterne-Weiler T, O'Hanlon D, Lin ZY, Chen GI, Easton LE, Ule J, Gingras AC, Eyras E, Blencowe BJ (2014)** A global regulatory mechanism for activating an exon network required for neurogenesis. *Mol Cell 56(1):90-103.*
- **Maslon MM, Heras SR, Bellora N, Eyras E, Cáceres JF (2014)** The translational landscape of the splicing factor SRSF1 and its role in mitosis. *Elife:e02028.*

Other relevant publications from last 10 years

- **Plass M, Codony-Servat C, Ferreira PG, Vilardell J, Eyras E (2012)** RNA secondary structure mediates alternative 3'ss selection in Saccharomyces cerevisiae. *RNA 18(6):1103-15.*
- **Althammer S, González-Vallinas J, Ballaré C, Beato M, Eyras E (2011)** Pyicos: a versatile toolkit for the analysis of high-throughput sequencing data. *Bioinformatics 27(24):3333-40.*
- **Corvelo A, Eyras E (2008)** Exon creation and establishment in human genes. *Genome Biol 9(9):R141.*

Postdocs: *Endre Sebestyén.*

PhD students: *Babita Singh, Isaac Kremsky and Amadís Pagès.*

Functional genomics Group

Robert Castelo

http://functionalgenomics.upf.edu

Research Outline

Our main research efforts are geared towards the development of statistical and computational methods for the analysis and comprehension of high-throughput genetics and genomics data.

Current Projects / Research lines

- **Reverse engineering the genotype-phenotype map.**
  Genes and molecules are activated in a coordinated manner under finely tuned regulatory programs. High-throughput genetics and genomics data offer a unique opportunity to witness this phenomenon by monitoring the simultaneous action of thousands of genes and millions of genotypes. We try to embrace this complexity by developing computational tools that enable estimating multivariate statistical models from these data, which have the potential to disentangle direct from indirect or spurious effects.

Selected publications 2014

· **Tur, I, Roverato A, Castelo R (2014)** Mapping eQTL networks with mixed graphical Markov models. *Genetics 198(4):1377-83*.

Other relevant publications from last 10 years

· **Castelo R, Roverato A (2006)** A robust procedure for Gaussian graphical model search from microarray data with p larger than n. *J Mach Learn Res 7:2621-50*.

· **Castelo R, Roverato A (2009)** Reverse engineering molecular regulatory networks from microarray data with qp-graphs. *J Comput Biol 16(2):213-27*.

· **Hänzelmann S, Castelo R, Guinney J (2013)** GSVA: gene set variation analysis for microarray and RNA-Seq data. *BMC Bioinformatics 14:7*.

PhD students: *Inma Tur and Pau Puigdevall*.

Integrative Biomedical Informatics Group

Ferran Sanz

http://grib.imim.es/research/integrative-biomedical-informatics/index.html
http://ibi.imim.es/

Research Outline

The huge wealth of biomedical information that is currently available is underused because the difficulties in seeking, integrating, analysing the relevant one. There is also a great difficulty for the identification and use of clinically actionable information. The goal of the Integrative Biomedical Informatics (IBI) group is to develop computational methods and tools to address these challenges, with the aim of better understanding human health and disease and contributing to the design of more effective and safe therapeutic interventions.

Current Projects / Research lines

The ongoing research lines of the IBI group are:

- New methods and tools for knowledge extraction and linkage from biomedical literature and other publicly available sources.
- Development of strategies for the research reuse of clinical data.
- Network biology for the study of human diseases and drug toxicity.
- Integrative knowledge management and exploitation in drug discovery and development.

The group is currently coordinating two EU-funded projects:

- IMI **eTOX** on the in silico prediction of drug toxicity.
- **MedBioinformatics** on the application of bioinformatics in translational research and clinical practice.

The group participates in other EU-funded IMI projects:

- **Open PHACTS** on knowledge discovery in pharmaceutical R&D using the semantic web technology.
- **EMIF** dealing with the creation and exploitation of a European Medical Information Framework.
- **iPIE** aiming to develop a predictive framework for the environmental impact of drugs.

Selected publications 2014

- **Marti-Solano M, Birney E, Bril A, Della Pasqua O, Kitano H, Mons B, Xenarios I, Sanz F. (2014)** Integrative knowledge management to enhance pharmaceutical R&D. *Nat Rev Drug Discov 13(4): 239-40.*
- **Carrió P, Pinto M, Ecker G, Sanz F, Pastor M (2014)** Applicability Domain Analysis (ADAN): A Robust Method for Assessing the Reliability of Drug Property Predictions. *J Chem Inf Model 54 (5): 1500-11.*
- **Grosdidier S, Ferrer A, Faner R, Piñero J, Roca J, Cosío B, Agustí A, Gea J, Sanz F, Furlong LI (2014)** Network medicine analysis of COPD multimorbidities. *Respir Res 15(1):111.*
- **Bravo A, Cases M, Queralt-Rosinach N, Sanz F, Furlong LI (2014)** A Knowledge-Driven Approach to Extract Disease-Related Biomarkers from the Literature. *BioMed Res International: 253128.*
- **Cases M, Briggs K, Steger-Hartmann T, Pognan F, Marc P, Kleinöder T, Schwab CH, Pastor M, Wichard J, Sanz F (2014)** The eTOX Data-Sharing Project to Advance in Silico Drug-Induced Toxicity Prediction. *Int J Mol Sci 15(11): 21136-54.*

Other relevant publications from last 10 years

- **Cases M, Furlong LI, Albanell J, Altman RB, Bellazzi R, Boyer S, Brand A, Brookes AJ, Brunak S, Clark TW, Gea J, Ghazal P, Graf N, Guigo R, Klein TE, Lopez-Bigas N, Maojo V, Mons B, Musen M, Oliveira JL, Rowe A, Ruch P, Shabo A, Shortliffe EH, Valencia A, van der Lei J, Mayer MA, Sanz F (2013)** Improving data and knowledge management to better integrate health care and research. *J Intern Med 274 (4): 321-8.*
- **Bauer-Mehren A, van Mulligen EM, Avillach P, Carrascosa MC, Garcia-Serna R, Piñero J, Singh B, Lopes P, Oliveira JL, Diallo G, Ahlberg Helgee E, Boyer S, Mestres J, Sanz F, Kors JA, Furlong LI (2012)** Automatic Filtering and Substantiation of Drug Safety Signals. *PLoS Comput Biol 8(4); e1002457*
- **Bauer-Mehren A, Furlong LI, Sanz F (2009)** Pathway databases and tools for their exploitation: benefits, current limitations and challenges. *Mol Syst Biol 5:290.*

Other PI: *Laura I. Furlong.*

Postdocs: *Miguel Angel Mayer, Pablo Carbonell, Núria Queralt and Alexia Giannoula.*

PhD students: *Alex Bravo, Janet Piñero and Alba Gutierrez.*

Project Manager: *Maria Saarela.*

PharmacoInformatics Group

Manuel Pastor

http://phi.imim.es

Research Outline

Our research is related with the application and development of computational methods in the field of pharmaceutical research and development. Regarding the application of computational methods, we make use of highly sophisticated computational simulations applied to G-protein coupled receptors in the context of the schizophrenia treatment, aimed to understand the molecular mechanisms involved and design safer and more effective drugs. Regarding the development of computational methods, we are authors of many novel methodologies, many of which have been implemented in scientific software with direct application in pharmaceutical research, mainly in the areas of discovery and preclinical drug safety evaluation.

Current Projects / Research lines

- **eTOX:** The objective of the IMIM/JU project eTOX is the development of in silico methods for the prediction of in vivo toxicity of novel drug candidates. This project, involving a large consortium of academic groups and pharmaceutical companies, has compiled one of the largest databases available of preclinical repeated dose toxicity, which is being exploited for developing integrated prediction models.
- **Open PHACTS:** The project is developing an open platform using the most advanced knowledge management technologies which integrates pharmacological data from a variety of information resources and provides tools and services to support pharmacological research.
- **Understanding antipsychotic effect:** Advanced computational methods are being applied for advancing in the understanding of the molecular mechanisms involved in the pharmacological effects of antipsychotic drugs. These involved milisecond scale molecular dynamic simulations to diverse G-protein coupled receptors for studying the effect of the membrane environment, their oligomerization or the action of biased ligands.

