



# ANNUAL REPORT



**2016**

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Institut de Biotecnologia i de Biomedicina

Parc de Recerca UAB, Mòdul B – Bellaterra (Cerdanyoladel Vallès) 08193

ibb@uab.cat

**Director:** Xavier Daura Ribera

**Manager:** Eva Vila Morros

**Administrative Support:** Natividad Infante Cabrera  
Manuela Romero Chávez  
Rosa Calzada Calvo  
María Teresa Jiménez Batista  
Alicia Zorrilla Guinot

**Technical Support:** Almudena Merino Palomar  
Francesca Mestres Folch  
Monica Serrano García  
Fernando Hernández Escoriza



## Genome Integrity and Instability

Group Leader	Rosa Miró Ametller
Senior Members	Montserrat García Caldés Aurora Ruíz-Herrera Ignasi Roig Immaculada Ponsa
PhD Students	Marina Marcet Ortega Ana Martínez Andros Maldonado Linares Covadonga Vara González Judith Bello Sonia Borao Sergi cumplido Judit fuentes Maria Teresa Guillot Yan Huang Eloi Miralles Ivan Pérez Carla Roca Claudia Tang

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## Overview

Our group's research focuses on three topics related to genome instability. Firstly, we study the mechanisms implicated in the origin of chromosome instability associated to solid tumors, in particular to colon and bladder cancer. We analyze the mechanisms involved in chromosome reorganizations and aneuploidy origin occurring in tumor cells. Secondly, we explore the implication of chromosome rearrangements as a possible source for the existing mammalian karyotype diversity and the involvement of meiotic recombination in these processes. Finally, we try to understand the mechanisms that control meiotic recombination in mammalian meiosis. Specially, we focus on identifying key players from the pathways that control double strand break repair and genome silencing during meiotic prophase.

## Projects

Explorando la plasticidad estructural del genoma de los mamíferos. CGL2014-54317-P. 2015-2017. PI: Aurora Ruiz-Herrera.

Estudio de los mecanismos que regulan la progresión de la profase meiótica en mamíferos. BFU2013-43965-P.. PI: Ignasi Roig.

## *Others*

### PhD thesis

Marina Marcet. Surveillance mechanisms in mammalian meiosis. 2016. Directors: I. Roig.

## Comparative and Functional Genomics

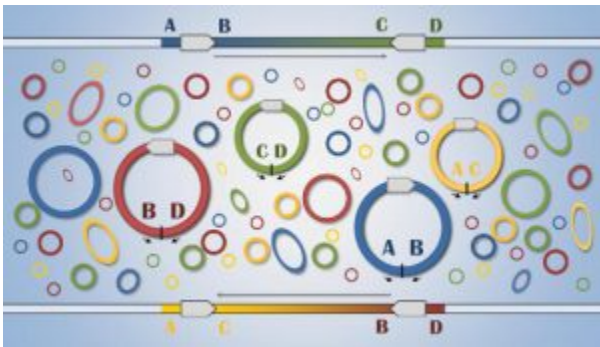
Group Leader	Mario Cáceres Aguilar
Postdoctoral Fellow	Marta Puig Font
	Marina Laplana Lafaja
PhD Students	Sarai Pacheco Piñol
	Carla Giner Delgado
	Jon Lerga Jaso
	Miguel Molina
	Noelia Pérez
	Ruth Gómez
	Tesera Soós
Lab Technicians	M <sup>o</sup> Alejandra Delprat Obeaga
	Sergi Villatoro Gómez

## Overview

Our laboratory is focused in the study of genome evolution and the genetic changes associated with individual and species differences, applying state of the art techniques and the wealth of available genomic data. In particular, a great degree of structural variation has been described in multiple organisms. In addition, we have information on the variation of expression levels of thousands of genes in different tissues and individuals. However, very little is known about the functional consequences of these changes and their role during evolution. To address these two questions, we use humans as a model and take a multidisciplinary approach that combines experimental and bioinformatic analysis, to generate results of interest in diverse fields.



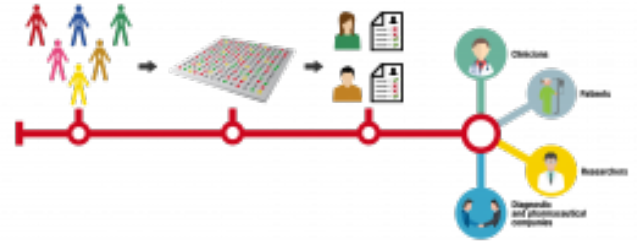
**Functional and evolutionary analysis of polymorphic inversions in the human genome.** Despite being one of the first types of genetic changes characterized, the difficulty in the study of inversions



is a big challenge to current structural variation analysis. Therefore, we are developing new experimental and bioinformatic methods to obtain a reliable catalogue of polymorphic inversions in the human genome, determine their distribution in world-wide human populations, and assess their functional and evolutionary impact, both with regard to their effect on gene expression and on nucleotide variation patterns.



**Genomic determinants of gene-expression changes in humans.** What makes us humans is a question that has attracted considerable interest for many years. Several research groups, including our own, have identified hundreds of genes with expression changes in the brain of humans and our closest primate relatives. However, due to the complexity of gene expression regulation, as the next step we need a better understanding of the molecular causes and the effects of these differences and their potential association to selective processes.



This research could provide important information on the regulatory mechanisms of gene-expression.

## Projects

La interpretacion de la variacion genomica desde la secuencia nucleotidica al fenotipo en drosophila y humanos. BFU2013-42649. IP: Mario Caceres

Análisis integrador del impacto funcional de las inversiones en genomas y caracteres fenotípicos. BFU2016-77244-R. IP: Mario Caceres

## Others

### MSc Thesis

Noelia Pérez Pereira. Detection of mosaicism for human inversions using ddPCR. 2016. Director: Mario Caceres

### Patent

M. Cáceres, S. Villatoro, C. Aguado. An in vitro method of genotyping multiple inversions". EU Patent Application EP13382296.5.

### Members of:

Coordinator of the Genomics and Proteomics Section of the Societat Catalana de Biologia.

### Editorial work

BMC Genomics Associate Editor.



## Bioinformatics of Genomics Diversity

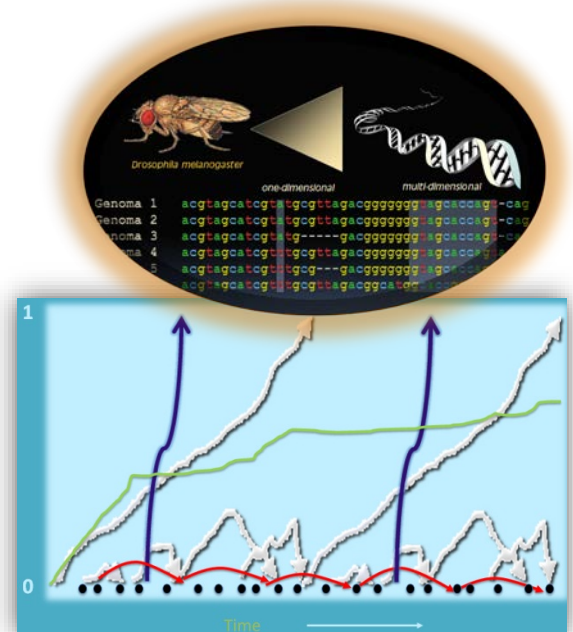
Group Leader	Antonio Barbadilla Prados
PhD Students	Sergio Hervás Fernández Marta Coronado Zamora
Lab Technicians	David Castellano Esteve

### Overview

In our research we develop and implement population genetics models and estimators to analyze and interpret the pattern of genomic variation. Among the most recent achievements, we have charted the first high resolution map of the trail of natural selection along the genome.

Key words:

- Population Genomics
- Natural selection mapping
- Bioinformatics Genome Variation
- Genome Wide Association ( GWA)
- Genome Variation Browsers



### Projects

BFU2013-42649-P. Understanding genome variation from nucleotides to phenotypes in *Drosophila* and humans. Ministerio de Ecolomía y Competitividad. IP: Dr. Antonio Barbadilla i Dr. Mario Cáceres. 2014-2016.

### Others

Members of:

Director of Bioinformatics Platform of campus UAB and UAB sphere Instituts of Health

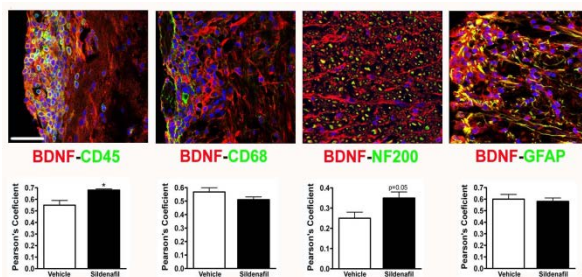
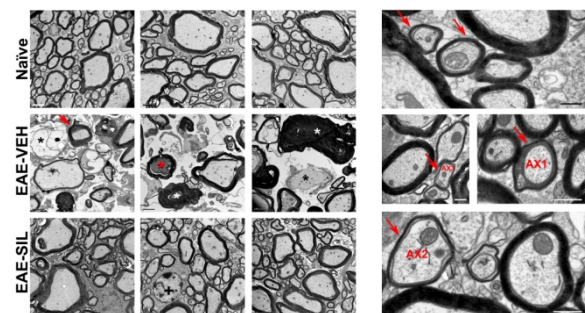
Promoter of a spin-off of Bioinformatics

## Neuroimmunology

Group Leader	Agustina García Sánchez
Senior Member	Maria Antonia Baltrons Soler
Postdoctoral Fellow	Beatriz Moreno Bruna
Predocctoral Fellow	Daniela del Valle Diaz Lucena

## Overview

Selective cyclic GMP phosphodiesterase 5 (PDE5) inhibitors, such as sildenafil (Viagra®), widely used for treatment of erectile dysfunction and pulmonary arterial hypertension, have been recently shown to exert neuroprotective actions in animal models of CNS injury and neurodegenerative diseases. Our group has demonstrated beneficial effects of PDE5 inhibitors in animal models of focal brain injury and of multiple sclerosis (MS) that are associated to down-regulation of neuroinflammation. In the later case, we have also shown that PDE5 inhibition can prevent demyelination and promote remyelination.



At present, we are investigating the mechanisms of the anti-inflammatory and remyelinating effects of PDE5 inhibitors in the animal model of MS, experimental autoimmune encephalomyelitis (EAE), as well as in immune cells from humans. Our final goal is to provide evidences that will support the notion of PDE5 as a therapeutic target for MS, taking it to a

preclinical stage. The group is also investigating if regulation of neuroinflammation is involved in the beneficial effects of sildenafil in cognition and  $\beta$ -amyloid burden reported by other groups in animal models of Alzheimer's disease.

