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Institut de Biotecnologia
i de Biomedicina

ANNUAL REPORT

2016

http://ibb.uab.cat
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Administrative Structure

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

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 mamiferos. CGL2014-54317-P. 2015-2017. PI: Aurora Ruiz-Herrera.

Estudio de los mecanismos que regulan la progresion de la profase meiotica en mamiferos. BFU2013-43965-P.. PI: Ignasi Roig.

Others

PhD thesis

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

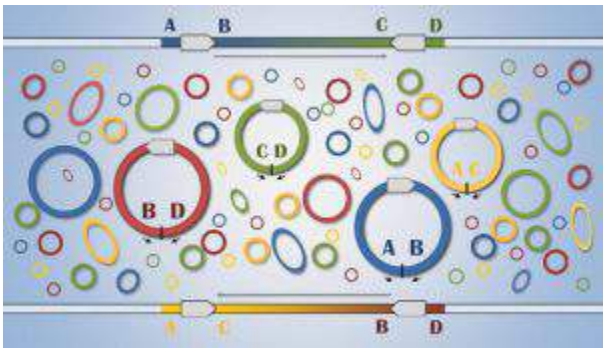
Comparative and Functional Genomics

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	Mº Alejandra Delprat Obeaga
	Sergi Villatoro Gómez

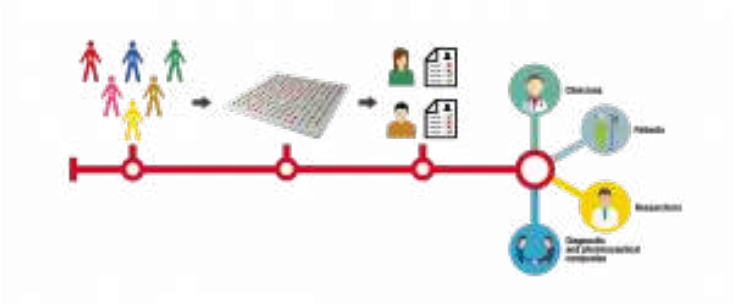
Overview

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 particualr, 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

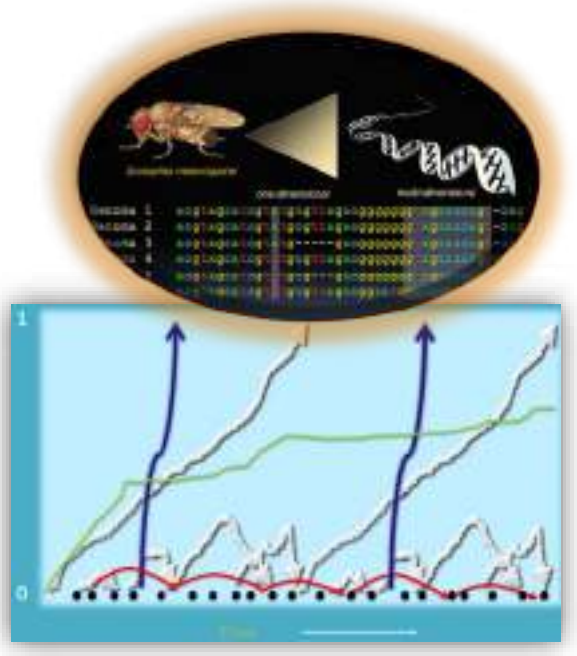
BMC Genomics Associate Editor.

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:

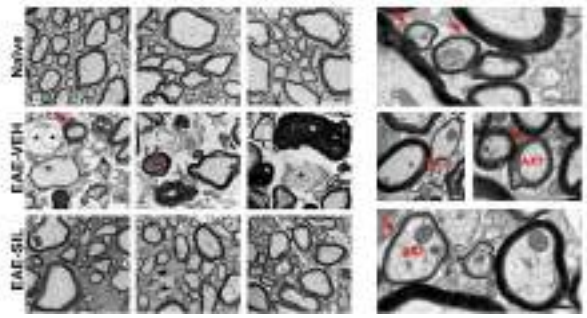
Director of Bioinformatics Platform of campus UAB and UAB sphere Instituts of Health

Promoter of a spin-off of Bioinformatics

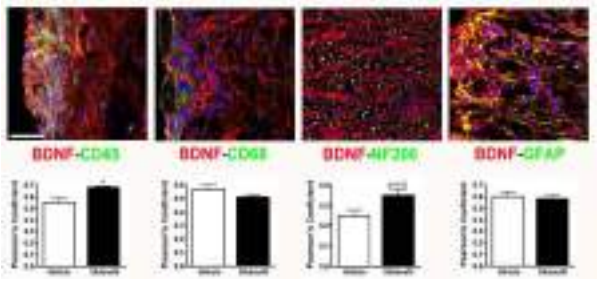
Neuroimmunology

Group Leader	Agustina García Sánchez
Senior Member	Maria Antonia Baltrons Soler
Postdoctoral Fellow	Beatriz Moreno Bruna
Predoctoral 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.