Selected publications 2014

- **Martí-Solano M, Sanz F, Pastor M, Selent JA (2014)** Dynamic View of Molecular Switch Behavior at Serotonin Receptors: Implications for Functional Selectivity. *Plos ONE 9(10):e109312. doi:10.1371/journal.pone.0109312.*
- **Selent J, Marti-Solano M, Rodríguez J, Atanes P, Brea J, Castro M, Sanz F, Loza MI, Pastor M (2014)** Novel insights on the structural determinants of clozapine and olanzapine multi-target binding profiles. *Eur J Med Chem 77:91-5.*
- **Guixà-González R, Rodriguez-Espigares I, Ramírez-Anguita JM, Carrió-Gaspar P, Martinez-Seara H, Giorgino T, Selent J (2014)** MEMBPLUGIN: studying membrane complexity in VMD. *Bioinformatics 30(10):1478-80.*
- **Carrió P, Pinto M, Ecker G, Sanz F, Pastor M (2014)** Applicability Domain Analysis (ADAN): A Robust Method for Assessing the Reliability of Drug Property Predictions. *J Chem Inf Model 54(5):1500-11 doi: 10.1021/ci500172z.*
- **Marti-Solano M, Birney E, Bril A, Della Pasqua O, Kitano H, Mons B, Xenarios I, Sanz F (2014)** Integrative knowledge management to enhance pharmaceutical R&D. *Nat Rev Drug Discov 13(4): 239-40. PMID: 24687050.*

Other relevant publications from last 10 years

- **Selent J, Sanz F, Pastor M, Fabritiis G (2010)** Induced effects of sodium ions binding on dopaminergic G-protein coupled receptors. *PLOS Computational Biology 6: pii:e1000884. PMID: 20711351.*
- **Selent J, Bauer-Mehren A, López L, Loza MI, Sanz F, Pastor M (2010)** A novel multilevel statistical method for the study of the relationships between multireceptorial binding affinity profiles and in vivo endpoints. *Mol Pharmacol 77(2):149-58 PMID: 19903829.*
- **Obiol-Pardo C, Gomis-Tena J, Sanz F, Saiz J, Pastor M (2011)** A Multiscale Simulation System for the Prediction of Drug-Induced Cardiotoxicity. *J Chem Inf Model; 51(2):483-92. PMID: 21250697.*

Senior Researcher: *Núria B. Centeno.*

Other PI: *Jana Selent.*

PhD students: *Maria Martí, Pau Carrió, Ramón Guixa and Oriol López.*

Technicians: *Inés Martinez.*

Structural Bioinformatics Group

Baldo Oliva

http://sbi.imim.es/web

Research Outline

Protein-protein interactions play a relevant role among the different functions of a cell. Identifying the protein-protein interaction network of a given organism (interactome) is useful to shed light on the key molecular mechanisms within a biological system. A paradox in protein-protein binding is to explain how the unbound proteins of a binary complex recognize each other among a large population within a cell and how they find their best docking interface in a short time-scale. We interrogate protein structure to unveil its function, generate the network of interactions and to relate genes/proteins with diseases by means of exploiting the topology of the network.

Current Projects / Research lines

- **Study of the relationship between sequence, structure and function of proteins.**
  Characterization of the structural motifs involved in the function and interactions between proteins. Development of statistical potentials and analysis of physico-chemical potentials helping to describe the fold and function of proteins and its interactions with other macro-molecules.
- **Prediction of protein-protein and protein-DNA interations.**
  Structural analysis of docking approaches and development of new techniques towards the prediction of binding sites and the mechanisms of interface selection of protein-protein and protein-DNA interactions.
- **Analysis of protein interaction networks and its use on bio-medicine, helping to detect potential targets and prioritization of candidate disease-genes.**
  Development of methods to study and integrate information for different types of networks and application on the study of metastasis. Prediction of signalling networks, such as the phosphorylation network and other post-transcriptional modifications, and integration with genomic data, such as microarrays.

Selected publications 2014

- **Oliva B, Fernandez-Fuentes N (2014)** Knowledge-based modeling of peptides at protein interfaces: PiPreD. Bioinformatics. *PMID 25540186*.
- **Bonet J, Segura J, Planas-Iglesias J, Oliva B, Fernandez-Fuentes N (2014).** Frag'r'Us: knowledge-based sampling of protein backbone conformations for de novo structure-based protein design. *Bioinformatics 30(13):1935-6*.
- **Guney E, García-García J, Oliva B (2014)** GUILDify: a web server for phenotypic characterization og genes through biological data integration and network-based priorization algorithms. *Bioinformatics 30 (12):1789-90*.
- **Guney E, Oliva B (2014)** Analysis of the robustness of network-based disease-gene prioritization methods reveals redundancy in the human interactome and functional diversity of disease-genes. *PLoS One 9(4): e94686*.
- **Guney E, Oliva B (2014)** Analysis of the robustness of network-based disease-gene prioritization methods reveals redundancy in the human interactome and functional diversity of disease-genes. *PLoS One 9(4): e94686*.

Other relevant publications from last 10 years

- **Wright RH, Castellano G, Bonet J, Le Dily F, Font-Mateu J, Ballaré C, Nacht AS, Soronellas D, Oliva B, Beato M (2012)** CDK2-dependent activation of PARP-1 is required for hormonal gene regulation in breast cancer cells. *Genes Dev 26(17):1972-83*.
- **Espadaler J, Aragüés R, Narayanan E, Marti-Renom MA, Querol E, Avilés FX, Sali A, Oliva B (2005)** Detecting Remotely Related Proteins by Their Interactions and Sequence Similarity. *PNAS 17;102(20):7151-6*.
- **Gitter A, Siegfried Z, Klutstein M, Fornés O, Oliva B, Simon I, Bar-Joseph Z (2009)** Backup in gene regulatory networks explains differences between binding and knockout results. *Mol Syst Biol. 5:276*.

Senior Researchers: *Narcís Fernández Fuentes.*

Postdocs: *Daniel Aguilar and Joan Planas.*

PhD students: *Javier García-García, Jaume Bonet, Oriol Fornés, Manuel Alejandro Marín, Bernat Antón and Daniel Poglayen.*

Genetics and Neurosciences Programme

Coordinator: Rafael Maldonado

The scientific goal of the GNP is to understand genetic and molecular basis of development, function and disease of the Nervous System.

The programme covers three main areas: (1) Developmental Neurobiology, focusing on the study of cellular and molecular mechanisms that operate during embryonic development to ensure patterning and cell fate specification in the Nervous System; (2) Genetics of Cognitive Functions, with a special emphasis in two pathologies, Williams-Beuren Syndrome and Autism Spectrum Disorder; and (3) Neuropharmacology, focused on the neurobiological substrate of drug addiction, pain, affective and eating disorders, aimed at the identification of new therapeutic targets in the Central Nervous System. The programme has participated in NIH grants. Research activities of the GNP have led to the creation of two spin-off, q-Genomics SL and ZeClinics, and several contracts with pharmaceutical companies, including the license of two patents to an external enterprise.

- **Laboratory of Neuropharmacology (NeuroPhar)**
  Rafael Maldonado
- **Human and Medical Genetics**
  Luis Alberto Pérez Jurado
- **Developmental Biology**
  Berta Alsina
- **Developmental Biology: Ear Development**
  Fernando Giráldez
- **Developmental Neurobiology**
  Cristina Pujades

Laboratory of Neuropharmacology (NeuroPhar)

Rafael Maldonado

www.upf.edu/neurophar

Research Outline

Our main interest is the identification of new therapeutical targets at the nervous system level. The group has focused its activities in the neurochemical and neuroanatomical bases of the dependence to opioids and cannabinoids employing murine models. We have also studied the possible use of some of these compounds in the treatment of pain, cognitive, affective and eating disorders. Therefore, we use a classical pharmacological strategy complemented with the use of genetically modified animals, in particular, knockout mice, and biochemichal techniques to quantify in vivo the concentration of several monoamines. We are also interested in studying the involvement of the endogenous opioid (EOS), cannabinoid (ECS) and hipocretinergic (EHS) systems in the physiopathology of affective disorders and cognitive deficits.