## Molecular Immunology

Group Leader  
Predoctoral Fellow

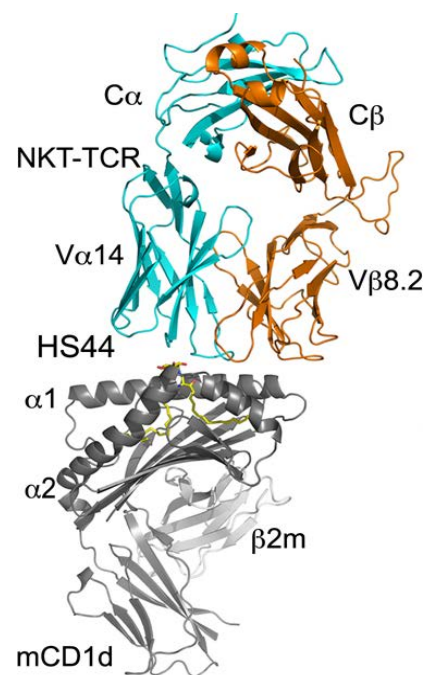
Ángel Raúl Castaño  
Ignasi Esteban

## Overview

Activation of iNKT cells by CD1d-ligands is a immunotherapeutic tool under intensive investigation.  $\alpha$ -GalCer is the prototypic agonist, but its excessive potency with contradictory activities hampers its potential therapeutic use. In search for novel ligands capable of overcoming these handicaps, we have obtained a series of synthetic analogs aiming for a controlled activation of the immune response

In vitro and in vivo studies demonstrate that some of these analogs are recognized by iNKT activating the immune response. One of them induces a robust IFN-g production, without the characteristic cytokine storm induced by  $\alpha$ -GalCer. Consequently, HS44 induces a very efficient antitumoral response in B16 tumor animal model able to completely avoid the establishment of lung metastasis. On the contrary, it is unable of inducing allergic responses making it suitable as immunotherapeutic reagent for future clinical applications.

New analogs aimed to further increase cellular Th1 response are being assayed as immune stimulants in “in vivo” models. Systemic induction of Th1 responses are being studied by wide spectrum serum cytokine analysis and their expected improved antitumoral capacities tested, and so far proved in one case, in tumor models. Cellular mechanism subjacent to their activation on the immune system, linking iNKT activation and antitumoral effectors, including movilization of innate cells from limfoïd organs and the chemokines directing such traficking are ongoing efforts in our lab.



## Projects

TV32013-130910. Antitumor activity of iNKT activators analogs of the  $\alpha$ -GalactosylCeramide: towards immunotherapeutical reagents. IP: Raul Castaño 2014-2016.

## Applied Immunology

Group Leader	Paz Martínez Ramírez
Senior Member	José Ramón Palacio
PhD Student	Meritxell Moreno Martín
Lab Technician	Ghizlaine El Korchi Zeriuoh

## Overview

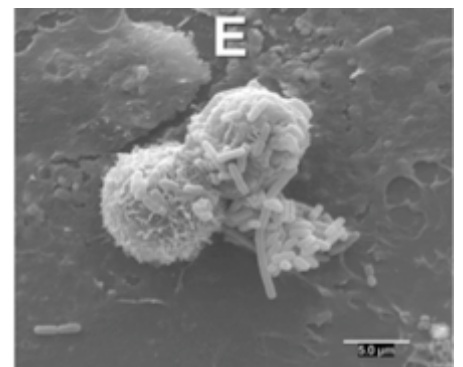
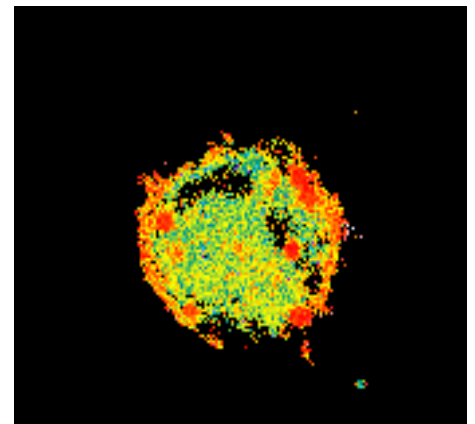
The group follows 3 main research lines:

1.- **Oxidative stress and inflammation in Reproduction.** Chronic inflammation together with oxidative stress modify the molecules which are involved in the materno-fetal dialogue during early embryo implantation. The study of antioxidant and/or anti-inflammatory therapies may contribute to the increase of implantation and pregnancy rates in assisted reproductive techniques.

2.- **Oxidative stress and biomembranes.** Lipid peroxidation may influence plasma membrane fluidity in cells from the innate and adaptative immune system (macrophages, lymphocytes). By using two-photon microscopy, a high resolution technique which allows the study of lipid dynamics *in vivo*, in individual cells, we detect how oxidative stress induces membrane changes so that the binding efficiency of ligand-receptor decreases, raft formation is prevented and cell activation may be inhibited.

A preliminary study on the relationship between oxidative stress, the biological age and quality of life in elderly people was performed. The influence of oxidative stress on membrane fluidity of immune cells, and how oxidative damage can modify the immune response is of great interest in the evaluation of disability in aging.

3.- **Nutrition and Immunology.** Probiotic and prebiotics have a protective role on several bacterial infections, so that they have been proposed as an alternative to the use of antibiotics and they are used in animal feeding to prevent neonatal diarrhea. We have investigated the protective effect of the probiotic *Saccharomyces cerevisiae* and a new developed prebiotic b-galactomannan, on epithelial intestinal cells and in a porcine model, and their immunomodulation ability in bacterial infections.



## Others

### MSc Thesis

Meritxell Moreno Martín. Analysis of cellular and soluble parameters as potential biomarkers of frailty in elderly people. 2016. Director: Paz Martínez

### Members of:

Soci ordinari de la Sociedad Española de Bioquímica, desde 1984.

Membre ordinari de la "European Society of Human Reproduction and Embryology", des de 1987.

Membre de la "International Society for Immunology of Reproduction" (I.S.I.R.) des de 1988.

Membre de la "American Society for Immunology of Reproduction" (A.S.I.R.) des de 1992.

Soci numerari de la Sociedad Española de Inmunología des de 1992.

Membre fundador de la European Society of Reproductive & Developmental Immunology (ESRADI)

Soci numerari de la Acadèmia de Ciències Mèdiques de Catalunya i de Balears des de 1996.

Directora científica del Servicio científico-técnico Cultivos Celulares, Producción de Anticuerpos y Citometría” de la UAB desde Junio de 2009



## Celular Immunology

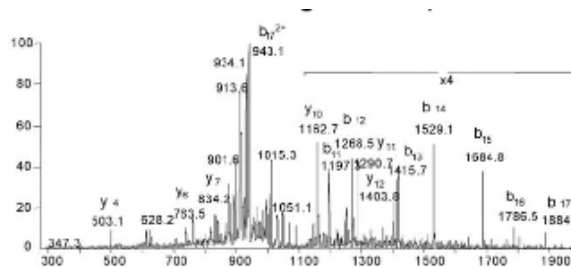
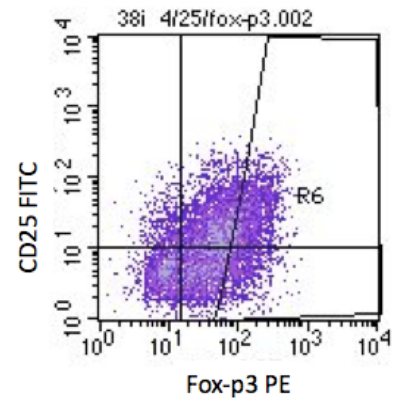
Group Leader	Dolores Jaraquemada
Senior Members	Mercè Martí Ripoll Iñaki Alvarez Pérez Carme Roura Mir
PhD Students	Erika M. Scholz Lorena Usero Roger Ferran Solé Soler Silio Lima de Moura Miguel Jiménez Rodríguez
Lab Technician	Annabel Segura

## Overview

The group's research interests are centered in the study of central tolerance, antigen processing, auto-antigen presentation and recognition in autoimmune diseases.

Specific lines include:

- Auto-antigen presentation in target organs.
- Autoreactive and regulatory T cells in autoimmunity.
- NKT Cells in Autoimmunity.
- Antigen processing in tolerance and autoimmunity.



# Response Mechanisms to Stress and Disease



## Projects

SAF2012-35344 (subprogram MED, CICYT, Spanish Science Ministry). From antigens to TCR. A systematic approach to the immune response in type 1 diabetes. IP: Dolores Jaraquemada. 2012 – 2015.

## Others

### PhD thesis

Lorena Usero. Estudi de la funció supressora de les cèl·lules iNKT en el control de la resposta autoimmunitària a la Diabetis Tipus 1 humana. 2016. Director: Dra. Carme Roura.

Cristina Xufré. Caracterització fenotípica i funcional de les cèl·lules T reguladores (naturals) en salut i malaltia (diabetis tipus 1). Director: Dra. M. Martí



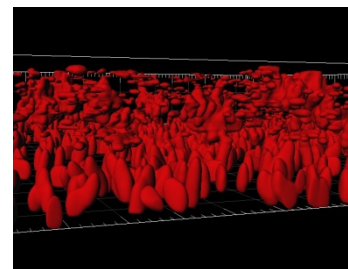
## Bacterial Molecular Genetics and Pathogenesis

Group Leader	Isidre Gibert González
Postdoctoral Fellows	Daniel Yero Corona
PhD Students	Celeste Gómez Camacho
	Pol Huedo Moreno
	Pablo Rodríguez Fernández
	Roser Márquez Gómez
	Xavier Coves Lozano

### Overview

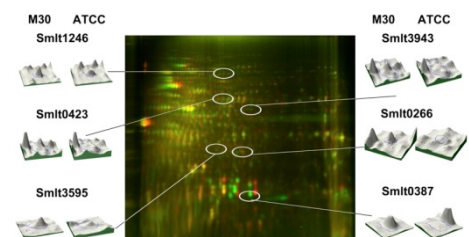
The main research interests of our group are:

- The molecular basis of bacterial pathogenesis and antimicrobial resistance.
- The identification and validation of new antimicrobial targets for Gram-negative pathogens.



Other research interest:

- Host-pathogen interactions and infection models: mouse, *C. elegans* and Zebrafish
- Bioinformatic approach to identify new potential candidates for vaccine and/or drug targets.



### Keywords

Bacterial Pathogenesis, Virulence, Host-Pathogen Interactions Molecular Genetics, Genomics, Proteomics, Gene Expression, Antimicrobial Resistance, Antimicrobial Drug



# Response Mechanisms to Stress and Disease



## Projects

Convenis de transferència i prestació de serveis en relació a programes de qualitat microbiològica amb Sociedad Española de Bioquímica Clínica y Patología Molecular i Fundació pel control de qualitat dels laboratoris clínics.