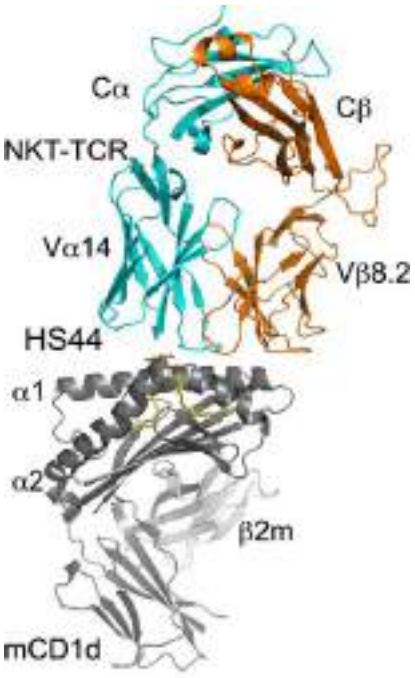
At present, we are investigating the mechanisms of the anti-inflammatory and remyelinating effects of PDE5 inhibitors in the animal model of MS, experimental autoimmune encephalomyelitis (EAE), as well as in immune cells from humans. Our final goal is to to provide evidences that will support the notion 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 β-amyloid burden reported by other groups in animal models of Alzheimer's disease.

Molecular Immunology

Group Leader Ángel Raúl Castaño
Predoctoral Fellow Ignasi Esteban

Overview

Activation of iNKT cells by CD1d-ligands is a immunotherapeutic tool under intensive investigation. α-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 α-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 limfoid organs and the chemokines directing such traficking are ongoing efforts in our lab.

Projects

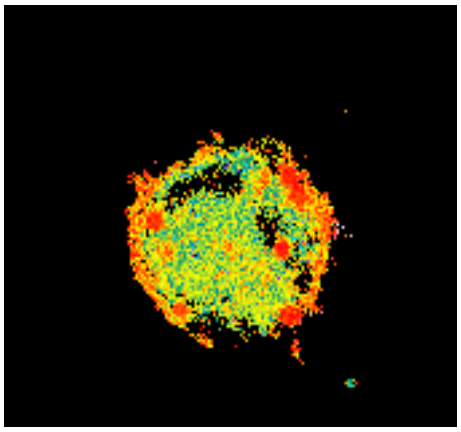
TV32013-130910. Antitumor activity of iNKT activators analogs of the a-GalactosylCeramide: towards immunotherapeutical reagents. IP: Raul Castaño 2014-2016.

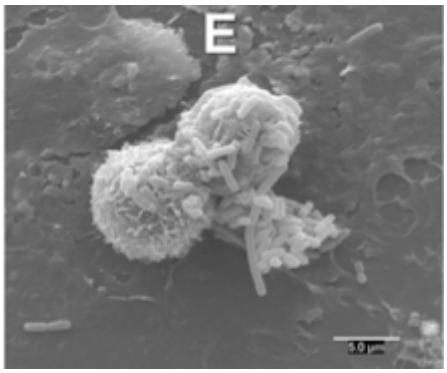
Applied Immunology

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

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 cerevisae* 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 de1992.

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 Mèdicas de Catalunya i de Baleares des de 1996.

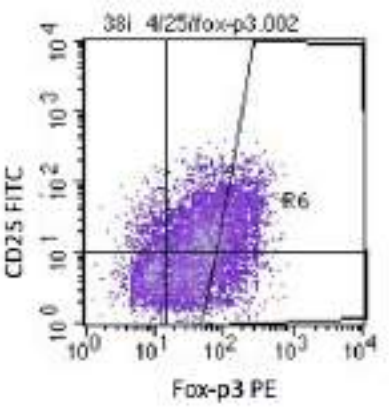
Directora científica del Servicio científico-técnico Cultivos Celulares, Producción de Anticuerpos y Citometría" de la UAB desde Junio de 2009

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

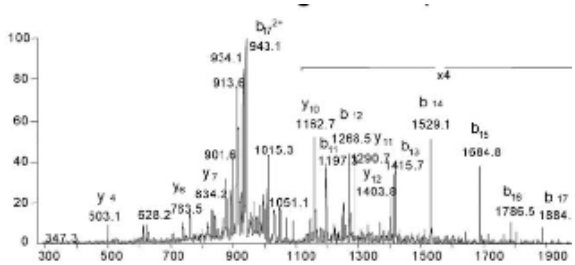
Overview

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.