Current Projects / Research lines

- Involvement of specific components of the EOS in the mechanisms underlying nicotine and cocaine addiction (RM)
- New therapeutic approaches for the treatment of drug addiction (RM)
- Involvement of specific components of the EOS and ECS in the mechanisms underlying palatable food-seeking behaviour (RM)
- Role of the EOS, ECS and serotonergic system in neuropathic, osteoarthritic and inflammatory pain, search for new pharmacological targets and analgesic compounds (RM)
- Participation of the ECS in the vulnerability of adolescents to alcohol consumption (RM)
- Evaluation of acylethanolamide-based neuroprotectants in animal models of perinatal and adult brain hypoxia (RM)
- Involvement of the EHS in the addictive properties of nicotine (relapse) and of cannabinoids (FB)
- Role of the EHS in the mechanisms underlying aversive memories (consolidation and extinction) (FB)
- Neurobiological mechanisms involved in the cognitive deficits associated with nicotine withdrawal (FB)
- Molecular and cellular mechanisms, e.g. mTOR pathway, involved in the cognitive function controlled by the ECS (AO)
- Targeting the ECS for pharmacological therapeutic approaches in fragile X syndrome (AO)
- Effects of chronic THC exposure in the brain (cognitive and fine motor coordination deficits) (AO)

Selected publications 2014

- **Vallée M, Vitello S, Bellocchio L, Hébert-Chatelain E, Monlezun S, Martin-Garcia E, Kasanetz F, Baillie GL, Panin F, Cathala A, Roullot-Lacarriere V, Fabre S, Hurst DP, Lynch DL, Shore DM, Deroche-Gamonet V, Spampinato U, Revest JM, Maldonado R, Reggio PH, Ross RA, Marsicano G, Piazza PV (2014)** Pregnenolone can protect the brain from cannabis intoxication. *Science, 343(6166):94-8.*
- **Pujadas Ll, Rossi D, Andrés R, Teixeira CM, Serra B, Parcerisas A, Maldonado R, Giralt E, Carulla N, Soriano E (2014)** Reelin interacts with AB42 oligomers, modulates amuloid-beta aggregation and rescues the cognitive deficits of Alzheimer's Disease. *Nature Communications, 5:3443.*
- **Gutierrez-Cuesta J, Burokas A, Mancino S, Kummer S, Martín-García E, Maldonado R (2014)** Effects of genetic deletion of endogenous opioid system components on the reinstatement of cocaine-seeking behavior in mice. *Neuropsychopharmacology, 39(13):2974-88.*
- **Chu Sin Chung P, Keyworth HL, Martin-Garcia E, Charbogne P, Darcq E, Bailey A, Filliol D, Matifas A, Scherrer G, Ouagazzal AM, Gaveriaux-Ruff C, Befort K, Maldonado R, Kitchen I, Kieffer BL (2014)** A Novel Anxiogenic Role for the Delta Opioid Receptor Expressed in GABAergic Forebrain Neurons. *Biological Psychiatry, 77(4):404-15.*
- **Planagumà J, Leypoldt F, Mannara F, Gutierrez-Cuesta J, Martin-Garcia E, Aguilar E, Marteen J, Petit-Pedrol M, Jain A, Balice-Gordon R, Lakadamyali M, Graus F, Maldonado R, Dalmau J (2014)** Human N-Methyl-D-Aspartate Receptor Antibodies Alter Memory and Behavior in Mice. *Brain. doi: 10.1093/brain/awu310. Epub 2014 Nov 11.*

Other relevant publications from last 10 years

- **Laurent P, Becker J.A, Valverde O, de Kerchove A, Schiffmann S.N, Maldonado R, Vassart G, Parmentier M (2005)** The prolactin-releasing peptide acts as a functional antagonist of the opioid system through its receptor GPR10. *Nature Neurosci 8: 1735-41.*
- **Puighermanal E, Marsicano G, Busquets-Garcia A, Lutz B, Maldonado R, Ozaita A (2009)** Cannabinoid modulation of hippocampal long-term memory is mediated by mTOR signaling. *Nat Neurosci 12(9):1152-8.*
- **Busquets-Garcia A, Gomis-González M, Guegan T, Agustín-Pavón C, Pastor A, Mato S, Pérez-Samartín A, Matute C, de la Torre R, Dierssen M, Maldonado R, Ozaita A (2013)** Targeting the endocannabinoid system in the treatment of fragile X syndrome. *Nature Med 19(5):603-7.*

Other PIs: *Fernando Berrendero Díaz, Andrés Ozaita Mintegui and Josep-Eladi Baños Díez.*

Postdocs: *Elena Martín García, Simona Andreea Bura, Antonio Ortega Álvaro, Sueli Mendonça Netto and David Cabañero Ferri.*

PhD students: *Xavier Viñals Álvarez, Carmen La Porta, Elk Kossatz de Mello, Samantha Mancino, Míriam Gutiérrez Martos, Victoria Salgado Mendialdúa, Laura Cutando Ruiz, Maria Gomis González, África Flores de los Heros, Rocío Saravia Santos, Roger Negrete Buela, Sami Kummer, Itzel Montserrat Lara Mayorga, Alba Navarro Romero, Miriam Martínez Navarro, Jefferson Pires Galvanho and Mireia Carcolé Estrada.*

Technicians: *Raquel Martín García, Cristina Fernández Avilés, Dulce Real Muñoz, Marta Linares López, Roberto Cabrera Ortega, Francisco Porrón López and Neus Morgui Valls.*

Project Manager: *Miquel-Àngel Serra Beltrán.*

Human and Medical Genetics

Luis Alberto Pérez Jurado

http://www.upf.edu/genetica/
http://www.qgenomics.com

Research Outline

The main focuses of our research are the genetic disorders caused by genomic mutations, the mutational mechanisms of the human genome, and some monogenic diseases of human development, integrating clinical and molecular research along with cellular and animal models. We search for better biomarkers for early diagnosis of germline and somatic disease, and provide appropriate genetic counseling to the families. Translation and transfer of the generated knowledge is achieved through the clinical services in the linked hospitals and the Spin-off qGenomics, developing specific tools and applications for personalized medicine.

Current Projects / Research lines

- **Structural human genome variation and disease susceptibility**
  We investigate molecular mechanisms of somatic and germline genome instability using improved tools for detection of complex structural changes of the genome.
- **Williams-Beuren (WBS) and duplication (DUP7) syndromes**
  WBS and DUP7 are reciprocal and recurrent genomic disorders caused by dosage imbalance of genes affecting the cardiovascular system, cognition and behavior. Clinical and molecular research, mouse models and patient-derived pluripotent cells are used to unravel these disorders and identify therapeutic targets.
- **Molecular bases of autism spectrum disorders and human malformations**
  Through the integration of clinical and multi-omic data, we investigate the etiology of these multifactorial developmental disorders to define biomarkers for early diagnosis and help families with genetic counseling.
- **Diagnosis of genetic diseases and personalized medicine**
  The Spin-off qGenomics offers valuable genetics and genomics products addressed to investigators and clinicians, developing specific tools for early translation into clinical diagnosis, prognosis and personalized medicine.

Selected publications 2014

- **González JR, Cáceres A, Esko T, Cuscó I, Puig M, Esnaola M, Reina J, Siroux V, Bouzigon E, Nadif R, Reinmaa E, Milani L, Bustamante M, Jarvis D, Antó JM, Sunyer J, Demenais F, Kogevinas M, Metspalu A, Cáceres M, Pérez-Jurado LA (2014)** A common 16p11.2 inversion underlies the joint susceptibility to asthma and obesity. *Am J Hum Genet 94:361-72*.
- **Argente J, Flores R, Gutiérrez-Arumí A, Verma B, Martos-Moreno GÁ, Cuscó I, Oghabian A, Chowen JA, Frilander MJ, Pérez-Jurado LA (2014)** Defective minor spliceosome mRNA processing results in isolated familial growth hormone deficiency. *EMBO Mol Med 6:299-306*.
- **Segura-Puimedon M, Sahún I, Velot E, Dubus P, Borralleras C, Rodrigues AJ, Valero MC, Valverde O, Sousa N, Herault Y, Dierssen M, Pérez-Jurado LA, Campuzano V (2014)** Heterozygous deletion of the Williams-Beuren syndrome critical interval in mice recapitulates most features of the human disorder. *Hum Mol Genet 23:6481-94*.
- **Martos Moreno GÁ, Serra-Juhé C, Pérez-Jurado LA*, Argente J* (2014)** Under-diagnosed Beckwith-Wiedemann syndrome among early-onset obese children. *Arch Dis Child. 99:965-7*.
- **Pérez-García D, Flores R, Brun-Gasca C, Pérez-Jurado LA (2014)** Lateral preference in Williams-Beuren syndrome is associated with cognition and language. *Eur Child Adolesc Psychiatry*.

Other relevant publications from last 10 years

- **Cuscó I, Medrano A, Gener B, Vilardell M, Gallastegui F, Villa O, González E, Rodríguez-Santiago B, Vilella E, Del Campo M, Pérez-Jurado LA (2009)** Autism-specific copy number variants further implicate the phosphatidylinositol signaling pathway and the glutamatergic synapse in the etiology of the disorder. *Hum Mol Genet 18:1795-804*.
- **Campuzano V, Segura M, Terrado V, Sánchez-Rodríguez C, Coustest M, Menacho-Márquez M, Nevado J, Bustelo XR, Francke U, Pérez Jurado LA (2012)** Reduction of NADPH-oxidase activity ameliorates the cardiovascular phenotype in a mouse model of Williams-Beuren syndrome. *PLoS Genet, 8(2):e1002458*
- **Jacobs K, Yeager M, Zhou W, Wacholder S, Wang Z, Rodríguez-Santiago B, Hutchinson A, Villa O,..(180 more authors)…, Pérez-Jurado LA*, Chanock SJ* (*co-last authors) (2012)** Detectable clonal mosaicism and its relationship to aging and cancer. *Nat Genet 44(6):651-8*.