Procesos biológicos no esenciales en *Stenotrophomonas maltophilia* como dianas para el diseño de nuevas estrategias antimicrobianas. BIO2015-66674-R. PI: Isidre Gibert and Xavier Daura

## Others

### MSc Thesis

Romero Martínez, Rosa Maria. El biofilm oral: Quin paper juga *Porphyromonas gingivalis*?. 2016. Director del treball: Isidre Gibert

Martín Martín, Sergio. Búsqueda de nuevas dianas en el tratamiento de *M. tuberculosis* multirresistente. 2016. Director del treball: Isidre Gibert

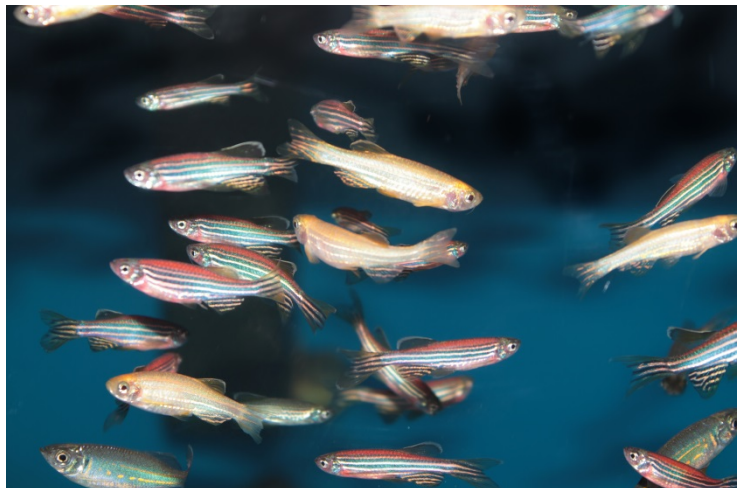
## Evolutionary Immunology

Group Leader	Nerea Roher Armentia
PhD Students	Debora Torrealba Sandoval
	Jie Ji
	Jofre Gasion
	Eva Vallejos
	Rosemary Thwaite

## Overview

### ➤ Development of nanovaccines for fish species of commercial interest

It's been a central focus of our work. We are searching for non-toxic, non-stressful and effective systems to protect commercial fish from diverse pathogenic challenges. Taking into account the particularities of the fish immune system, we have recently completed a nanoformulation (Ruyra et al., 2013) able to increase the survival of bacterial challenged fish (Ruyra et al, manuscript in preparation). The development of sustainable aquaculture, a strategic sector to feed the ever-increasing



human population (Khan et al, 2011), relies on disease prevention through the implementation of preventive immunostimulation and effective vaccination strategies (Evensen et al., 2009). In particular, fish immunologists face now a major challenge trying to prevent the massive economic losses caused by viral diseases. Development of novel vaccines to protect fish from viral diseases such as Spring Viremia Carp Virus, SVCV or Viral haemorrhagic septicemia viruses, VHSV (Gomez-Casado et al., 2011) will be a major goal of our research efforts during the next years. In collaboration with a fish virologist (Dr. A. Estepa) we aim to encapsulate plasmids coding for antigenic viral proteins into nanoliposomes and characterise them in zebrafish to finally, test the formulations in the real host. A hallmark of our work in the next five years would be to design and develop new nanovaccines against SVCV and VHSV.

### ➤ The evolution of pathogen recognition in vertebrates

In the last 7 years we have been investigating the molecular basis of the fish immune system, and we have been trying to decipher the particularities of its innate immune response. Most fish species lack the TLR4 receptor that senses the LPS presented in the outer membrane of bacterial cells. We are



interested to tackle the characterization of the molecule responsible for LPS sensing and why fish are less sensitive to the toxic and pro-inflammatory effects of LPS. Genomic tools have been of great importance for the fish research field during the last years. Fish genomes such as fugu, puffer fish, medaka, cod or salmon among others start to be available to the scientific community. A major achievement in fish biology has been the completion of the zebrafish reference genome sequence, with publication of the Zv9 assembly. The Sanger Institute provides the research community with a high-quality zebrafish genome sequence. The number of identified protein-coding genes in the zebrafish genome now stands at around 24000 and fish supplied by the Zebrafish Mutation Resource (Sanger Institute) can be used to study a wide range of biological processes such as response to pathogens, cancer, diabetes etc. Our lab will be provided with INF $\gamma$  and IL-1 $\beta$  mutant fish that will be used to investigate the anti-viral and the inflammatory response respectively. Our fish facility is open to house other mutants of interest for the research of groups in the IBB-MRB.

➤ **Defense mechanisms in *Branchiostoma lanceolatum***

Lastly, besides the above mentioned research lines, we will have an additional long-term research line aimed to explore the defense mechanisms in a non-vertebrate marine organism, the amphioxus (*Branchiostoma lanceolatum*) that would allow us for a better understanding of the vertebrate immune system. From an evolutionary point of view the amphioxus is an excellent living organism to study what was going on before vertebrates arose. The amphioxus is a cephalochordate with a small genome and simple body architecture that makes it very suitable for evolutionary studies. In collaboration with Dr. Bayes (IIB, Hospital de Sant Pau) we will study different aspects of amphioxus biology such as nervous system architecture, defense mechanisms or tolerance and biodistribution of nanoliposomes.

## Projects

Desarrollo de sistemas específicos de nanodelivery para especies de interés acuícola: delivery mediante nanoliposomas y mediante nanopartículas proteicas. AGL2015-65129-R (01/01/2016 – 31/12/2018).

# Response Mechanisms to Stress and Disease

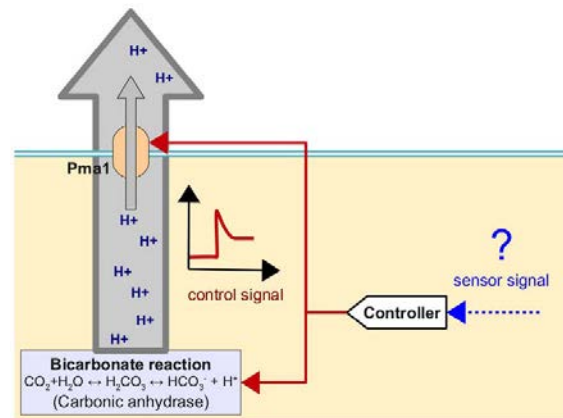


## Yeast Molecular Biology

Group Leader	Joaquin Ariño Carmona
Senior Member	Antonio Casamayor Gracia
Postdoctoral Fellows	Maria López
PhD Students	Carlos Calafí
	Albert Serra Cardona
	Cristina Molero Merinero
	Diego Velázquez
	Chun-Yi Zhang
	Carlos Santolaria Bello
	Marcel Albacar Carot
Lab Technician	Montse Robledo Costas

## Overview

Our group is interested in different aspects of the biochemistry, molecular biology and genomics of the yeast *Saccharomyces cerevisiae*, particularly in those involving cell signaling via phospho-dephosphorylation processes. This includes research on ion homeostasis, response to various forms of stress or cell cycle regulation. Particular emphasis is given to the interaction between ion and nutrient homeostases. The ultimate goal is to obtain a comprehensive view of the yeast response to perturbations in their environment that may lead to a deeper insight into the biology of this organism, as well as to new biotechnological applications. As an example, we are carrying out a project to develop new strains tolerant to acetic acid, to improve the fermentative processes involved in the generation of bio-alcohol from plant debris.



C) Plasmid	YPD	8.0 pH
YCp50 Ø		
YCp50-RAS2*		
YEplac112 Ø		
YEplac112-GPA2*		



## Projects

Exploración de los mecanismos de homeostasis de cationes monovalentes como nueva diana antifúngica. (Ref. BFU2014-54591-C2-1-P). PI: Joaquin Ariño.

## Others

### MSc Thesis

Rebeca Kenda Nana Barrantes. Screen for high-copy suppressors of the deleterious effect of Ppz1 overexpression. (Master in Molecular Biotechnology, UB). 2016. Joaquin Ariño.

Marcos Barba. Vías nutricionales: ¿podemos usarlas como dianas terapéuticas? (Máster Oficial de Microbiología Aplicada, UAB). 2016. Joaquin Ariño.

María Coca Jimeno. La homeostasis iónica como posible diana para el desarrollo de antifúngicos. (Máster Oficial de Microbiología Aplicada, UAB) 2016. Joaquin Ariño.

### Members of:

Joaquín Ariño ha sido nombrado miembro del Editorial Board de la nueva revista Microbial Cell (<http://microbialcell.com/>), editada por Shared Science Publishers OG. Editorial work.

# Applied Proteomics and Protein Engineering



## Computational Biology

Group Leader	Xavier Daura Ribera
PhD Students	Michael Cristòfol Clough
Lab Technician	Oscar Conchillo Solé

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## Overview

The group's trajectory has been, until recent years, largely based on the use of molecular-dynamics simulation methods to study biomolecular systems at atomic resolution, mostly in connection with the process of polypeptide folding. Since 2007, however, the group has expanded its scope towards the proteomic analysis of pathogenic bacteria for the identification of antigens and putative drug targets. This expansion has been enabled by the incorporation of new members with expertise on additional computational and experimental techniques, and by teaming up with IBB's Bacterial Molecular Genetics group. Currently, the group has active projects, often intertwined, in the following topics:

- Study of biophysical properties of peptides and proteins by molecular-dynamics simulation methods.
- Computational compound screening and redesign for drug discovery.
- Bioinformatic and experimental identification and characterization of proteins of pathogenic bacteria for vaccine and antibacterial-drug development.

In general each of these topics is being developed within the context of a collaborative project.

## Projects

Procesos biológicos no esenciales en *Stenotrophomonas maltophilia* como dianas para el diseño de nuevas estrategias antimicrobianas. BIO2015-66674-R. PI: Isidre Gibert and Xavier Daura

## Others

### MSc Thesis

Aniol Valera: Genome-wide screening method to detect putative antimicrobial targets. 12/09/2016.  
Xavier Daura

### Commissions of trust

Member of Three Delegate Commissions of UAB's Governing Council: Research (since 2011), Knowledge Transfer and Strategic Projects (since 2012) and Doctorate (since 2013).

Project evaluation for EU's H2020, since 2014.

Project evaluation for the Italian Association for Cancer Research (AIRC), Italy, since 2011.

Project evaluation for the Partnership for Advanced Computing in Europe (PRACE), EU, since 2012.

Peer review for several journals, including Journal of the American Chemical Society, Angewandte Chemie International Edition, PLoS Computational Biology, Journal of Chemical Theory and Computational, Bioinformatics, etc.

### Patent

D. Yero, M. Indarte, O. Conchillo, I. Gibert, X. Daura. Enhanced antibiotic composition.

## Theoretical Molecular Biology

Group Leader	Josep M. Lluch
Senior Members	Àngels González Lafont Mireia García Viloca Laura Masgrau
PhD Students	Patricia Saura Martínez Sonia Romero Téllez Maria Fernanda Mendoza

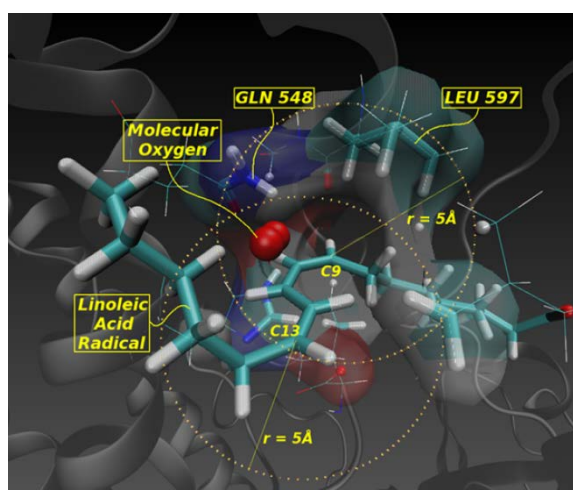
## Overview

In the Theoretical Molecular Biology group we are interested in understanding how enzymes work at the atomic/molecular level. We are particularly specialized on the theoretical study of the chemical reactions taking place inside enzymes and in identifying the main actors that make possible these exquisite catalytic processes. Among other mechanistic aspects, for example, we analyse how the high regio and stereospecificity of this biological catalysis is achieved. Our final aim is to use all that knowledge to force conveniently modified enzymes to work in the way we need to achieve outstanding biomedical and biotechnological applications.

To do this, we apply and develop Theoretical and Computational Chemistry methods, including hybrid quantum mechanics/molecular mechanics methods on the solvated enzyme-substrate(s) system, molecular dynamics simulations, free energy calculations, the EA-VTST/MT scheme and protein-ligand dockings.