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

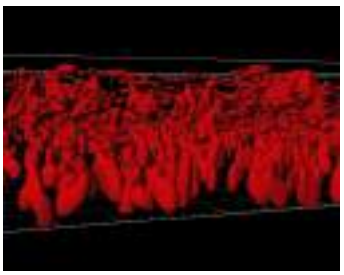
Bacterial Molecular Genetics and Pathogenesis

Group Leader	Isidre Gibert Gonzàlez
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.

<u>*Keywords*</u>

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

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

Evolutive Immunology

Group Leader	Nerea Roher Armentia
PhD Students	Debora Torrealba Sandoval
	Jie Ji
	Jofre Gasion
	Eva Vallejos
	Rosermary 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 INFφ and IL-1b 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

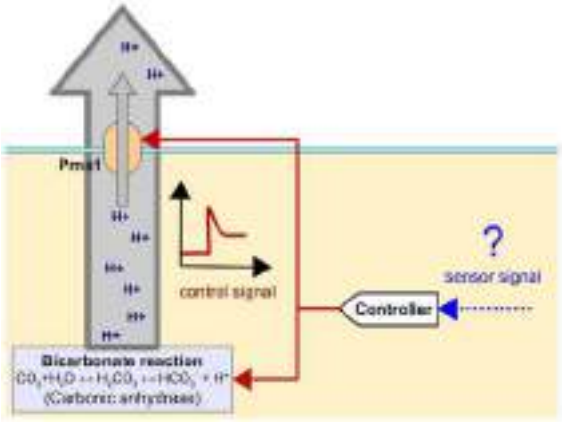
Desarrollo de sistemas específicos de nanodelivery para especies de interés acuícola: delivery mediante nanoliposomas y mediante nanopartículas proteicas. AGL2015-65129-R (01/01/2016 – 31/12/2018).

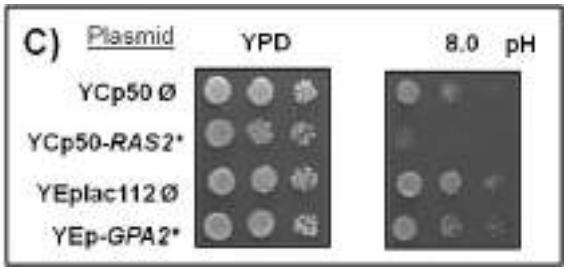
Yeast Molecular Biology

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 give 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.





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 Microbiologia Aplicada, UAB). 2016. Joaquin Ariño.

María Coca Jimeno. La homeostasis iónica como posible diana para el desarrollo de antifúngicos. (Máster Oficial de Microbiologia 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.

Computational Biology

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

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 rewiew for several journals, including Journal of the american Chemical society, Andgewandte 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.

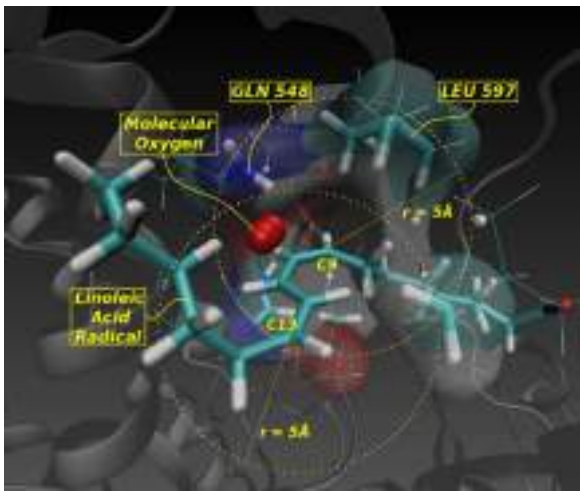
Theoretical Molecular Biology

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 anb 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.



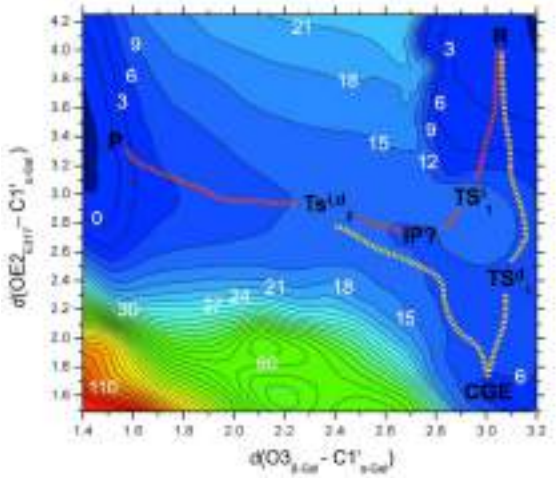
From Suardíaz *et al.*, J Phys Chem B , 2013

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 stereosecific in the hydroperoxidation reaction they catalyse; specificity required for its correct physiological function. We have been analysing the possible causes of this regiospecificity in the oxygen attack step catalysed by rabbit 15S-LO. Our results conclude that, among the different possibilities proposed