Other PIs: *Mª Victoria Campuzano Uceda, Miguel del Campo Casanelles, Ivon Cuscó Martí and Lluís Armengol Dulcet (qGenomics director).*

Postdocs: *Benjamín Rodríguez Santiago, Olaya Villa Marcos, Cristina Hernando Davalillo, Clara Serra Juhé and Roser Corominas Castiñeira.*

PhD students: *Aïda Homs Raubert, Marta Codina Solà, Armand Gutiérrez Arumí, Judith Reina Castillón, Débora Pérez García and Cristina Borralleras Fumaña.*

Technicians: *Raquel Flores Peirats, Manel García Aragonés and Sònia Cano Redondo.*

IT technician: *Xavier Armengol Dulcet.*

Research Manager CIBERER: *Research Manager CIBERER.*

Developmental Biology

Berta Alsina

http://lavandula.imim.es/Alsina_Group

Research Outline

Our research focuses in understanding the molecular and cellular events underlying the development of the inner ear. This organ, a highly sophisticated sensory organ of our head, is responsible for the senses of hearing and balance. Its dysfunction causes the most prevalent sensorineural deficit in our society. We want to understand which genes are implicated in the development of sensory neurons and hair cells and whether their dysfunction causes deafness. We also focus on mechanisms of hair cell regeneration. Combined with genetic manipulations and gene regulatory network analysis, we focus in the morphogenetic events taking place during inner ear development to understand how cells organize and generate an organ with a precise 3D shape. The laboratory combines cell tracing, genetic, in vivo imaging and biomechanical approaches.

Current Projects / Research lines

- **Neurosensory Development of the inner ear.**
  We are studying the transcription factors and signaling pathways involved in early specification of neuronal and sensory progenitors of the inner ear. Developmental genes causing deafness are also investigated to link developmental processes with disease.
- **Morphogenesis of the inner ear.**
  We are studying several morphogenetic processes taking place during inner ear development. On one side, how a cavity develops inside the organ and the inner ear transits from a 2D structure to a 3D structure. Our data is can be translated to other organs with cavities such as the gut, brain or heart. On the other, we are analyzing the epithelial-mesenchymal transition (EMT) events underlying neuronal delamination.
- **Regeneration of hair cells.**
  Humans cannot regenerate damage hair cells, which leads to deafness. A central goal in inner ear biology is to find possible pathways involved in hair cell regeneration that could be used in future therapeutic strategies. We have found that retinoic acid signaling has a central role in hair cell regeneration and we are currently investigating its target genes.

Selected publications 2014

- **Radosevic M, Fargas L, Alsina B (2014)** The role of her4 in inner ear development and its relationship with proneural genes and Notch signalling. *PLoS One, 9(10):e109860. doi: 10.1371.*
- **Maier EC, Saxena A, Alsina B, Bronner ME, Whitfield TT (2014)** Sensational placodes: Neurogenesis in the otic and olfactory systems. *Dev Biol 126(Pt 1):53-9.*

Other relevant publications from last 10 years

- **Radosevic M, Robert-Moreno A, Coolen M, Bally-Cuif L and Alsina B (2011)** Her9, a zebrafish Hes1 ortholog, represses neurogenic fate in the inner ear downstream of Tbx1 and RA. *Development 138(3):397-408.*
- **Abelló B, Khatri S, Scotting P, Giráldez F, Alsina B (2010)** Independent regulation of Sox3 and Lmx1b by FGF and BMP signaling gradients determines the neurogenic and non-neurogenic domains in the otic placode. *Dev Biol 339(1):166-78.*
- **Naranjo S, Voesenek K, de la Calle-Mustienes E, Robert-Moreno A, Kokotas H, Grigoriadou M, Economides J, Van Camp G, Hilgert N, Moreno F, Alsina B, Petersen M, Kremer H, Gomez-Skarmeta JL (2010)** Multiple enhancers located in a 1 Mb region upstream of POU3F4 promote expression during inner ear development and may be required for hearing. *Hum Genet 128(4):411-9.*

Postdocs: *Esteban Hoijman.*

PhD students: *Davide Rubbini and Laura Fargas.*

Technicians: *Marta Linares and Miquel Sas.*

Developmental Biology: Ear Development

Fernando Giráldez

www.upf.edu/devbiol/projectes/progenitors.html

Research Outline

One basic problem in development is to understand how specific cell types are generated from pluripotent progenitors throughout embryonic life. We address this question by exploring the development of neurons and hair cells in the inner ear. We study the genetic networks that specify the onset of hair cells and neurons in the ear how this is timed during development. This knowledge is crucial for developing new tools for regenerative therapies directed to alleviate hearing impairment.

Current Projects / Research lines

- **The origin of hair cells in the embryo:**
  Atonal1 (Atoh1) is a basic Helix-Loop-Helix transcription factor that behaves as a master gene for the development of inner ear hair cells. Atoh1 is necessary and sufficient for hair cell development. Atoh1 is able also to drive cell production also in the adult inner ear and to convert non-sensory cells into hair cells. The regulation of Atoh1, therefore, is at the heart of hair cell development and regeneration. Our goal is to understand the molecular regulation of Atoh1 in ear precursors and the production of hair cells in the embryo. This work is supported by MINECO.
- **Regenerating hair cells.**
  Tissue regeneration may be improved by reactivating similar genetic programs that operate during embryonic life. This is the value of research on hair cell development as applied to alleviate hearing loss. Studies on the molecular regulation of Atoh1 are focused on finding the conditions that favour its activation during transdifferentiation procedures in different cellular contexts. This work is oriented to design better techniques for hair cell regeneration and hearing repair. For this purpose we collaborate with Thomas Schimmang (IBGM, CSIC-UVA) and Marcelo Rivolta within a project supported by Fundació La Marató TV3.

Selected publications 2014

- **Petrovic J, Formosa-Jordan J, Luna JC, Abelló G, Ibañes M, Neves J, Giraldez F (2014)** Ligand dependent Notch signaling strength orchestrates lateral induction and lateral inhibition in the developing inner ear. *Development 141(11):2313-24*
- **Petrovic J, Abelló G, Gálvez H, Neves J, Giraldez F (2014)** Differential regulation of Hes/Hey genes during inner ear development. *Developmental Neurobiology doi: 10.1002/dneu.22243.*

Other relevant publications from last 10 years

- **Kamaid A, Neves J, Giraldez F (2010) Id gene regulation and function in the prosensory domains of the chicken inner ear: a link between BMP signaling and Atoh1. J.Neuroscience 30(34):11426-34.**
- **Dominguez-Frutos E, Lopez-Hernandez I, Vendrell V, Neves J, Gallozzi M, Gutsche K, Quintana L, Sharpe J, Knoepfler P, Eisenman R, Trumpp A, Giraldez F, Schimmang T (2011) N-myc controls proliferation, morphogenesis and patterning of the inner ear. J Neuroscience 11;31(19):7178-89.**
- **Neves J, Parada C, Chamizo M, Giraldez F (2011) Jagged1 regulates the restriction of Sox2 expression in the developing chicken inner ear: a mechanism for sensory organ specification. Development 138: 735-44.**

Postdocs: *Gina Abelló.*

PhD students: *Héctor Gálvez.*

Technicians: *Miquel Sas and Marta Linares.*

Developmental Neurobiology

Cristina Pujades

www.upf.edu/devbiol/projectes/cns.html

Research Outline

We are interested in understanding how sensory inputs from the inner ear are conveyed and relayed into the hindbrain, and how neural circuits are then established within the brain. Our approach has been to dissect how neural elements of both structures are generated upon morphogenesis, in order to understand how they can connect later on. We use zebrafish embryos because they allow us to combine genetic tools with high resolution imaging techniques. We think this approach will provide us understanding in different biological processes such as patterning and morphogenesis, and reveal principles underlying how the circuits in the brain produce behavior.

Current Projects / Research lines

- We have generated the complete lineage tree of the neurosensory elements of the inner ear; now we want to **uncover the proneural gene requirements controlling different neurosensory progenitor potential** and how are environmentally regulated. We seek to understand whether different functional modalities rely on sensory neuron birthplace and position within the SAG.
- To **generate a 3D-functional map of the hindbrain**. We want to **monitor the neural activity brain-wide** upon evoked stimulation and to **identify the central neuronal circuits responsible of vestibular/acoustic sensory modalities**. We will address these questions on the zebrafish larva, which exhibit stereotyped behavioral responses to various stimuli associated with several sensory modalities.
- **How the precise regulation of neurogenesis is achieved in specific regions of the hindbrain** and how the progenitor capacity is allocated. We combine high resolution imaging and transcriptional activation/gene signature analyses. We will **generate the lineage of the boundary cell population** –generated at the rhombomere interface- by cell tracing in transgenic fish lines specifically labelling this cell population.