Our current main lines of research focus on:

- **Mammalian lipoxygenases (LOs)**: LOs are implicated in the pathogenesis of inflammatory and hyperproliferative diseases. Moreover, some isoforms like the 15S-LO, are highly regio and stereospecific in the hydroperoxidation reaction they catalyse; specificity required for its correct physiological function. We have been analysing the possible causes of this regioselectivity in the oxygen attack step catalysed by rabbit 15S-LO. Our results conclude that, among the different possibilities proposed

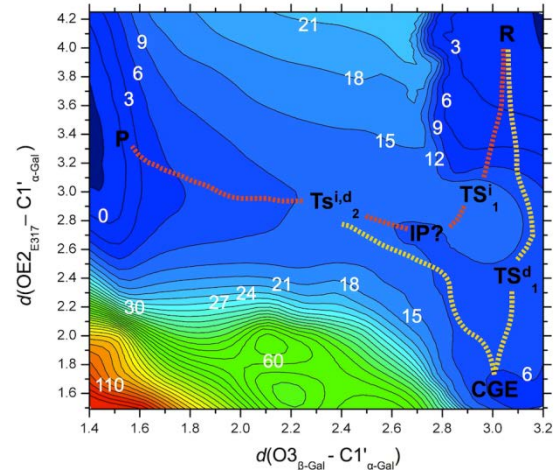


From Suardiàz *et al.*, J Phys Chem B, 2013

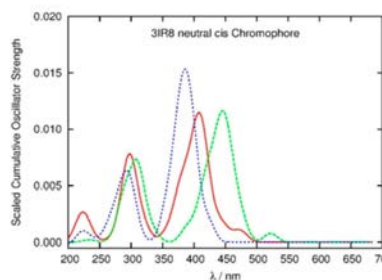
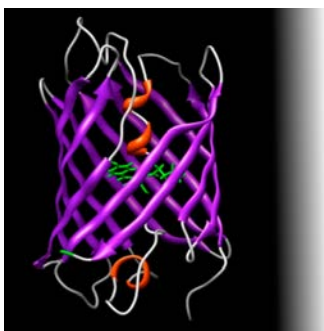
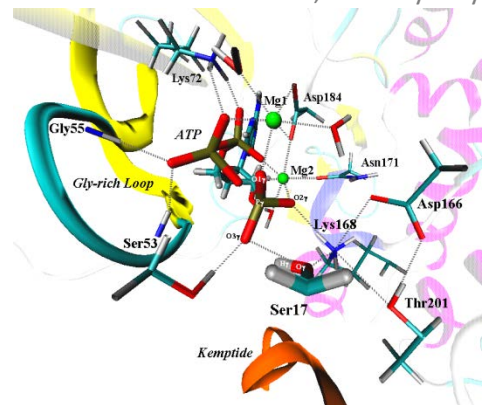


in the literature, the steric-shielding hypothesis seems to be the operating one in this enzyme. On another hand, we have started the study of the hydrogen abstraction step.

- **Computational chemical glycobiochemistry:** the biosynthesis of glycans has been the focus of this research line. In particular, we are providing computational evidences that are helping clarify the catalytic mechanism used by retaining glycosyltransferases, a matter that has been under debate for the last decades and has remained as one of the unanswered fundamental questions in glycosciences. We have studied *in silico* several of these enzymes, some of these works being compiled in the PhD thesis of H. Gómez, defended in October 2013.



- **Serine-threonine kinases:** The cAMP-dependent protein kinase A (PKA) is a prototypical kinase that plays pivotal roles in numerous signaling pathways. During this period, important progress has been done on the study of the reaction mechanisms (dissociative and associative) of the phosphoryl transfer catalyzed by PKA and the Asp166Ala mutant. As Asp166 has a fundamental role in the dissociative mechanism, the only way to explain the experimental activity observed for the mutant enzyme is via an associative process never taken into account by other modeling studies of this important catalytic process. The energetic and structural analysis of the catalytic reaction pathway performed in our laboratory is shedding some light on the origin of transition state stabilization within the kinase family.



- **Fluorescent Proteins:** Part of our group has a strong background in the study of chemical reactivity in excited states. In the last years, this experience is also being applied to investigate several aspects related to the fluorescence phenomena in fluorescent proteins, which have many applications in biomedicine as *in vivo* biomarkers. The Green Fluorescence Protein (GFP) and many members of the Red Fluorescence Protein (RFP) family are being the focus of

Protein (GFP) and many members of the Red Fluorescence Protein (RFP) family are being the focus of

# Applied Proteomics and Protein Engineering



our research. Especially we are working on the design of RFP variants that excite and emit in the optical window in which mammalian tissues are relatively transparent to light. This new fluorescent proteins for imaging in mammals should be useful for following biological processes “in vivo”.

## *Projects*

Adscribed at the Department of Chemistry of the UAB.

# Applied Proteomics and Protein Engineering



## Nanobiotechnology

Group Leader  
Senior Members

Antonio P. Villaverde  
Neus Ferrer

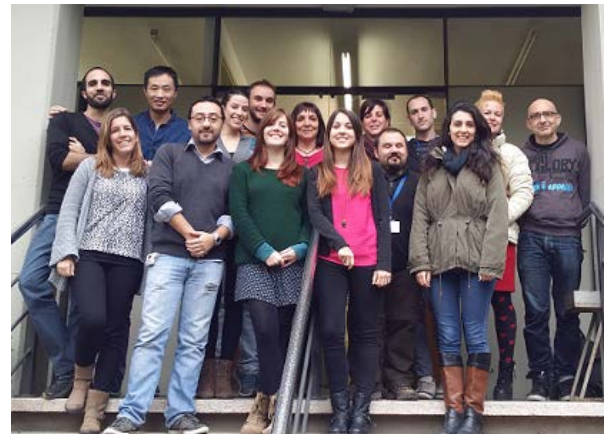
Esther Vazquez  
José Luis Corchero  
Elena Garcia Fruitós  
Joaquin Seras

PhD Students

Mireia Pesarrodonà  
Paolo Saccardo  
Ugutzu Unzueta  
Naroa Serna  
Laura Sanchez  
Fabián L. Rueda  
Esther Martínez  
José Vicente Carratalá  
Marianna Teixeira de Pinho  
Raquel Díaz Ocaña  
Diana Patricia Florez Lemos  
Hèctor López Laguna  
Laura Domènech Amorós  
Núria Bosch Galan

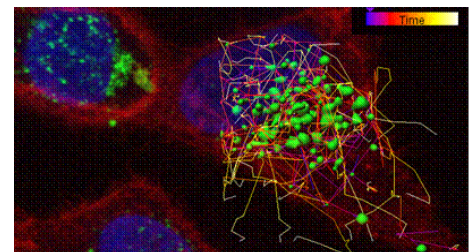
Lab Technician

Rosa Mendoza  
Mercedes Márquez Martínez



## Overview

- Development of self-assembling protein nanoparticles for non-viral gene therapy.
- Development of new bacterial nanomaterials for tissue engineering.
- Design and production of enzymes and antibodies for cell therapy.
- Design of processes for production of recombinant proteins of therapeutic interest in bacteria, insect cells and mammal cells.
- Study of cell stress responses to the production of proteins of pharmacological interest.
- Study of the physiology and genetics of protein aggregation in recombinant bacteria.
- Generation and engineering of virus-like-particles of biomedical interest.
- Design of functionalized proteins for targeted drug delivery, endosomal escape and blood-brain barrier crossing.



## Projects

Genotoxic nanoparticles targeting colorectal cancer stem cells. TV32013-132031. IP Antoni Villaverde

Ingeniería de nanopartículas proteicas para la entrega dirigida de proteínas terapéuticas y de ácidos nucleicos. BIO2013-41019-P. IP Antoni Villaverde.

2014 SGR 132 Microbiologia bàsica i aplicada. . IP Antoni Villaverde

Diseño de nanoconjugados inteligentes para el tratamiento del cáncer colorrectal metastásico. PI15/00272. IP Esther Vazquez Gomez.

Desenvolupament d'un nanoconjugat antitumoral dirigit a tumors sòlids i neoplàsies hamatològiques CXCR4 positius. 14640 FIRHSCSP. IP Esther Vazquez Gomez.

Desenvolupament d'un nanoconjugat antitumoral dirigit a tumors CXCR4 positius. 14641 FIRHSCSP. IP Esther Vazquez Gomez.

FIRHSCSP-Servei producció Nanopartícula. 14461. IP Esther Vazquez Gomez.

FIRHSCSP-Servei síntesi nanoconjugat T22. 14462. IP Esther Vazquez Gomez.

Desenvolupament d'un nanoconjugat antitumoral dirigit a cèl·lules mare de càncer de pàncrees CXCR4 positius . IP Esther Vazquez Gomez.

Personalized nanomedicine for triple negative breast cancer stem cells. TV32013-133930. IP Esther Vazquez Gomez.

Diseño de nanoconjugados inteligentes para el tratamiento del cáncer colorrectal metastásico. PI15/00272. IP Esther Vazquez Gomez.

## Others

### MSc Thesis

Olivia Cano. Production of protein nanomaterials in lactic acid bacteria for human and animal medicine. 2016 . E.Garcia Fruitós, A.Villaverde

Fabian Rueda. Self-structured protein nanomaterials produced in endotoxin-free microbial cells. 2016. E.Garcia Fruitós, A.Villaverde.

## Patent

Olivier LACZKA, Francisco Javier DEL CAMPO, Francisco Xavier MUÑOZ PASCUAL, Antonio P. VILLAVERDE CORRALES, Neus FERRER MIRALLES, Rosa María FERRAZ COLOMINA. Biosensor for detecting anti-hiv antibodies. WO2010026275A1. US20110233073 A1

Marco Colás, María Pilar; Pascual Durán, Nuria; Pastells Díez, Carme; Sanchez Baeza, Francisco; Villaverde Corrales, Antonio Pedro; Rodríguez Carmona, Escarlata. Haptens y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa. WO2014135730 A. US20160033489.

Miro Jaume Veciana, Bastardas Inmaculada Ratera, GIL César DÍEZ, Corrales Antonio Pedro Villaverde, Gómez Esther Vázquez, Fruitós Elena García. Inclusion bodies, bacterial cells and compositions containing them and uses thereof. WO2010026275A1. US20110233073 A1.

Miro Jaume Veciana, Bastardas Inmaculada Ratera, GIL César DÍEZ, Corrales Antonio Pedro Villaverde, Gómez Esther Vázquez, Fruitós Elena García. Inclusion bodies, bacterial cells and compositions containing them and uses thereof. WO2010076361 A1. US20110268773.

Rigat Isolda Casanova, Navarro María Virtudes Céspedes, Miralles Neus Ferrer, Bafalluy Ramon Mangues, Elorza Ugutz Unzueta, Gómez Esther Vázquez, Corrales Antonio Villaverde. Methods and reagents for efficient and targeted delivery of therapeutic molecules to cxcr4 cells. WO2012095527 A1. WO2012095527 A1.

## Members of:

Member of CIBER en Biomateriales, Bioingeniería y Nanomedicina (ISCIII) since 2006.

Member of the Spanish Platform on Nanomedicine since 2007.

Member of the European technological Platform in Nanomedicine since 2008 and UAB representative.

Chairman B-DEBATE on "Nanotechnology in human and animal health". Barcelona, Spain, 2013.

Chairman 2st Workshop on Nanomedicine UAB-CEI. Barcelona, Spain, 2013.

Scientific advisor of the la TWAS, The academy of sciences for the developing world, since 2013

## Editorial work:

BMC Genomics Associate Editor.

Editor-in-Chief de Microbial Cell Factories (ISSN: 1475-2859).

Editor de Microorganisms (ISSN 2076-2607) desde 2012.

Editor de Medical Sciences (ISSN 2076-3271) desde 2012.