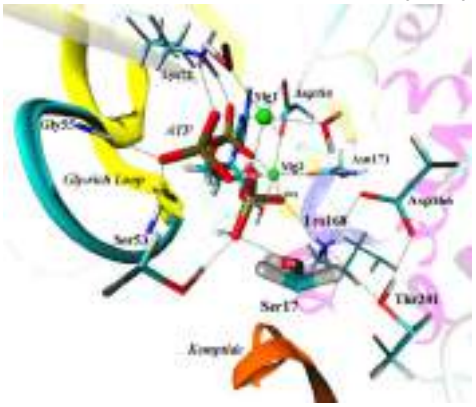
in the literature, the steric-shielding hypothesis seems to be the operating one in this enzyme. On another hand, we have started the study of the hydrogen abstraction step.

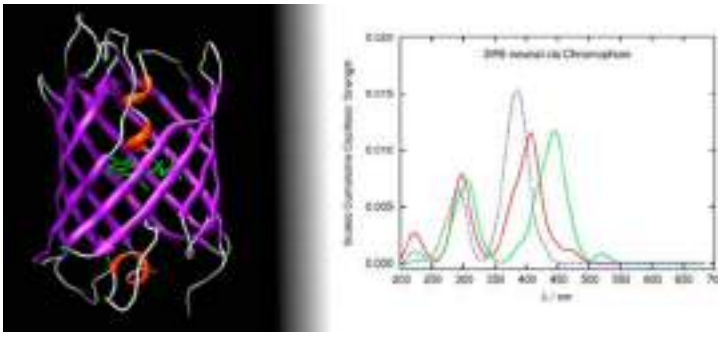
- **Computational chemical glycobiology:** the biosynthesis of glycans has been the focus of this research line. In particular, we are providing computational evidences that are helping clarify the catalytic mechanism used by retaining glycosyltransferases, a matter that has been under debate for the 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.



From Gómez *et al.*, J Am Chem Soc , 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 applyied 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

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”.

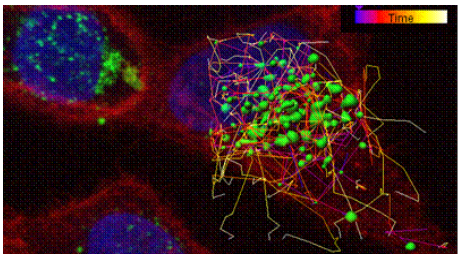
Projects

Adscribed at the Department of Chemistry of the UAB.

Nanobiotechnology

Group Leader	Antonio P. Villaverde
Senior Members	Neus Ferrer
	Esther Vazquez
	José Luis Corchero
	Elena Garcia Fruitós
	Joaquin Seras
PhD Students	Mireia Pesarrodona
	Paolo Saccardo
	Ugutz 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

Ingenieria de nanoparticulas proteicas para la entrega dirigida de proteinas terapeuticas y de acidos 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 microbialcells. 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. Haptenos 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.

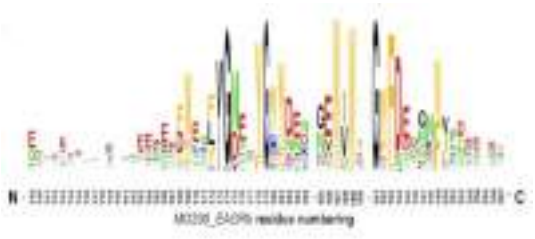
Editor de Medical Sciences (ISSN 2076-3271) desde 2012.

Molecular Biology

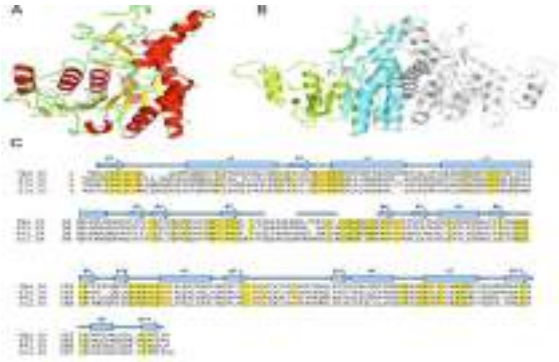
Group Leader	Enrique Querol Murillo
Senior Members	Jaume Piñol Ribas
	Josep A. Perez Pons
Postdoctoral Fellow	Ángel Mozo
	Oscar Quijada
PhD Students	Isaac Amela Abellán
	Juan Aibar
	Gemma Elias Bosch
	Luis González González
	Miguel González Martín
	Ignasi Granero Moya
	Esther Gútiez García
	Luis Franco Serrano
	Ana María, Martínez
	Luis García Morales
	Mario Huerta Casado
	Marta Hernández Solans
	Marta Huguet 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.