Selected publications 2014

- **Calzolari S, Terriente J, Pujades C (2014)** Cell segregation in the rhombomeric boundaries relies in physical mechanisms based in an actomyosin cable. *EMBO J 33(7):686-701*.
- **Joya X, Garcia-Algar O, Vall O, Pujades C (2014)** Transient exposure to ethanol during zebrafish embryogenesis results in defects in neuronal differentiation: an alternative model system to study FASD. *PLoS ONE 9(11):e112851. doi: 10.1371/journal.pone.0112851*.
- **Joya X, Garcia-Algar O, Salat-Batlle J Pujades C Vall O (2014)** Advances in the development of novel antioxidant therapies as an approach for fetal alcohol syndrome prevention. *Birth Defects Res A Clin Mol Teratol doi: 10.1002/bdra.23290*.

Other relevant publications from last 10 years

- **Sapède D, Dyballa S, Pujades C (2012)** Cell lineage analysis reveals three different progenitor pools for neurosensory elements in the otic vesicle. *J Neurosc 32(46):16424-34*.
- **Jimenez-Guri E, Udina F, Colas JF, Sharpe J, Padrón L, Torres M, Pujades C (2010)** Clonal analysis in mice underlines the importance of positional information during hindbrain segmentation. *PLoS ONE 5(4): e10112*.
- **Sapède D, Pujades C (2010)** Hedgehog signaling governs the development of sensory epithelium and its associated innervation in the zebrafish inner ear. *J Neurosc 30:3612-23*.

Postdocs: *Javier Terriente*.

PhD students: *Andrea Zecca,Sylvia Dyballa and Adrià Voltes*.

Master's students: *Ivan Belzunce*.

Transversal Programme: Public Health and Education in Health Sciences

Coordinator: Fernando García-Benavides

The main objective of this programme is to improve the social perspective of health and education in life and health sciences. The Programme has three goals: (i) a scientific objective, which studies how social and economic policies, such as environmental and working conditions, are affecting the health of population, (ii) to serve as a bridge between basic research produced in other programmes and hospitals and other public health centres, and (iii) the development of educational research in order to improve teaching's quality.

The link and knowledge transfer between basic research and public health is ensured by the inclusion of the Centre for Research in Occupational Health (CiSAL), the Research Centre Environmental Epidemiology (CREAL) and the Health Service Research Unit in the IMIM-Parc Salut Mar, where Hospital del Mar plays a central role. Academic work is published through scientific reports and papers, and transferred by workshops and guidelines, assisting and influencing others to act on the recommendations.

The educational research to improve teaching's quality is carried out by the Research Group in Health Sciences Education.

- **Center for Research in Occupational Health (CiSAL)**
  Fernando García-Benavides
- **Research Group in Health Sciences Education**
  Jordi Pérez & Josep Eladi Baños

Center for Research in Occupational Health (CiSAL)

Fernando García-Benavides

www.upf.edu/cisal/en/Publications/

Research Outline

The objective of the CiSAL is to study occupational health issues (mainly injuries, mental and musculoskeletal disorders) and their implications for employees, businesses and governments. All of them particularly relevant for Social Welfare Systems. Our group aims to serve as an academic venue producing and disseminating useful scientific knowledge to inform policy with the ultimate goal of improving the health of workers.

Current Projects / Research lines

- Intervention and evaluation to minimize occupational incapacity from musculoskeletal disorders (INTEVAL) project is a European project (11 countries are involved) that aims to implement an innovative intervention in the workplace that minimizes the adverse impact of disabling MSDs on workers' well-being and the financial cost of sickness absence for employers and social security systems.
- Social welfare state and health (EBISA) project analyses the relationship between labour market trajectories, permanent disability and mortality in a cohort of more than 1 million of workers affiliated to the Social Security System.
- Traffic-related occupational injuries (LTT) project involves analyzing data on work-related road traffic injuries in Spain between 2000 and 2012 from the information available in the records from Traffic Authority.
- Central American Survey of Working Conditions and Health (ECCTS) project, in collaboration with seven other Central American Universities (SALTRA), pursues to evaluate employment and working conditions and health indicators in Central America.

Selected publications 2014

- **Benavides FG, Duran X, Gimeno D, Vanroelen C, Martínez JM (2014)** Labour market trajectories and early retirement due to permanent disability: a study based on 14 972 new cases in Spain. *Eur J Public Health. pii: cku204.*
- **Benavides FG, Wesseling C, Delclos GL, Felknor S, Pinilla J, Rodrigo (2014)** Working conditions and health in Central America: a survey of 12.024 workers in sin six countries. *Occup Environ Med 71(7):459-65.*
- **López-Ruíz M, Martínez JM, Pérez K, Novoa AM, Tobías A, Benavides FG (2014)** Impact on road safety interventions on traffic-related occupational injuries in Spain, 2004-2010. *Accid Anal Prev. 66:114-9.*
- **Gimeno D, Bultmann U, Benavides FG, Alexanderson K, Abma FI, Ubalde-Lopez M, Roelen CA, Kjeldgård L, Delclos GL (2014)** Cross-national comparisons of sickness absence systems and statistics: towards common indicators. *Eur J Public Health 24(4):663-6.*
- **Robert G, Martinez JM, Garcia AM, Benavides FG, Ronda E (2014)** From the boom to the crisis: changes in employment conditions of immigrants in Spain and their effects on mental health. *Eu J Public Health 24(3):404-9.*

Other relevant publications from last 10 years

- **Ronda Pérez E, Benavides FG, Levecque K, Love JG, Felt E, Van Rossem R (2012)** Differences in working conditions and employment arrangements among migrant and non-migrant workers in Europe. *Ethn Health 17(6):563-77.*
- **Ubalde-Lopez M, Delclos GL, Calvo E, Benavides FG (2013)** Influence of new secondary diagnoses on the duration of non-work related sickness absence episodes. *J Occup Environ Med 55(4):460-4.*
- **Coggon D, Ntani G, Vargas-Prada S, Martinez JM, Serra C, Benavides FG, Palmer KT, et al (2013)** International variation in absence from work attributed to musculoskeletal illness: findings from the CUPID study. *Occup Environ Med 70(8):575-84.*

Seniors Researchers: *Consol Serra, Jordi Delclós and David Gimeno.*

Postdocs: *Jose María Ramada Rodilla, Sergio Vargas-Prada, Xavier Duran Rodilla and Albert Sánchez.*

PhD students: *María López, Mónica Ubalde, María Andrée López, Elena Zaballa, Clara Gual, Pamela Merino, Esther Colell, Dinora Bernal, Marianela Rojas, Núria Mancebo, Rocio Villar and Joan Mirabent.*

Technicians: *Montserrat Fernandez and Sandra Garrido.*

Project Manager: *Bàrbara Pons.*

Research Group in Health Sciences Education

Jordi Pérez & Josep Eladi Baños

Research Outline

The Group of Research on Education in Health Sciences (GRECS) has four main objectives:

1. To improve the educational project of the FCSV of UPF.
2. To enhance the initiatives which improve the university teaching.
3. To facilitate the contact with secondary education whit an increase of scientific interest of young students.
4. To bring closer together society and science.

To achieve these aims, GRECS has four domains of activities:

1. Evaluation of teaching of the bachelors of the FCSV of UPF
2. Activities in educative research.
3. Innovation and development in education.
4. Communication and public engagement activities.