# Applied Proteomics and Protein Engineering

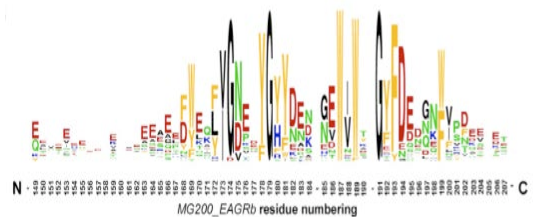


## Molecular Biology

Group Leader	Enrique Querol Murillo
Senior Members	Jaume Piñol Ribas Josep A. Perez Pons
Postdoctoral Fellow	Ángel Mozo Oscar Quijada
PhD Students	Isaac Amela Abellán Juan Aibar Gemma Elias Bosch Luis González González Miguel González Martín Ignasi Granero Moya Esther Gútiérrez García Luis Franco Serrano Ana María, Martínez Luis García Morales Mario Huerta Casado Marta Hernández Solans Marta Huguete Ramon Ariadna Izquierdo Pérez Marina Marcos Silva Carlos Martínez Torró Carmen Muñoz Navarro Arturo Rodríguez Banqueri Cristian Ponce Basco Lucia Sánchez Alba Rubén Sebastian Pérez Sergi Torres Puis

## Overview

- Mycoplasma genitalium as a model of minimal cell and genome. Functional proteomics, adhesion and gliding mechanism, pathogenicity.





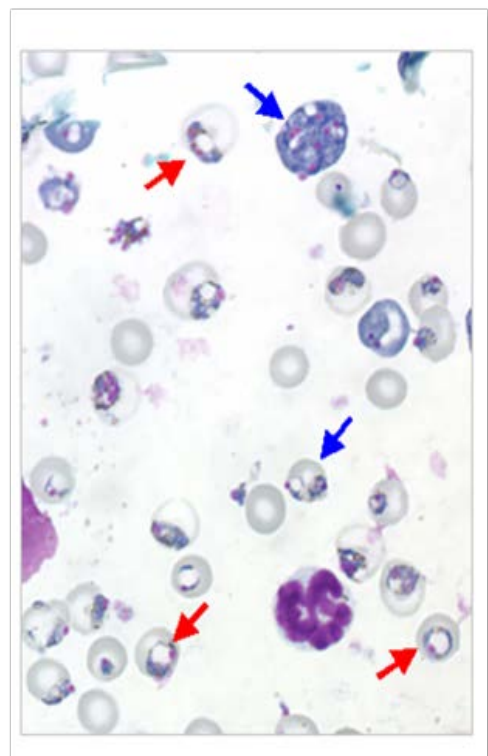
## Protein Engineering and Proteomics

Group Leader	Francesc X. Avilés Puigvert
Senior Members	Josep Vendrell Roca Julia Lorenzo Rivera
PhD Students	Giovanny Covalada Noemí Contreras Pereda Diana Flores León Carolina Frías Botella Javier García Pardo Sergi Montané Bel Sarah Moreira Castro Esther Berenguer de la Cuesta María del Carmen García Guerrero Sergi Montané Bel David Montpeyó García-Moreno Irantzu Pallarés Goitiz Eric Rovira Cal David Martínez Elisa Rioja Blanco Mariana Edith Tellechea Threpthimol Ponnoth Sergi Rodríguez

## Overview

Our group's interests lie in protein engineering, focusing on the study of protease precursors and inhibitors in general, and on metalloproteinases in particular. Among this lines we work in redesigning proteins or organoproteic molecules capable of keeping these enzymes inactive, and in such way finding out determinant factors for their activation and inactivation.

We also develop methodologies for high-throughput proteomics as well as for the classification, structural prediction / simulation and modeling of proteins, ligand design, drug design and protein engineering in general.





# Applied Proteomics and Protein Engineering



## Projects

ICN2-Estudis citotoxicitat nanomaterials. Nueva tecnología en sensores en muestras microbiológicamente muertas y vivas. 2016. IP: F. X. Avilés.

Interactómica diseño de sondas e imagen de carboxipeptidasas. en transito de la función a la aplicabilidad. BIO2013-44973-R.2014. IP: F. X. Avilés

Proteómica de proteasas y de oxidoreductasas. Una estrategia binaria en el descubrimiento de inhibidores y su aplicabilidad biotecnológica. BIO2016-78057-R. IP: F. X. Avilés

## Protein Folding and Conformational Diseases

Group Leader

Salvador Ventura Zamora

Postdoctoral Fellow

Susana Navarro Cantero

PhD Students

Patrizia Marinelli

Anita Carija

Marta Díaz Caballero

Francisca Pinheiro

Ricardo Sant'Anna Oliveira

Alex Mur

Joan Serrano

Jordi Pujols

Marcos Gil

Valentin Iglesias Mas

Cristina Visentin

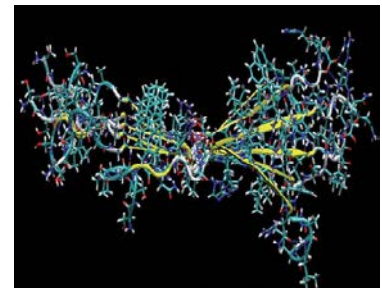
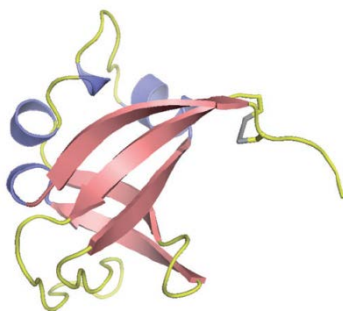
Weiqiang Wang

## Overview

We aim to understand the chemistry and biology of protein folding and how this reaction is competed in the cell by misfolding and aggregation processes, leading to the onset of a variety of human conformational diseases.

Among other achievements, in the present year:

1.- Using atomic force microscopy, single molecule force spectroscopy and molecular dynamics we have addressed the inner forces that stabilize amyloid fibrillar structures (Valle-Delgado JJ. et al. 2012)

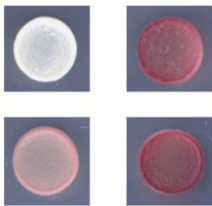
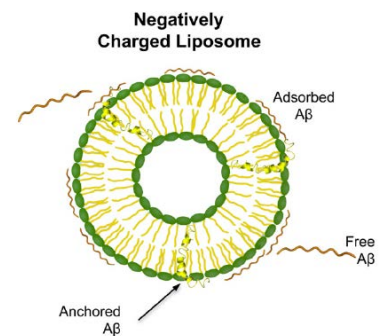


2.- We have deciphered the role played by disulfide bonds on the thermodynamic stability of proteins, folding kinetics and specially on the their aggregation into amyloid fibrils. They act as key molecular elements promoting the formation of stable functional forms and precluding the population of aggregating species that might trigger pathological processes. (Grana-Montes R, et al. 2012)



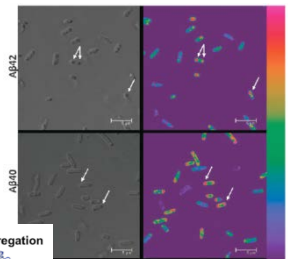
3.- The formation of aggregates by misfolding polypeptides is inherently toxic for the cell, decreasing cellular fitness. Using bacteria as a model organism we have developed a robust system to model and quantify the impact of protein aggregation in cell homeostasis. (Villar-Pique et al., 2012a)

4- The neurotoxicity of the amyloid peptide Aβeta is exerted through interactions with neuronal membranes. Using liposomes as model membranes, we have shown that it is the balance between peptide insertion and adsorption in the membrane that modulates its aggregation and toxicity (Sabate et al 2012a).

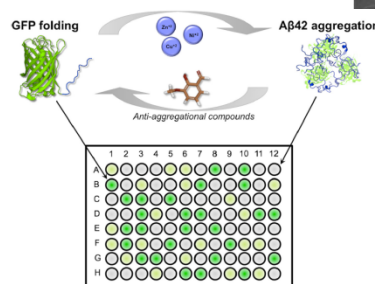


5- We have shown that bacterial cells might form infective amyloid structures and therefore that they can be used to generate and study prion proteins (Espargaro et al 2012a).

6- We have developed a method that exploits flow-cytometry to screen the impact of genetic mutations or chemical compounds in the aggregation of proteins involved in different pathologies (Espargaro et al 2012b).



7- We have developed a method based on GFP identify chemical compounds that promote or aggregation of biotechnological/biomedical (Villar-Pique et al., 2012a).



refolding to avoid the relevant proteins

## Projects

Grup d'estudis de proteïnes autoagregatives (2014SGR 938) 2014. Generalitat de Catalunya.

Descubrimiento, caracterización y diseño de nuevos amiloides funcionales auto-replicativos. BFU2013-44763-P. IP: Salvador Ventura.

Deciphering the role of a  $\alpha$ -synuclein strains in prion-like synucleopathy induction and spreading. TV3-2014-4330. IP: Salvador Ventura.

## Protein Structure

Group Leader

David Reverter Cendrós

Postdoctoral Fellow

Nathalia Varejão Nogueira da Paz

PhD Students

Bing Liu

Hèctor López

Jara Lascorz

Jéssica Angulo

Roger Canton

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## Overview

- Structural characterization of the activation cascade by the mitotic kinases NEK6, NEK7 and NEK9.
- Structural and functional studies of the de-ubiquitin proteases USP25 and USP28 regulated by SUMO modification.
- Structural characterization of the complex SMC5/SMC6 and its roles as a SUMO E3 ligase.

## Projects

Caracterización estructural de la modificación por sumo en procesos de reparación de DNA. (Ref. BFU2015-66417-P).IP: David Reverter.

## NMR Applications in Biomedicine (GABRMN)

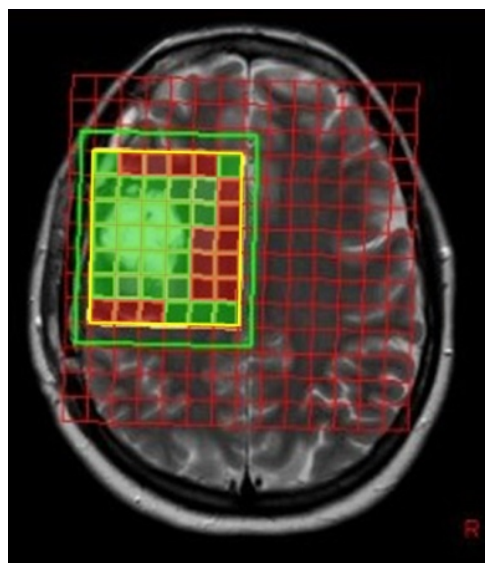
Group Leader	Carles Arús Caraltó
Senior Members	Margarida Julià Sapé Ana Paula Candiota
PhD Students	Victor Mocioiu Laura Ferrer Font Daniel Ulinic Xavier Serra Mocioiu Yanisleydis Hernández

### Overview

GABRMN stands for "Grup d'Aplicacions Biomèdiques de la Ressonància Magnètica Nuclear".

Our research group is located jointly at the IBB and at the Unitat de Biociències of the Departament de Bioquímica i Biologia Molecular, located at the Faculty of Biosciences of the Universitat Autònoma de Barcelona, UAB.

The GABRMN@IBB hosts all infrastructure and personnel related to bioinformatics developments needed to fulfil our research lines. The GABRMN@IBB hosts, jointly with the Servei de Ressonància Magnètica (Nuclear Magnetic Resonance Facility) (SeRMN) (<http://sermn.uab.cat/>) of the UAB, one of the CIBER-BBN platform units, the Platform of Biomedical Applications of Nuclear Magnetic Resonance at the Universitat Autònoma de Barcelona.