- Bioinformatics: Analysis of protein structure and function. Gene expression algorithms. Vaccine and drug target identification.
- Biotechnology: vaccine and diagnostic kits design.



Projects

Analisis de los mecanismos de virulencia y patogenicidad en micoplasmas: diseño de vacunas contra algunas especies de interes clinico. BIO2013-48704-R. IP Jaume Piñol.

Others

PhD thesis

Sergio Hernández. Análisis bioinformático de las proteinas multifuncionales (moonlighting). 2016. Directors: E.Querol.

Mario Huerta. Solving the Glucocorticoid Paradox in Cancer Using Expression Data. 2016. Directors: J.Cedano, E.Querol.

Patent

Inventores:, L. González, J. Piñol, J. Montane, M. Camats, E. Querol, M. Sitja. "Cepas mutantes de *Mycoplasma hyopneumoniae*" WO2014/009586 A2. "Vectors for transforming *Mycoplasma hyopneumoniae*, transformed *M. hyopneumoniae* straints, and use thereof "EP 2 684959 A1".

Inventors Gonzalez Luis Gonzalez, RIBAS Jaume PIÑOL, Giralt Jordi Montane, Malet Maria Camats, Murillo Enrique Querol, ARNAU Marta SITJA. WO2014135730 A1. Haptenos y conjugados derivados de piocianina, anticuerpos de los mismos, y método inmunoquímico para la detección de infecciones provocadas por pseudomonas aeruginosa. US20160033489

RIBAS Jaume PIÑOL, Virgili Sergi Bru, SOLER Laura FERRER, ARNAU Marta SITJA, Murillo Enrique Querol. WO2014009586 A3. Cepa viva atenuada de actinobacillus pleuropneumoniae. US20150306200.

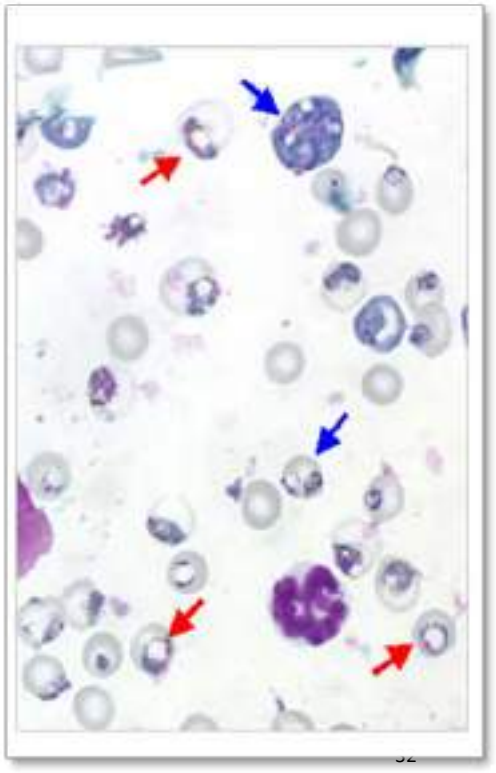
Protein Engineering and Proteomics

Group Leader	Francesc X. Avilés Puigvert
Senior Members	Josep Vendrell Roca
	Julia Lorenzo Rivera
PhD Students	Giovanny Covaleda
	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 metallocarboxipeptidases 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.



UAB
Universitat Autònoma de Barcelona

Projects

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

Interactomica diseño de sondas e imagen de carboxipeptidasas. en transito de la funcion 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.

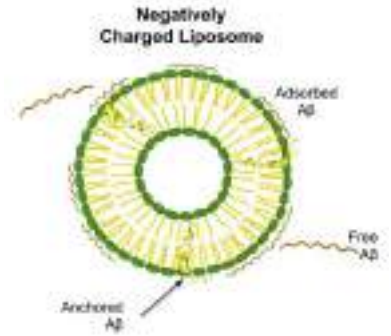
Among other achievements, in the present year:

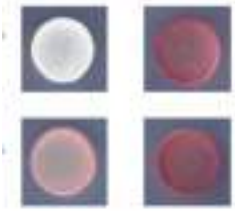
1.- Using atomic force microscopy, single molecule force spectroscopy and molecular dynamics we have addressed the inner forces that stabilize amyloid fibrillar structures (Valle-Delgado JJ. et al. 2012)

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)

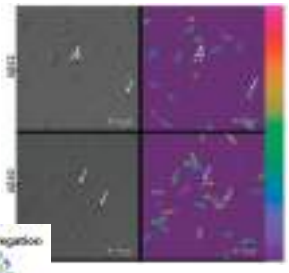
4- The neurotoxicity of the amyloid peptide Abeta is exerted through interactions with neuronal membranes. Using liposomes as model membranes, we have shown that it is the balance between peptide insertion and adsortion in the membrane that modulates its aggregation and toxicity (Sabate et al 2012a).