Current Projects / Research lines

a) Evaluation of teaching projects at FCSB of UPF

- Problem-based learning (PBL)
- Students' mentoring
- Portfolio for generic competencies

b) Research in education:

- Inquiry-based methods and the contextualization of science in daily life, social and scientific facts to promote the interests of young people in science.
- Inquiry-based methods (ABP), evaluation of learning (effects of PBL, continuous evaluation and final outcomes, learning styles and recall), academic stress (stress sources and psychological and physical discomfort)

c) Innovation and educative development

- Teaching material
- Interdisciplinary didactic units
- Communication and information technologies to stimulate the cooperative work of teachers
- Activities to enhance the interest of science for young students (many in collaboration with PRBB)

d) Science, Communication and Society

- NERRI, Neuroenhancement and Responsible Research and Innovation
- KiiCS, Knowledge innovation in Incubation and Creation for Science
- Quiral, Health and Medicine Information in media
- Recercaixa Communication and Society

Selected publications 2014

- **Andión, O.; Cañellas, M.; Baños, JE. (2014)** Physical well-being in postoperative patients: a survey in patients, nurses and physicians. *Journal of Clinical Nursing, 23: 1421-1429.*
- **Revuelta G. (2014)** Impacts of science communication on publics, cities and actors. JCOM. *(2014); 01(C01).*
- **Pérez, J.; Aramburu, J.; Baños, JE.; Bosch, F.; Díez, J.; Farré, M.; Girvent, M.; Sentí, M.; Valverde, O. (2014)** Uso del cine comercial como herramienta docente en estudios en ciencias de la salud. Una experiencia multidisciplinar y colectiva. *Fundación Educación Médica, 17: 131-135.*
- **Agell,L.; Soria, V.; Carrió, M. (2014)** Using Role Play to Debate Animal Testing, *Journal of Biological Education, DOI: 10.1080/00219266.2014.943788*
- **Rodríguez, G.; Baños, JE. (2014).** Frankenstein: un mito más allá del cine de ciencia ficción. *Revista Medicina y Cine, 10: 37-44.*

Other relevant publications from last 10 years

- **Farré, M.; Arribas, S.; Pérez, J.; Baños, J.E. (2013).** Bioethical principles, clinical research and popular movies. *Medical Education, 47: 1141-1142.*
- **Carrio, M.; Larramona, P. Baños, J.E.; Pérez, J. (2011)** The effectiveness of the hybrid problem-based learning approach in the teaching of biology: a comparison with lecture-based learning. *Journal of Biological Education, 45: 229-235.*
- **Gaskell G, Allansdottir A, Allum N, Castro P, Esmer Y, Fischler C, Jackson J, Kronberger N, Hampel J, Mejlgaard N, Quintanilha A, Rammer A, Revuelta G, Stares S, Torgersen H and Wagner W. (2011)** The 2010 Eurobarometer on the life sciences. *Nature Biotechnology, 29: 113-114.*

Seniors Researchers: **Education:** *Laia Agell, Eva Baillés, Mar Carrió, Nuria B. Centeno, Silvia Lope, Miguel Angel Mayer, Elisabeth Moyano, Meritxell Girvent, Mariano Sentí, Vanessa Soria and Mireia Valero.* **Communication:** *Gema Revuelta, Vladimir de Semir, Emma Cots, Carme Pérez and Núria Saladié.*

PhD students: *Gemma Rodríguez.*

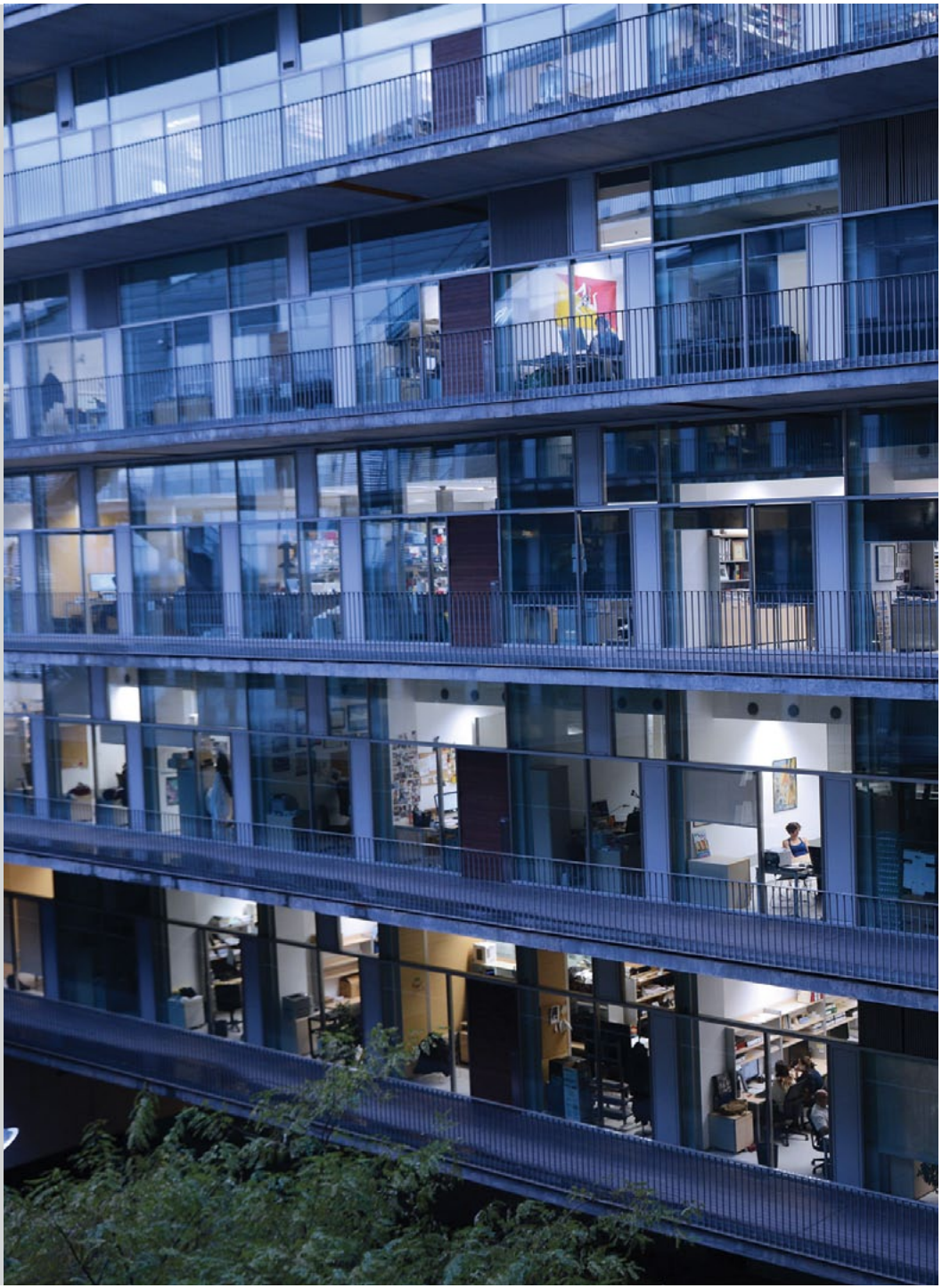
Technicians: *Pilar Larramona.*

Core facilities

Our faculty has access to cutting-edge Core Facilities in the PRBB offering the latest technologies in their fields. The Genomics, Peptide Synthesis and Scientific Information Technologies Core Facilities are run directly by the DCEXS, and they are open to the whole PRBB community, while the Proteomics and Flow Cytometry facilities are jointly managed with the CRG. The UPF also contributes to the Advanced Light Microscopy Unit (CRG-UPF) and has access to other facilities belonging to the rest of institutions in the PRBB.

The Genomics unit offers a wide variety of methodologies for nucleic acid analyses and features state-of-the-art instruments for high-throughput genetic analysis and functional genomics, as well as de novo sequencing. The Proteomics Unit focuses on ultimate technology mass spectrometry for hypothesis free as well as targeted proteomics. Applications include identification of proteins and posttranslational modifications, biomarker analysis, and quantitative proteomics using label free quantification, iTRAQ and SILAC. The Peptide Synthesis produces custom peptides and performs the conjugation of peptides to carrier proteins to generate antibodies. The Flow Cytometry Unit, with its six analyzers and two sorters, is one of the most comprehensive facilities and the largest Becton Dickinson site in Spain. The Microscopy Unit covers the whole spectrum of advanced microscopy applications with a recent focus on super-resolution microscopy. Among the facilities ran by other institutions, we could mention the PRBB's animal facility, one of the most complex and automated in Europe, with capacity for 70,000 mice under SPF conditions and for 6,000 mice in standard conditions (UBIOMEX), as well as 50,000 zebrafish. As of June 2010, the programme of care and use of laboratory animals has the full accreditation from the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).

- **CRG/UPF Advanced Light Microscopy Unit (ALMU)**
  Timo Zimmermann (CRG)
- **UPF/CRG Joint Flow Cytometry Unit**
  Òscar Fornas
- **Genomics Core Facility**
  Ferran Casals
- **Peptide Synthesis Facility**
  David Andreu
- **Proteomics Unit**
  Eduard Sabidó (CRG)



CRG/UPF Advanced Light Microscopy Unit (ALMU)

Timo Zimmermann (CRG)

www.crg.eu/en/core/programmes-groups/advanced-light-microscopy-unit

Service & Research

In 2014, the total booked microscope usage time of the unit reached 18300 hours in approx. 5000 separate bookings. This corresponds to approximately seven hours of daily usage on the bookable microscope systems plus many additional hours on equipment without mandatory booking and on special equipment. During the year, 120 users from 28 CRG research groups and 52 users from 27 UPF-CEXS groups have used the unit. Additionally the unit was used by 33 users from 13 groups of other PRBB institutes and for projects from external visitors. On average, 88 investigators use the unit every month.

The ALMU was one of the few sites worldwide that performed beta-testing of the latest 3D STED technology for Leica Microsystems. The unit also hosted the first Lightsheet Z1 system from Carl Zeiss Microimaging Spain for the first half of the year. The unit was involved in several additional tests of not yet released microscopy equipment.