The bioinformatics platform @IBB, with a total storage capacity of 12TB, is accessible through the UAB network ([agarcia@gabrmn.uab.es](mailto:agarcia@gabrmn.uab.es) for access). It hosts two multicentre databases (INTERPRET and eTUMOUR), with NMR and clinical data for more than 1000 human brain tumour patients and provides consultancy in processing and mathematical analysis of MRSI data, preclinical and clinical.

The platform also distributes GABRMN software packages such as the INTERPRET decision-support system for human brain tumour diagnosis based on MRS and SpectraClassifier, for pattern recognition of in vivo MRS data.

# Applied Proteomics and Protein Engineering



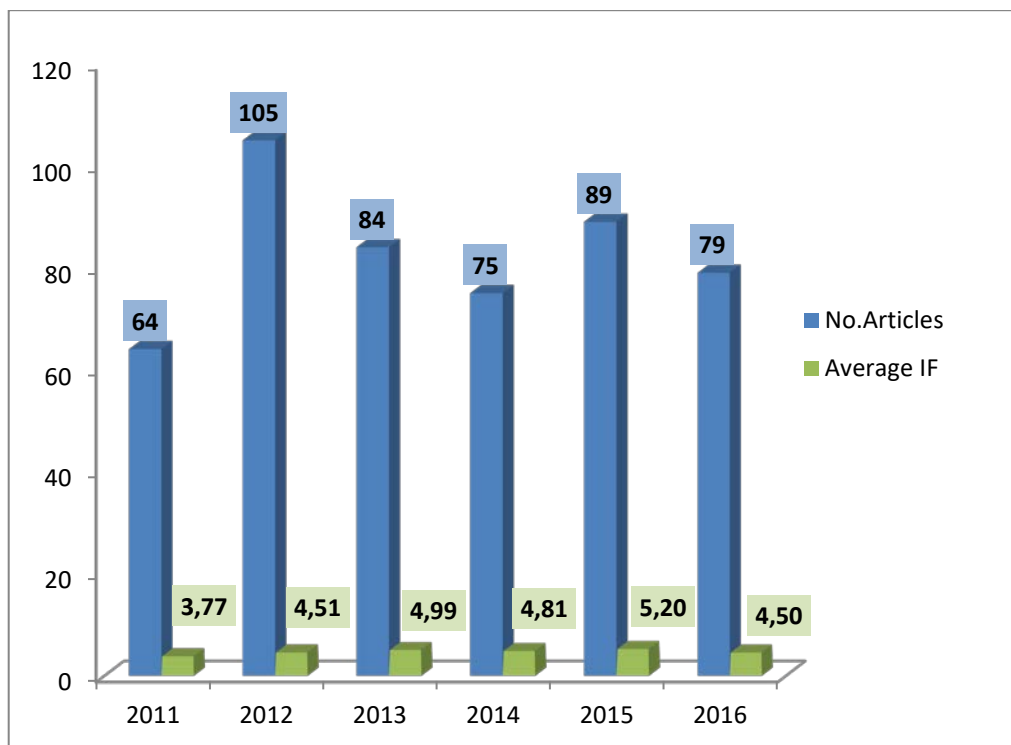
## *Others*

### Editorial work

Carles Arús is member of the editorial board of “MAGMA Magnetic Resonance Materials in Physics, Biology and Medicine”.

## Publications

Year	No.Articles	Total IF	Average IF
2011	64	241,49	3,77
2012	105	473,86	4,51
2013	84	418,86	4,99
2014	75	360,66	4,81
2015	89	462,45	5,20
2016	79	355,33	4,50



Adel, S., F. Karst, A. Gonzalez-Lafont, M. Pekarova, P. Saura, L. Masgrau, J. M. Lluch, S. Stehling, T. Horn, H. Kuhn and D. Heydeck (2016) Evolutionary alteration of ALOX15 specificity optimizes the biosynthesis of antiinflammatory and proresolving lipoxins. *Proceedings of the National Academy of Sciences of the United States of America*. 113, E4266-E4275.

Aillaud, C., C. Bosc, Y. Saoudi, E. Denarier, L. Peris, L. Sago, N. Taulet, A. Cieren, O. Tort, M. M. Magiera, C. Janke, V. Redeker, A. Andrieux and M. J. Moutin (2016) Evidence for new C-terminally truncated variants of alpha- and beta-tubulins. *Molecular Biology of the Cell*. 27, 640-653.

Arinez-Soriano, J., J. Albalad, A. Carne-Sanchez, C. S. Bonnet, F. Busque, J. Lorenzo, J. Juanhuix, M. W. Terban, I. Imaz, E. Toth and D. Maspoch (2016) pH-Responsive Relaxometric Behaviour of Coordination Polymer Nanoparticles Made of a Stable Macrocyclic Gadolinium Chelate. *Chemistry-a European Journal*. 22, 13162-13170.

Armengol, P., R. Gelabert, M. Moreno and J. M. Lluch (2016) Chromophore interactions leading to different absorption spectra in mNeptune1 and mCardinal red fluorescent proteins. *Physical Chemistry Chemical Physics*. 18, 16964-16976.

Bru, S., J. M. Martinez-Lainez, S. Hernandez-Ortega, E. Quandt, J. Torres-Torronteras, R. Marti, D. Canadell, J. Arino, S. Sharma, J. Jimenez and J. Clotet (2016) Polyphosphate is involved in cell cycle progression and genomic stability in *Saccharomyces cerevisiae*. *Molecular Microbiology*. 101, 367-380.

Cabrera, I., I. Abasolo, J. L. Corchero, E. Elizondo, P. R. Gil, E. Moreno, J. Faraudo, S. Sala, D. Bueno, E. Gonzalez-Mira, M. Rivas, M. Melgarejo, D. Pulido, F. Albericio, M. Royo, A. Villaverde, M. F. Garcia-Parajo, S. Schwartz, N. Ventosa and J. Veciana (2016) alpha-Galactosidase-A-Loaded Nanoliposomes with Enhanced Enzymatic Activity and Intracellular Penetration. *Advanced Healthcare Materials*. 5, 829-840.

Cabrera-Munoz, A., L. Rojas, D. F. Gil, Y. Gonzalez-Gonzalez, M. Mansur, A. Camejo, J. R. Pires and M. Antigua (2016) Heterologous expression of *Cenchrus muricatus* protease inhibitor II (CmPI-II) in *Pichia pastoris* system: Purification, isotopic labeling and preliminary characterization. *Protein Expression and Purification*. 126, 127-136.

Calderon-Gomez, E., H. Bassolas-Molina, R. Mora-Buch, I. Dotti, N. Planell, M. Esteller, M. Gallego, M. Marti, C. Garcia-Martin, C. Martinez-Torro, I. Ordas, S. Singh, J. Panes, D. Benitez-Ribas and A. Salas (2016) Commensal-Specific CD4(+) Cells From Patients With Crohn's Disease Have a T-Helper 17 Inflammatory Profile. *Gastroenterology*. 151, 489-+.

Canadell, D. and J. Arino (2016) Interactions Between Monovalent Cations and Nutrient Homeostasis. *Yeast Membrane Transport*. Ramos, J., Sychrova, H. and Kschischo, M. (eds.), pp 271-289

Cano-Garrido, O., M. V. Cespedes, U. Unzueta, P. Saccardo, M. Roldan, A. Sanchez-Chardi, R. Cubarsi, E. Vazquez, R. Mangues, E. Garcia-Fruitos and A. Villaverde (2016) CXCR4(+)-targeted protein nanoparticles produced in the food-grade bacterium *Lactococcus lactis*. *Nanomedicine*. 11, 2387-2398.

Carija, A., S. Navarro and S. Ventura (2016) Data on correlation between Abeta42 structural aggregation propensity and toxicity in bacteria. *Data in brief*. 7, 143-7.

Castells Domingo, X., L. Ferrer-Font, M. Davila, A. Paula Candiota, R. V. Simoes, A. Fernandez-Coello, A. Gabarros, S. Boluda, A. Barcelo, J. Arino and C. Arus (2016) Improving Ribosomal RNA Integrity in Surgically Resected Human Brain Tumor Biopsies. *Biopreservation and Biobanking*. 14, 156-164.

Ciezka, M., M. Acosta, C. Herranz, J. M. Canals, M. Pumarola, A. P. Candiota and C. Arus (2016) Development of a transplantable glioma tumour model from genetically engineered mice: MRI/MRS/MRSI characterisation. *Journal of Neuro-Oncology*. 129, 67-76.

Collado, R., A. Prenafeta, L. Gonzalez-Gonzalez, J. A. Perez-Pons and M. Sitja (2016) Probing vaccine antigens against bovine mastitis caused by *Streptococcus uberis*. *Vaccine*. 34, 3848-3854.

Contreras Rodriguez, A. R., J. Saiz-Poseu, J. Garcia-Pardo, B. Garcia, J. Lorenzo, I. Ojea-Jimenez, D. Komilis, J. Sedo, F. Busque, A. Sanchez, D. Ruiz-Molina and X. Font (2016) Biocompatible polydopamine-like particles for the removal of heavy metals at extremely low concentrations. *Rsc Advances*. 6, 40058-40066.

Corchero, J. L. (2016) Eukaryotic aggregates: from a model of conformational diseases to an emerging type of immobilized biocatalyzers. *Applied Microbiology and Biotechnology*. 100, 559-569.

Domingo, X. C., L. Ferrer-Font, M. Davila, A. P. Candiota, R. V. Simoes, A. Fernandez-Coello, A. Gabarros, S. Boluda, A. Barcelo, J. Arino and C. Arus (2016) Improving Ribosomal RNA Integrity in Surgically Resected Human Brain Tumor Biopsies. *Biopreservation and Biobanking*. 14, 156-164.

Fa, M., D. Puzzo, R. Piacentini, A. Staniszewski, H. Zhang, M. A. Baltrons, D. D. Li Puma, I. Chatterjee, J. Li, F. Saeed, H. L. Berman, C. Ripoli, W. Gulisano, J. Gonzalez, H. Tian, J. A. Costa, P. Lopez, E. Davidowitz, W. H. Yu, V. Haroutunian, L. M. Brown, A. Palmeri, E. M. Sigurdsson, K. E. Duff, A. F. Teich, L. S. Honig, M.