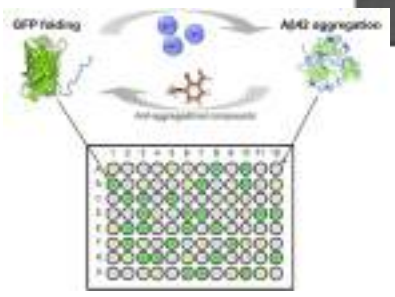




5- We have shown that bacterial cells might form infective amyloid structures and therefore that they can be used to generate and study prion proteins (Espargaro et al 2012a).

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 refolding to identify chemical compounds that promote or avoid the aggregation of biotechnological/biomedical relevant proteins (Villar-Pique et al., 2012a).

Projects

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

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

Deciphering the role of a a-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 Varejáo Nogueira da Paz
PhD Students	Bing Liu
	Hèctor López
	Jara Lascorz
	Jéssica Angulo
	Roger Canton

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

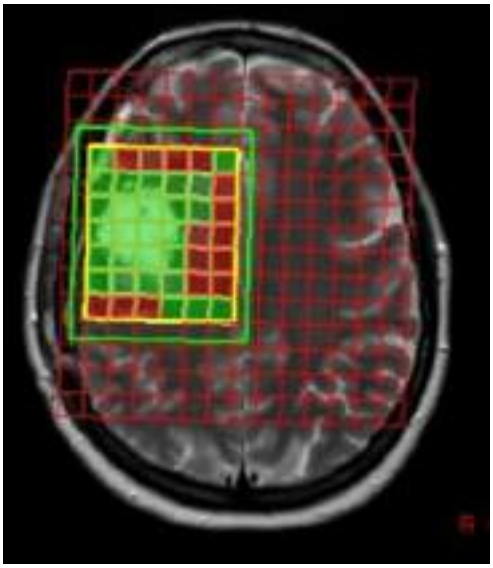
Caracterización estructural de la modificación por sumo en procesos de reparación de DNA. (Ref. BFU2015-66417-P).IP: David Reverter.

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 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.

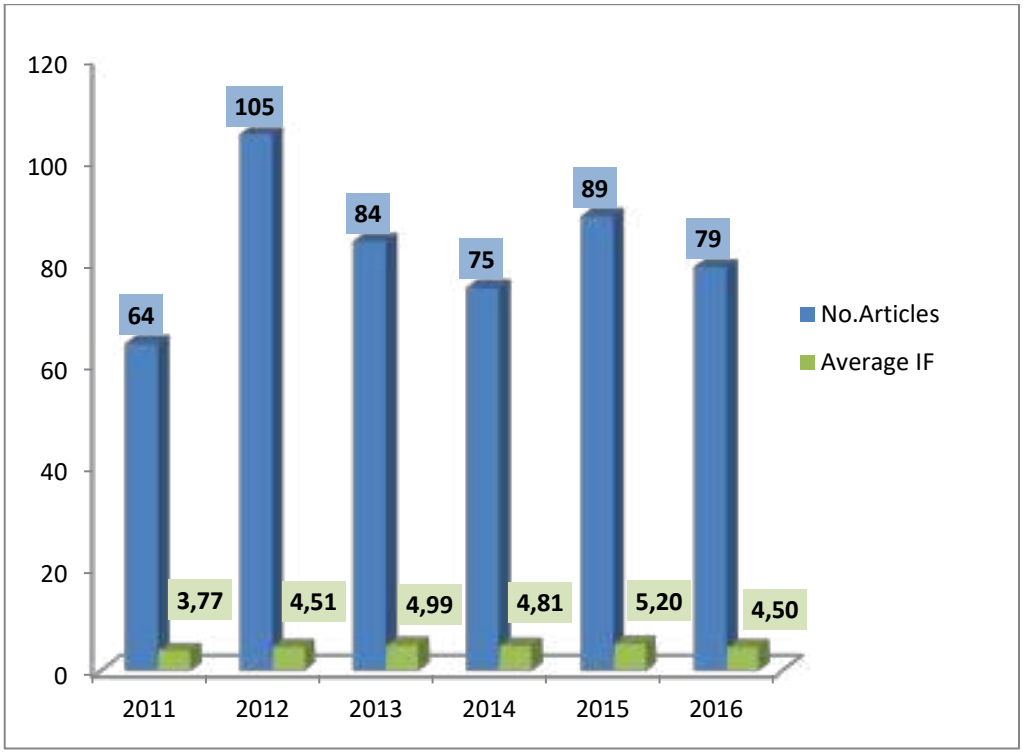
Others

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 Cenchritis 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.