Selected publications 2014

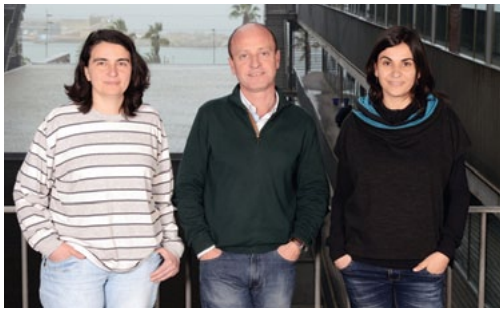
- **Pérez-Vilaró G, Fernández-Carrillo C, Mensa L, Miquel R, Sanjuan X, Forns X, Pérez-Del-Pulgar S, Díez J.** Hepatitis C virus infection inhibits P-body granule formation in human livers. *J Hepatol. 2015 Apr;62(4):785-90. [doi: 10.1016/j.jhep.2014.11.018]. Epub 2014 Nov 21.*

Other relevant publications from last 10 years

- **Grünberg R, Burnier JV, Ferrar T, Beltran-Sastre V, Stricher F, van der Sloot AM, Garcia-Olivas R, Mallabiabarrena A, Sanjuan X, Zimmermann T, Serrano L.** Engineering of weak helper interactions for high-efficiency FRET probes. *Nat Methods. 2013 Oct;10(10):1021-7. [doi: 10.1038/nmeth.2625]. Epub 2013 Sep 1.*

Technicians: *Xavier Sanjuan (UPF), Raquel García (CRG), Arrate Mallabiabarrena (CRG), Raúl Gómez (CRG) and Thomas Pengo (CRG).*

UPF/CRG Joint Flow Cytometry Unit



Òscar Fornas

www.upf.edu/sct/en/citometria/presentacio

Service & Research

The mission of the UPF/CRG Joint Flow Cytometry Unit is to provide researchers with technical expertise and training to access the state-of-the-art instrumentation, as well as technical and scientific advice to develop efficient and reliable flow cytometric assays with the highest quality control standards and productivity. Currently the Unit assists around 180 users within around 70 research groups. The Unit is one of the largest Flow Cytometry Unit in Spain and Europe. Currently equipped with state of the art instrumentation with 5 analyzers and 2 advanced cell sorters.

The Unit supports the use of a wide range of flow cytometry applications and new ones are developed and/or implemented responding to the facility needs or under user demand.

Since 2013, the UPF/CRG Flow Cytometry Unit is the Spanish Becton Dickinson Reference Site into the Becton Dickinson South Europe Delegation, due to its international recognition of excellence. That agreement facilitates national and international collaborations to develop and implement new methodologies and applications for the scientific community (see below) as well as offering special advanced training. The Unit also is a member of Core4fife strategic alliance (www.coreforlife.eu), the Excellence Alliance of Life Science Core Facilities in Europe, with the mission to explore the potential of coordinating and bundling core facility expertise and resources across institutes and countries in order to advance knowledge and to benefit the entire scientific and technological community.

Selected publications 2014

During last 3 years, the facility has been established as a reference site for single particle/cell sorting and nano-particle detection and sorting. On that direction we have developed and established relevant flow Cytometry methodologies and/or applications for the scientific community as follows:

- Flow Karyotyping: Has been established (2012-2014) in collaboration with Dr. Paul Lizzardi from Yale University, USA, for single chromosome sorting and sequencing *(pending to publish)*.
- Single virus sorting: Has been established (2013-2014) in collaboration with Dr. Manuel Martínez from Universidad de Alicante, Spain *(pending to publish)*.
- Extra Cellular Vesicles (EVs) detection and sorting: Project under development (2014) in collaboration with Dr. Ana Merino from IDIBELL, Spain *(pending to publish)*.

Technicians: *Eva Julià (IMIM) and Erika Ramírez (CRG).*

Genomics Core Facility

Ferran Casals

Service & Research

The Genomics Core Facility at the UPF provides a wide variety of methods for DNA and RNA analyses. Available equipments include liquid handling robots to automate pipeting tasks, capillary sequencers for Sanger sequencing and fragment analysis, DNA quantification and quality control with Picogreen and Bioanalyzer, real-time PCR and OpenArray system for absolute and relative quantification of nucleic acids (genotyping and gene expression), and two next-generation sequencing platforms from Illumina: MiSeq, ideal for targeted and small genome sequencing and NextSeq, a highly flexible platform performing a broad range of applications, from targeted resequencing to RNA profiling and whole-exome or genome sequencing.

The Genomics Core facility is also committed to research for the development of new technologies for genetic analysis. The laboratory develops its own research projects or in collaboration with other laboratories, mostly focusing in studies requiring the development of new laboratory methods for sample preparation. The projects include studies on rare diseases, degraded and non-invasive samples, small RNA or single cell sequencing.

The Genomics Core Facility also organizes courses on the new sequencing methodologies and pioneers some of their applications to medical genomics.

Selected publications 2014

- Population and genomic lessons from genetic analysis of two Indian populations. **Juyal G, Mondal M, Luisi P, Laayouni H, Sood A, Midha V, Heutink P, Bertranpetit J, Thelma BK, Casals F.** *Hum Genet. 2014 Oct;133(10):1273-87*

PhD students: *Guillem De Valles.*

Technicians: *Roger Anglada, Núria Bonet and Raquel Rasal.*

Peptide Synthesis Facility

David Andreu

Service & Research

During 2014 the facility has performed 151 custom synthesis jobs for 22 users, 9 from PRBB, 13 external. Sizes have ranged from 3 to 50 residues, with an average of 20. Special requests have included sequences with special (phosphorylated, acetylated, methylated, lipidated, D-) amino acids, fluorescent tags, etc. We have also performed conjugations of peptides to carrier protein for anti-peptide antibody production. Average turnover time for most jobs (including synthesis, HPLC purification, analytical documentation) is 1 week.

Technicians: *Javier Valle.*

UPF/CRG Joint Proteomics Unit

Eduard Sabidó (CRG)

Service & Research

The Proteomics Unit is a joint effort of Universitat Pompeu Fabra (UPF) and the Center of Genomic Regulation (CRG) to create an innovative core facility that provides high quality proteomics services to its final users, by providing proper expertise and advice, and by developing new methods and techniques.

The Proteomics Unit provides full service in a variety of proteomics applications including sample preparation, protein quantification, identification of post-translational modifications, and data analysis, among others. In addition to the services provided to the research community, the Proteomics Unit also promotes internal technology-driven research as an essential task to keep the unit at the forefront of the proteomics field.

As a reference proteomics center, the Unit has state-of-the-art equipment consisting on high resolution liquid chromatography and electrophoresis systems, and four advanced mass spectrometers to identify and quantify the proteins of interest.

The Proteomics Unit is part of the "Plataforma de Recursos Biomoleculares y Bioinformáticos (ProteoRed, Instituto Carlos III)" and "Proteomics Research Infrastructure Maximizing knowledge EXchange and access (PRIME-XS)", a prestigious international consortium of twelve partners that grants access to state-of-the-art proteomics technology to the European biological and biomedical research community.

Selected publications 2014

- Validation of semaphorin 7A and ala-β-his-dipeptidase as biomarkers associated with the conversion from clinically isolated syndrome to multiple sclerosis. **Cantó E, Tintoré M, Villar LM, Borràs E, Alvarez-Cermeño JC, Chiva C, Sabidó E, Rovira A, Montalban X, Comabella M.** J Neuroinflammation. *2014 Nov 13;11:181. doi: 10.1186/s12974-014-0181-8.*
- Influence of the digestion technique, protease, and missed cleavage peptides in protein quantitation. **Chiva C, Ortega M, Sabidó E.** *J Proteome Res. 2014 Sep 5;13(9):3979-86. doi: 10.1021/pr500294d. Epub 2014 Jul 28.*
- Profiling the secretome and extracellular proteome of the potato late blight pathogen Phytophthora infestans. **Meijer HJ, Mancuso FM, Espadas G, Seidl MF, Chiva C, Govers F, Sabidó E.** *Mol Cell Proteomics. 2014 Aug;13(8):2101-13. doi: 10.1074/mcp.M113.035873. Epub 2014 May 28.*
- Lifelong exercise training modulates cardiac mitochondrial phosphoproteome in rats. **Ferreira R, Vitorino R, Padrão AI, Espadas G, Mancuso FM, Moreira-Gonçalves D, Castro-Sousa G, Henriques-Coelho T, Oliveira PA, Barros AS, Duarte JA, Sabidó E, Amado F.** *J Proteome Res. 2014 Apr 4;13(4):2045-55. doi: 10.1021/pr4011926. Epub 2014 Mar 4.*
- Quantification of ErbB network proteins in three cell types using complementary approaches identifies cell-general and cell-type-specific signaling proteins. **Kiel C, Ebhardt HA, Burnier J, Portugal C, Sabidó E, Zimmermann T, Aebersold R, Serrano L.** J *Proteome Res. 2014 Jan 3;13(1):300-13. doi: 10.1021/pr400878x. Epub 2013 Dec 9.*