- Sierks, J. G. Moe, L. D'Adamio, C. Grassi, N. M. Kanaan, P. E. Fraser and O. Arancio (2016) Extracellular Tau Oligomers Produce An Immediate Impairment of LTP and Memory. *Scientific Reports*. 6, 15.
- Ferrer-Font, L., E. Alcaraz, M. Plana, A. P. Candiota, E. Itarte and C. Arus (2016) Protein Kinase CK2 Content in GL261 Mouse Glioblastoma. *Pathology & Oncology Research*. 22, 633-637.
- Ferrer-Navarro, M., G. Torrent, E. Mongiardini, O. Conchillo-Sole, I. Gibert and X. Daura (2016) Proteomic analysis of outer membrane proteins and vesicles of a clinical isolate and a collection strain of *Stenotrophomonas maltophilia*. *Journal of Proteomics*. 142, 122-129.
- Franco, L., S. Hernandez, A. Calvo, G. Ferragut, I. Amela, J. Cedano and E. Querol (2016) Moonlighting proteins: a bioinformatics analysis of their biochemical characteristics. *New Biotechnology*. 33, 432-433.
- Garcia-Morales, L., L. Gonzalez-Gonzalez, E. Querol and J. Pinol (2016) A minimized motile machinery for *Mycoplasma genitalium*. *Molecular Microbiology*. 100, 125-138.
- Giannotti, M. I., I. Abasolo, M. Oliva, F. Andrade, N. Garcia-Aranda, M. Melgarejo, D. Pulido, J. L. Corchero, Y. Fernandez, A. Villaverde, M. Royo, M. F. Garcia-Parajo, F. Sanz and S. Schwartz, Jr. (2016) Highly Versatile Polyelectrolyte Complexes for Improving the Enzyme Replacement Therapy of Lysosomal Storage Disorders. *Acs Applied Materials & Interfaces*. 8, 25741-25752.
- Gomez, A., N. Andreu, M. Ferrer-Navarro, D. Yero and I. Gibert (2016) Triclosan-induced genes Rv1686c-Rv1687c and Rv3161c are not involved in triclosan resistance in *Mycobacterium tuberculosis*. *Scientific Reports*. 6.
- Klionsky, D. J., et al. (2016) Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy*. 12, 1-222.
- Lazaro, D. F., M. C. Dias, A. Carija, S. Navarro, C. S. Madaleno, S. Tenreiro, S. Ventura and T. F. Outeiro (2016) The effects of the novel A53E alpha-synuclein mutation on its oligomerization and aggregation. *Acta Neuropathologica Communications*. 4.
- Lopez, L. C., O. Varea, S. Navarro, J. A. Carrodegua, N. S. de Groot, S. Ventura and J. Sancho (2016) Benzbromarone, Quercetin, and Folic Acid Inhibit Amylin Aggregation. *International Journal of Molecular Sciences*. 17, 12.
- Lorenzo, J. and A. M. Montana (2016) The molecular shape and the field similarities as criteria to interpret SAR studies for fragment-based design of platinum(IV) anticancer agents. Correlation of physicochemical properties with cytotoxicity. *Journal of Molecular Graphics & Modelling*. 69, 39-60.
- Luis Corchero, J. (2016) Eukaryotic aggresomes: from a model of conformational diseases to an emerging type of immobilized biocatalyzers. *Applied Microbiology and Biotechnology*. 100, 559-569.
- Macedo, B., Y. Cordeiro and S. Ventura (2016) Mammalian prion amyloid formation in bacteria. *Prion*. 10, 112-118.
- Marcilla, M., I. Alvarez, A. Ramos-Fernandez, M. Lombardia, A. Paradela and J. P. Albar (2016) Comparative Analysis of the Endogenous Peptidomes Displayed by HLA-B\*27 and Mamu-B\*08: Two MHC Class I Alleles Associated with Elite Control of HIV/SIV Infection. *Journal of Proteome Research*. 15, 1059-1069.
- Marinelli, P., I. Pallares, S. Navarro and S. Ventura (2016) Dissecting the contribution of *Staphylococcus aureus* alpha-phenol-soluble modulins to biofilm amyloid structure. *Scientific Reports*. 6.
- Martinelli, L., L. Garcia-Morales, E. Querol, J. Pinol, I. Fita and B. M. Calisto (2016) Structure-Guided Mutations in the Terminal Organelle Protein MG491 Cause Major Motility and Morphologic Alterations on *Mycoplasma genitalium*. *Plos Pathogens*. 12.
- Mendoza, F., H. Gomez, J. M. Lluch and L. Masgrau (2016) alpha 1,4-N-Acetylhexosaminyltransferase EXTL2: The Missing Link for Understanding Glycosidic Bond Biosynthesis with Retention of Configuration. *Acs Catalysis*. 6, 2577-2589.
- Moreno, M., R. Gelabert and J. M. Lluch (2016) The Quest for Photoswitches Activated by Near-Infrared Light: A Theoretical Study of the Photochemistry of BF<sub>2</sub>-Coordinated Azo Derivatives. *Chemphyschem*. 17, 2824-2838.
- Mozo-Villarias, A., J. Cedano and E. Querol (2016) Vector description of electric and hydrophobic interactions in protein homodimers. *European Biophysics Journal with Biophysics Letters*. 45, 341-346.
- Navarro, S., A. Carija, D. Munoz-Torrero and S. Ventura (2016) A fast and specific method to screen for intracellular amyloid inhibitors using bacterial model systems. *European Journal of Medicinal Chemistry*. 121, 785-792.
- Pallares, I., V. Iglesias and S. Ventura (2016) The Rho Termination Factor of *Clostridium botulinum* Contains a Prion-Like Domain with a Highly Amyloidogenic Core. *Frontiers in Microbiology*. 6.
- Pallares, I. and S. Ventura (2016) Understanding and predicting protein misfolding and aggregation: Insights from proteomics. *Proteomics*. 16, 2570-2581.
- Pantano, L., M. R. Friedlander, G. Escaramis, E. Lizano, J. Pallares-Albanell, I. Ferrer, X. Estivill and E. Marti (2016) Specific small-RNA signatures in the amygdala at premotor and motor stages of Parkinson's

disease revealed by deep sequencing analysis. *Bioinformatics*. 32, 673-681.

Pastor-Flores, D., J. O. Schulze, A. Bahi, E. Suss, A. Casamayor and R. M. Biondi (2016) Lipid regulators of Pkh2 in *Candida albicans*, the protein kinase ortholog of mammalian PDK1. *Biochimica Et Biophysica Acta-Molecular and Cell Biology of Lipids*. 1861, 249-259.

Perez-Sampietro, M., A. Serra-Cardona, D. Canadell, C. Casas, J. Arino and E. Herrero (2016) The yeast Aft2 transcription factor determines selenite toxicity by controlling the low affinity phosphate transport system. *Scientific Reports*. 6.

Pesarrodona, M., Y. Fernandez, L. Foradada, A. Sanchez-Chardi, O. Conchillo-Sole, U. Unzueta, Z. Xu, M. Roldan, S. Villegas, N. Ferrer-Miralles, S. Schwartz, Jr., U. Rinas, X. Daura, I. Abasolo, E. Vazquez and A. Villaverde (2016) Conformational and functional variants of CD44-targeted protein nanoparticles bio-produced in bacteria. *Biofabrication*. 8.

Petrenyi, K., C. Molero, Z. Konya, F. Erdodi, J. Arino and V. Dombradi (2016) Analysis of Two Putative *Candida albicans* Phosphopantothenoylcysteine Decarboxylase / Protein Phosphatase Z Regulatory Subunits Reveals an Unexpected Distribution of Functional Roles. *Plos One*. 11.

Petrezselyova, S., M. Lopez-Malo, D. Canadell, A. Roque, A. Serra-Cardona, M. C. Marques, E. Vilaprinyo, R. Alves, L. Yenush and J. Arino (2016) Regulation of the Na<sup>+</sup>/K<sup>+</sup>-ATPase Ena1 Expression by Calcineurin/Crz1 under High pH Stress: A Quantitative Study. *Plos One*. 11.

Petrov, D., X. Daura and B. Zagrovic (2016) Effect of Oxidative Damage on the Stability and Dimerization of Superoxide Dismutase 1. *Biophysical Journal*. 110, 1499-1509.

Popa, C., L. Li, S. Gil, L. Tatjer, K. Hashii, M. Tabuchi, N. S. Coll, J. Arino and M. Valls (2016) The effector AWR5 from the plant pathogen *Ralstonia solanacearum* is an inhibitor of the TOR signalling pathway. *Scientific Reports*. 6, 14.

Pulido, P., E. Llamas, B. Llorente, S. Ventura, L. P. Wright and M. Rodriguez-Concepcion (2016) Specific Hsp100 Chaperones Determine the Fate of the First Enzyme of the Plastidial Isoprenoid Pathway for Either Refolding or Degradation by the Stromal Clp Protease in *Arabidopsis*. *Plos Genetics*. 12.

Reig-Viader, R., M. Garcia-Caldes and A. Ruiz-Herrera (2016) Telomere homeostasis in mammalian germ cells: a review. *Chromosoma*. 125, 337-351.

Rey, S., V. Moiche, S. Boltana, M. Teles and S. MacKenzie (2017) Behavioural fever in zebrafish larvae. *Developmental and Comparative Immunology*. 67, 287-292.

Rey, S., L. Ribas, D. M. Capdevila, A. Callol, F. A. Huntingford, M. Pilarczyk, S. Kadri and S. MacKenzie (2016) Differential responses to environmental challenge by common carp *Cyprinus carpio* highlight the importance of coping style in integrative physiology. *Journal of Fish Biology*. 88, 1056-1069.

Rey, S., V. Moiche, S. Boltana, M. Teles and S. MacKenzie (2016a) Behavioural fever in zebrafish larvae. *Developmental and comparative immunology*.

Rodríguez, A. R. C., J. Saiz-Poseu, J. Garcia-Pardo, B. Garcia, J. Lorenzo, I. Ojea-Jimenez, D. Komilis, J. Sedo, F. Busque, A. Sanchez, D. Ruiz-Molina and X. Font (2016) Biocompatible polydopamine-like particles for the removal of heavy metals at extremely low concentrations. *Rsc Advances*. 6, 40058-40066.

Roque, A., S. Petrezselyova, A. Serra-Cardona and J. Arino (2016) Genome-wide recruitment profiling of transcription factor Crz1 in response to high pH stress. *Bmc Genomics*. 17.

Rueda, F., M. V. Cespedes, A. Sanchez-Chardi, J. Seras-Franzoso, M. Pesarrodona, N. Ferrer-Miralles, E. Vazquez, U. Rinas, U. Unzueta, U. Mamat, R. Mangués, E. Garcia-Fruitos and A. Villaverde (2016) Structural and functional features of self-assembling protein nanoparticles produced in endotoxin-free *Escherichia coli*. *Microbial Cell Factories*. 15.

Saccardo, P., J. L. Corchero and N. Ferrer-Miralles (2016) Tools to cope with difficult-to-express proteins. *Applied Microbiology and Biotechnology*. 100, 4347-4355.

Salazar, V. A., J. Arranz-Trullen, S. Navarro, J. A. Blanco, D. Sanchez, M. Moussaoui and E. Boix (2016) Exploring the mechanisms of action of human secretory RNase 3 and RNase 7 against *Candida albicans*. *Microbiologyopen*. 5, 830-845.

Sanchez-Garcia, L., L. Martin, R. Mangués, N. Ferrer-Miralles, E. Vazquez and A. Villaverde (2016) Recombinant pharmaceuticals from microbial cells: a 2015 update. *Microbial Cell Factories*. 15.

Sant'Anna, R., M. R. Fernandez, C. Batlle, S. Navarro, N. S. de Groot, L. Serpell and S. Ventura (2016a) Characterization of Amyloid Cores in Prion Domains. *Scientific Reports*. 6.

Sant'Anna, R., P. Gallego, L. Z. Robinson, A. Pereira-Henriques, N. Ferreira, F. Pinheiro, S. Esperante, I. Pallares, O. Huertas, M. R. Almeida, N. Reixach, R. Insa, A. Velazquez-Campoy, D. Reverter, N. Reig and S. Ventura (2016a) Repositioning tolcapone as a potent inhibitor of transthyretin amyloidogenesis and associated cellular toxicity. *Nature Communications*. 7.

Sant'Anna, R., S. Navarro, S. Ventura, L. Paraoan and D. Foguel (2016b) Amyloid properties of the leader peptide of variant B cystatin C: implications for Alzheimer and macular degeneration. *Febs*

Letters. 590, 644-654.

Saura, P., J. D. Marechal, L. Masgrau, J. M. Lluch and A. Gonzalez-Lafont (2016a) Computational insight into the catalytic implication of head/tail-first orientation of arachidonic acid in human 5-lipoxygenase: consequences for the positional specificity of oxygenation. *Physical Chemistry Chemical Physics*. 18, 23017-23035.