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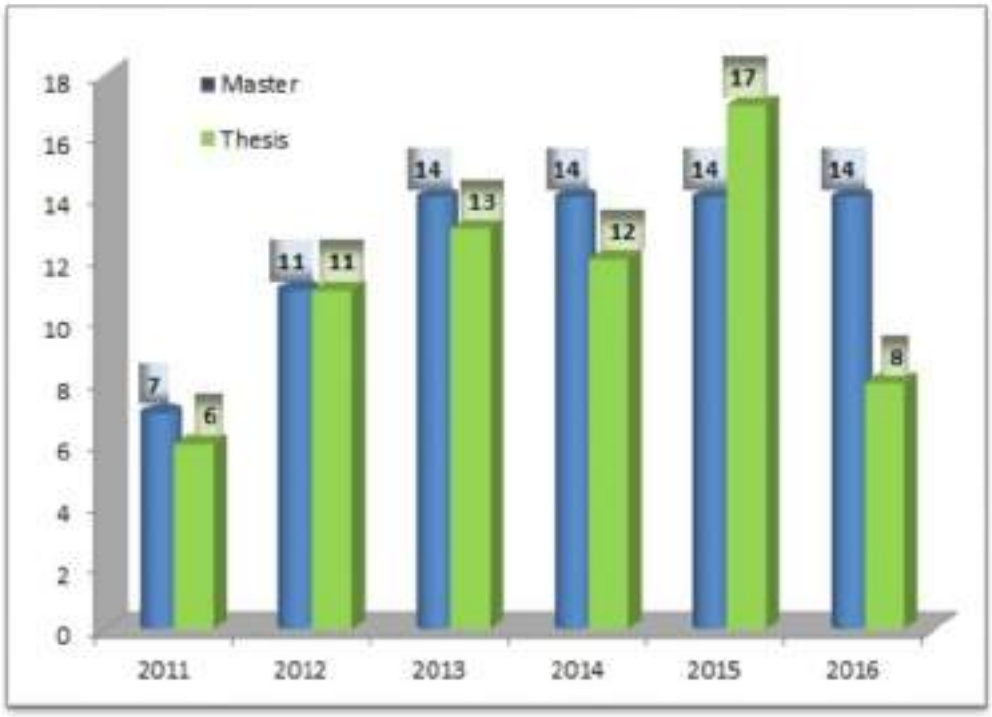
Thesis