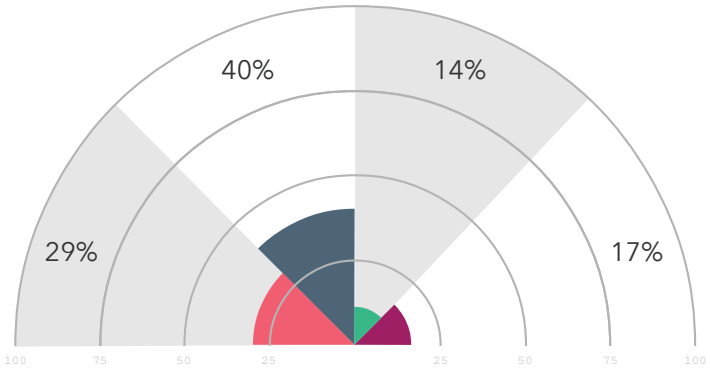
Postdocs: *Salvatore Cappadona (CRG).*

PhD students: *Mireia Ortega.*

Technicians: *Eva Borràs, PhD (UPF), Cristina Chiva, PhD (UPF), Guadalupe Espadas-Garcia (CRG) Francesco Mancuso (CRG), Ivonne Peña (UPF) and Jennifer Garcia (CRG).*

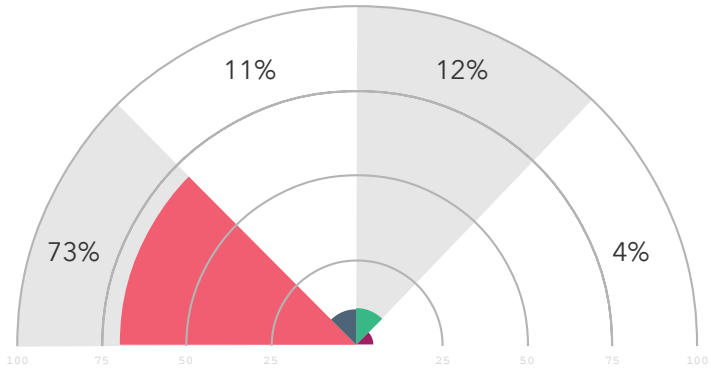
The DCEXS in numbers

External funding obtained in 2014



Competitive funding (origin)

	€000
International Admin (including FP7)	2672
State Administration	3707
Autonomical Administration	1291
Companies and Institutions	1623
Total	9293

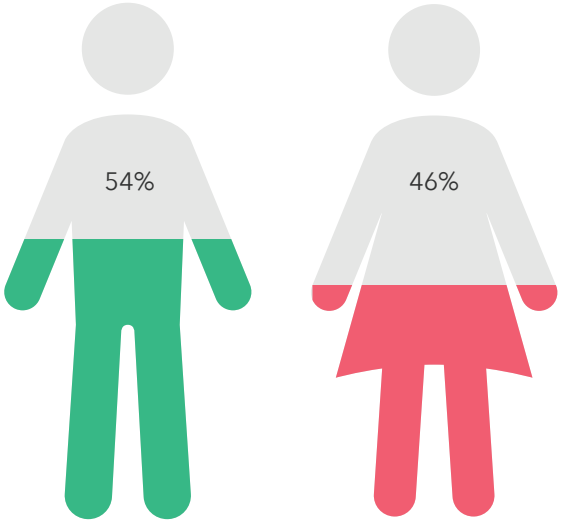


Competitive funding (type of grant)

	€000
Competitive	6819
Non competitive	973
Human Resources	1094
Infraestructure and institutional grants	407
Total	9293

The DCEXS in numbers

Personnel



	Men	Women
Group Leaders	30	10
Other PIs	7	3
Senior Researchers	7	3
Postdocs	42	51
PhD Students	62	83
Technicians	13	32
Project Managers	3	8

PhD in Biomedicine 2013/14

Total PhD students registered	**431**
New PhD students	119
Continuing PhD students	312

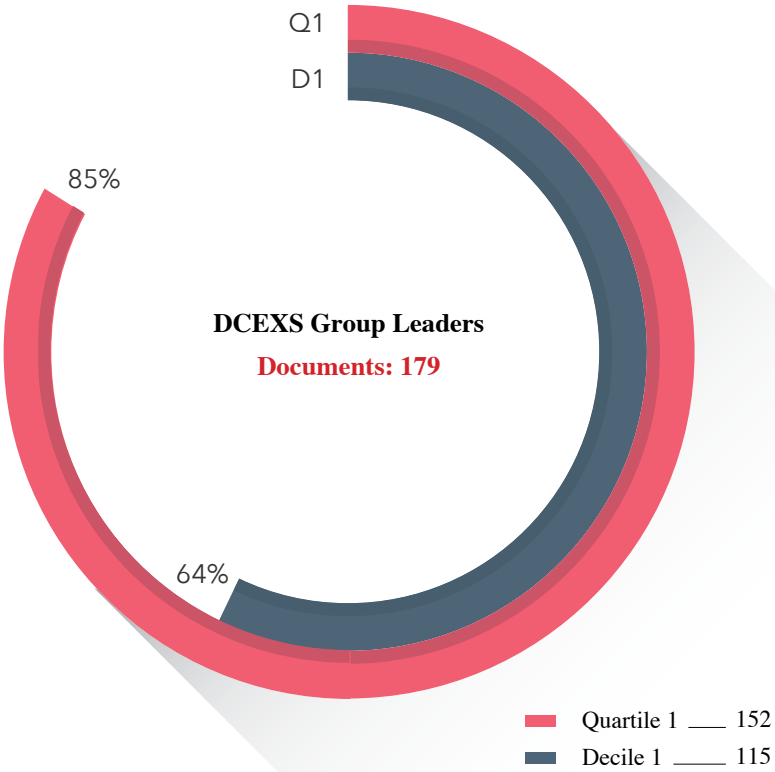
New PhD registrations per home university	
Catalunya	78
Rest of Spain	8
EU countries	21
Other countries	12

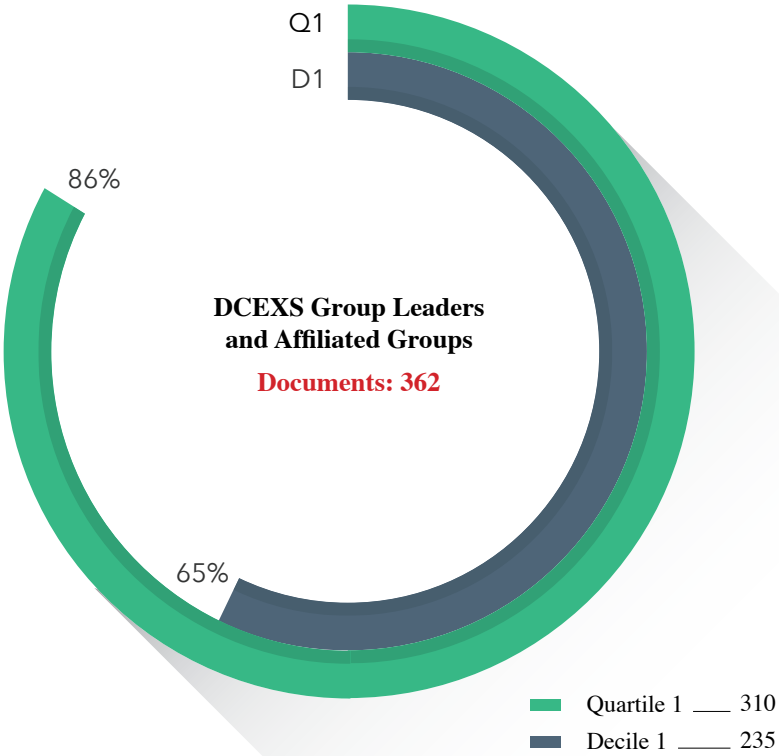
Doctoral theses defended	
Total PhD theses defended	79
PhD theses awarded European Mention in Doctoral Diploma	11
Length average of thesis development	4,05 academic years

Extraordinary award 2013/14	
PhD theses proposed	36
PhD theses awarded	7

The DCEXS in numbers

Publications





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Evolutionary Population Genetics
Elena Bosch

Evolutionary Genomics
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Complex Systems
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Berta Alsina

Developmental Biology: Ear Development
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Developmental Neurobiology
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