Saura, P., L. Masgrau, D. Heydeck, H. Kuehn, J. M. Lluch and A. Gonzalez-Lafont (2016b) Is Regioselectivity in the Enzyme-Catalyzed Hydroperoxidation of Arachidonic Acid Necessarily Determined by Hydrogen Abstraction? The Case of Rabbit Leu597Ala/Ile663Ala ALOX15 Mutant. *Chemphyschem*. 17, 3321-3332.

Scholz, E., A. Mestre-Ferrer, X. Daura, N. Garcia-Medel, M. Carrascal, E. A. James, W. W. Kwok, F. Canals and I. Alvarez (2016) A Comparative Analysis of the Peptide Repertoires of HLA-DR Molecules Differentially Associated With Rheumatoid Arthritis. *Arthritis & Rheumatology*. 68, 2412-2421.

Seras-Franzoso, J., A. Sanchez-Chardi, E. Garcia-Fruitos, E. Vazquez and A. Villaverde (2016) Cellular uptake and intracellular fate of protein releasing bacterial amyloids in mammalian cells. *Soft Matter*. 12, 3451-3460.

Serna, N., M. V. Cespedes, P. Saccardo, Z. K. Xu, U. Unzueta, P. Alamo, M. Pesarrodona, A. Sanchez-Chardi, M. Roldan, R. Mangués, E. Vazquez, A. Villaverde and N. Ferrer-Miralles (2016) Rational engineering of single-chain polypeptides into protein-only, BBB-targeted nanoparticles. *Nanomedicine-Nanotechnology Biology and Medicine*. 12, 1241-1251.

Soler, J., P. Saura, D. Garcia-Lopez, L. Masgrau, J. M. Lluch and A. Gonzalez-Lafont (2016) How Can Linoleic Acid Be the Preferential Substrate of the Enzyme 15-Lipoxygenase-1? A QM/MM Approach. *Journal of Physical Chemistry B*. 120, 1950-1960.

Suardiaz, R., P. G. Jambrina, L. Masgrau, A. Gonzalez-Lafont, E. Rosta and J. M. Lluch (2016) Understanding the Mechanism of the Hydrogen Abstraction from Arachidonic Acid Catalyzed by the Human Enzyme 15-Lipoxygenase-2. A Quantum Mechanics/Molecular Mechanics Free Energy Simulation. *Journal of Chemical Theory and Computation*. 12, 2079-2090.

Taglialegna, A., S. Navarro, S. Ventura, J. A. Garnett, S. Matthews, J. R. Penades, I. Lasa and J. Valle (2016) Staphylococcal Bap Proteins Build Amyloid Scaffold Biofilm Matrices in Response to Environmental Signals. *Plos Pathogens*. 12, 34.

Tatjer, L., A. Gonzalez, A. Serra-Cardona, A. Barcelo, A. Casamayor and J. Arino (2016) The *Saccharomyces cerevisiae* Ptc1 protein phosphatase attenuates G2-M cell cycle blockage caused by activation of the cell wall integrity pathway. *Molecular Microbiology*. 101, 671-687.

Tatjer, L., A. Sacristan-Reviriego, C. Casado, A. Gonzalez, B. Rodriguez-Porrata, L. Palacios, D. Canadell, A. Serra-Cardona, H. Martin, M. Molina and J. Arino (2016b) Wide-Ranging Effects of the Yeast Ptc1 Protein Phosphatase Acting Through the MAPK Kinase Mkk1. *Genetics*. 202, 141-+.

Torrealba, D., D. Parra, J. Seras-Franzoso, E. Vallejos-Vidal, D. Yero, I. Gibert, A. Villaverde, E. Garcia-Fruitos and N. Roher (2016) Nanostructured recombinant cytokines: A highly stable alternative to short-lived prophylactics. *Biomaterials*. 107, 102-114.

Vallejos-Vidal, E., F. Reyes-Lopez, M. Teles and S. MacKenzie (2016) The response of fish to immunostimulant diets. *Fish & Shellfish Immunology*. 56, 34-69.

Vazquez, E., R. Mangués and A. Villaverde (2016a) Functional recruitment for drug delivery through protein-based nanotechnologies. *Nanomedicine*. 11, 1333-1336.

Ventura, S. (2016) Curing bacterial infections with protein aggregates. *Molecular Microbiology*. 99, 827-830.

Villar-Pique, A., A. Espargaro, S. Ventura and R. Sabate (2016) In vivo amyloid aggregation kinetics tracked by time-lapse confocal microscopy in real-time. *Biotechnology Journal*. 11, 172-177.

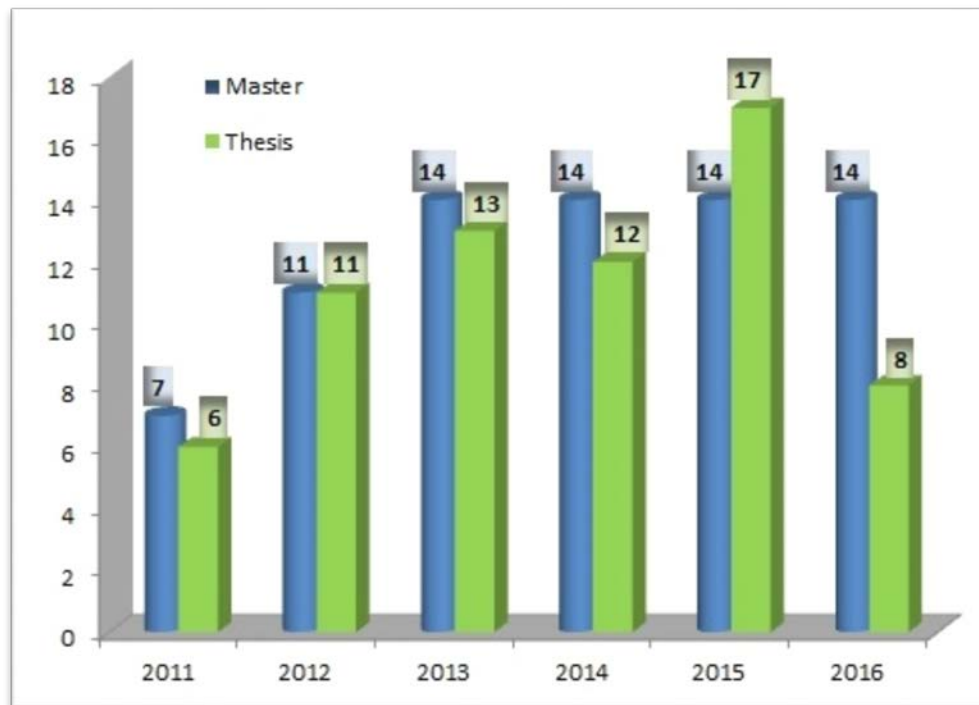
Villar-Pique, A., T. L. da Fonseca, R. Sant'Anna, E. M. Szegoe, L. Fonseca-Ornelas, R. Pinho, A. Carija, E. Gerhardt, C. Masaracchia, E. A. Gonzalez, G. Rossetti, P. Carloni, C. O. Fernandez, D. Foguel, I. Milosevic, M. Zweckstetter, S. Ventura and T. F. Outeiro (2016a) Environmental and genetic factors support the dissociation between alpha-synuclein aggregation and toxicity. *Proceedings of the National Academy of Sciences of the United States of America*. 113, E6506-E6515.

Virtudes Cespedes, M., Y. Fernandez, U. Unzueta, R. Mendoza, J. Seras-Franzoso, A. Sanchez-Chardi, P. Alamo, V. Toledo-Rubio, N. Ferrer-Miralles, E. Vazquez, S. Schwartz, Jr., I. Abasolo, J. Luis Corchero, R. Mangués and A. Villaverde (2016) Bacterial mimetics of endocrine secretory granules as immobilized in vivo depots for functional protein drugs. *Scientific Reports*. 6.

Vozdova, M., A. Ruiz-Herrera, J. Fernandez, H. Cernohorska, J. Frohlich, H. Sebestova, S. Kubickova and J. Rubes (2016) Meiotic behaviour of evolutionary sex-autosome translocations in Bovidae. *Chromosome Research*. 24, 325-338.

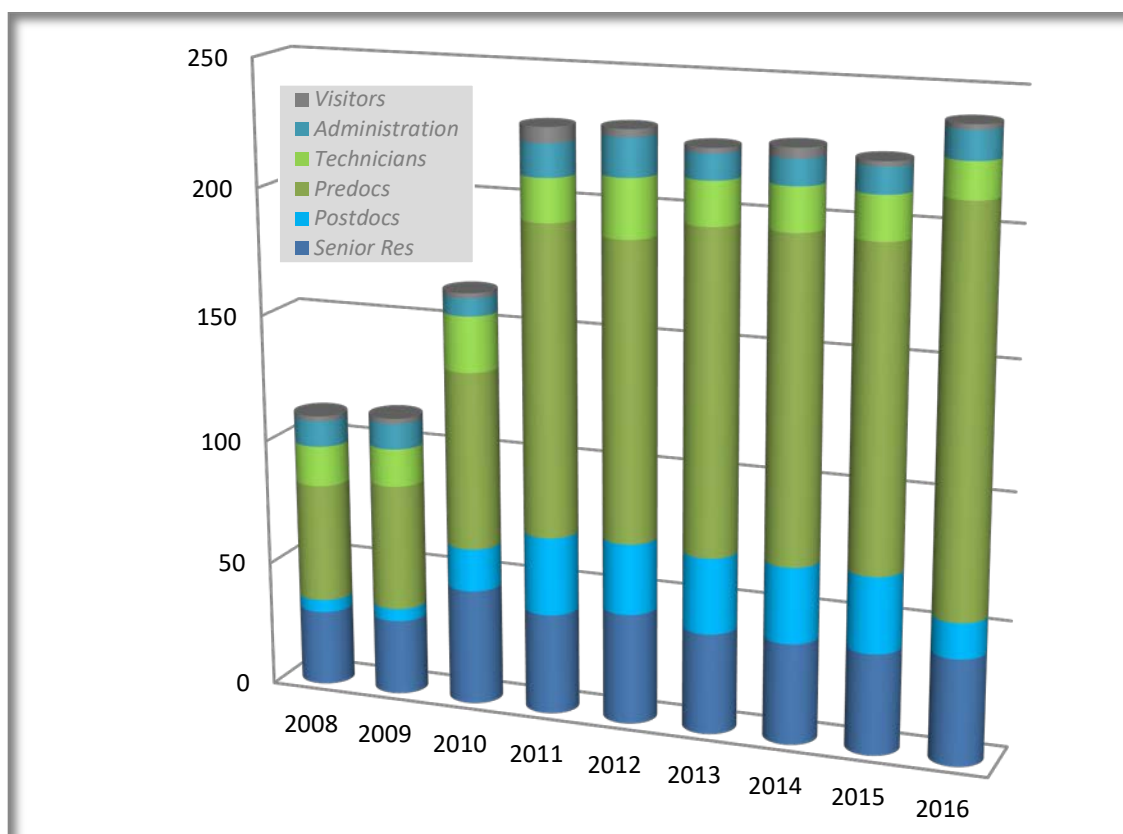
## Thesis

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## Human Resources

	Senior Res	Postdocs	Predocs	Technicians	Administration	Visitors	Total
2008	30	5	47	16	10	2	110
2009	30	5	50	15	10	2	112
2010	46	17	70	22	7	2	164
2011	40	31	122	17	13	6	229
2012	44	28	117	23	15	3	230
2013	40	30	126	17	10	2	225
2014	40	30	126	17	10	4	227
2015	40	30	125	17	10	2	224
2016	42	14	156	14	11	2	239



# Key figures

## Funding