Master
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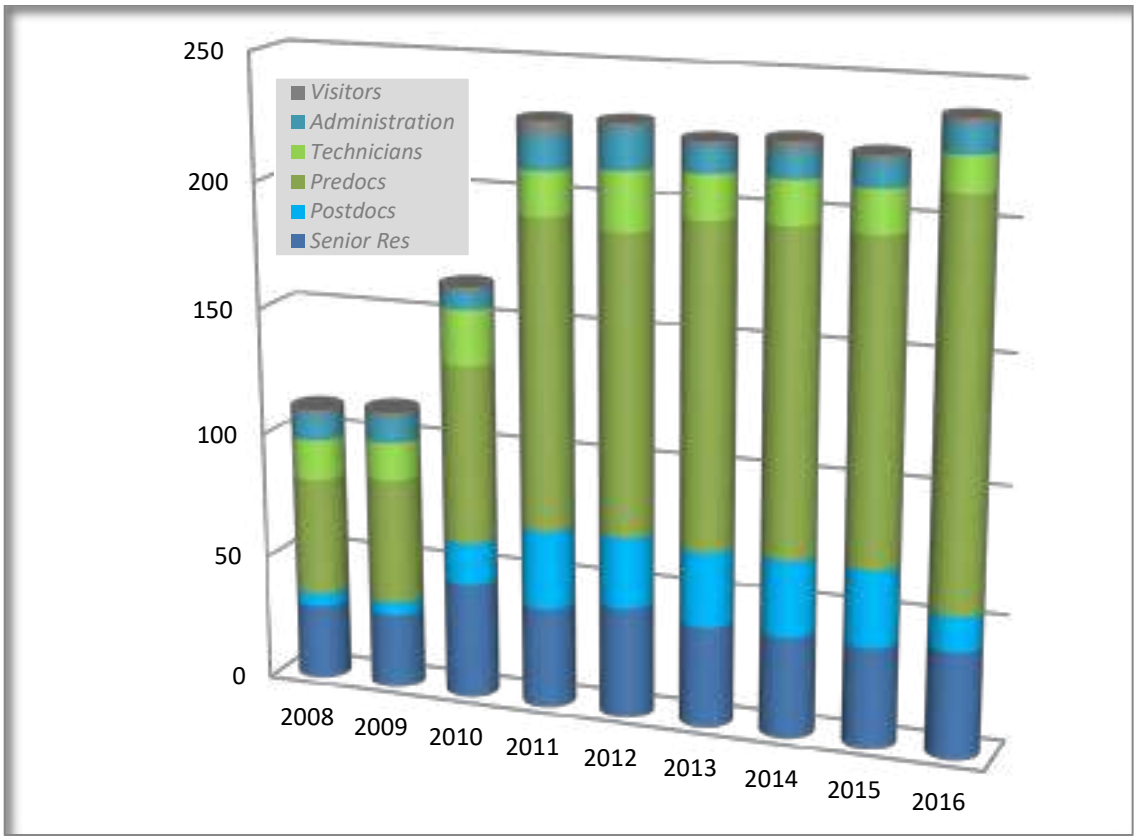
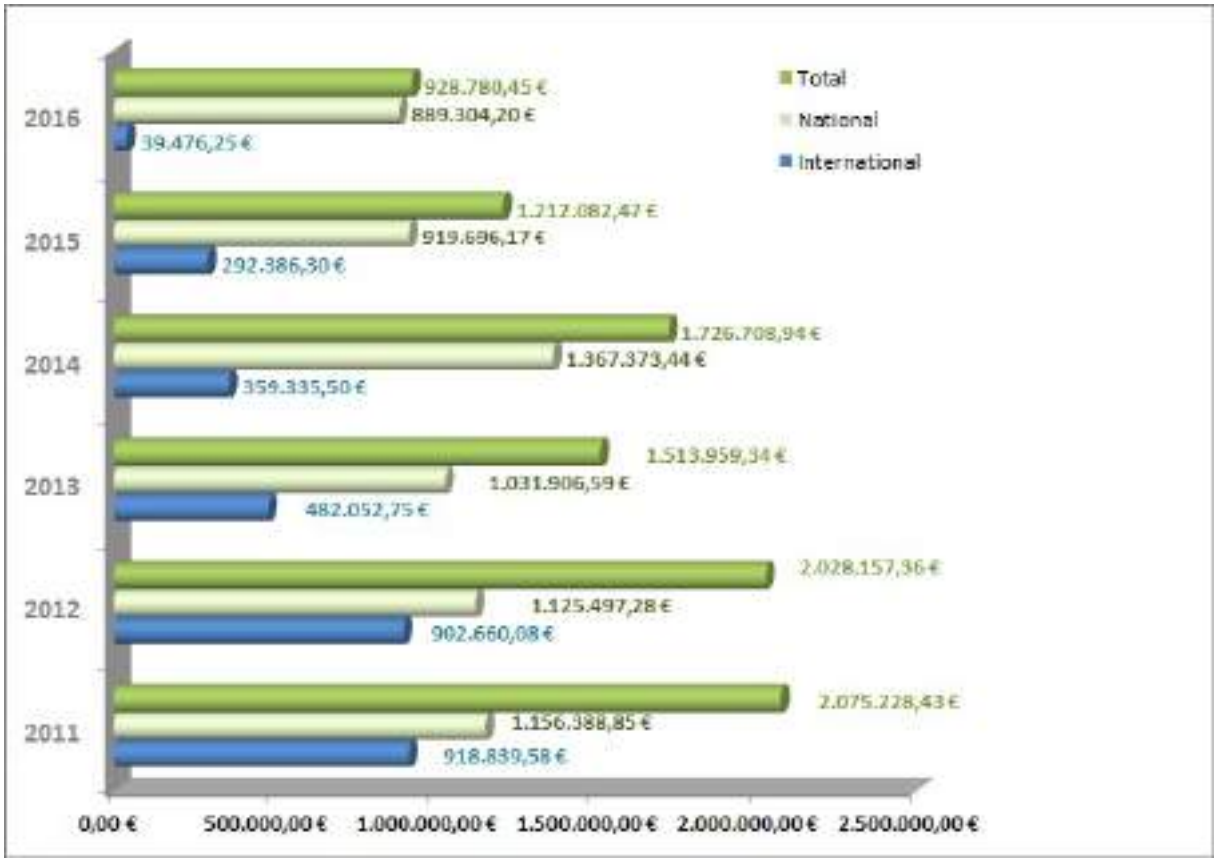
2011
2012
2013
2014
2015
2016

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



Funding


Total
National
International
2016
928.780,45 €
889.304,20 €
39.476,25 €
2015
1.212.082,47 €
919.696,17 €
292.386,30 €
2014
1.726.708,94 €
1.367.373,44 €
359.335,50 €
2013
1.513.959,34 €
1.031.906,59 €
482.052,75 €
2012
2.028.157,36 €
1.125.497,28 €
902.660,08 €
2011
2.075.228,43 €
1.156.388,85 €
918.839,58 €
0,00 €
500.000,00 €
1.000.000,00 €
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