IRB
BARCELONA

INSTITUTE
FOR RESEARCH
IN BIOMEDICINE

THE YEAR'S SCIENCE

Research Programmes

CELL AND DEVELOPMENTAL BIOLOGY

Ferran Azorín: Chromatine Structure and Function

Group Members

Group Leader

Ferran Azorín

Research Associates

Jordi Bernués
María Lluisa Espinas

Postdoctoral Fellows

Anne Daulny
Eva Maria Mejía
Tomas Ernesto Morán
Olga Moreno
Mònica Torras

PhD Students

Sergi Cuartero
Roman Kessler
Marta Lloret
Sònia Medina
Salvador Pérez
Olivera Vujatovic

Research Assistants

Carles Bonet
Gemma Molla
Alicia Vera

Lab Technician

Estefania Freire

Highlights

- We have unveiled the essential function of linker histone H1 in the maintenance of genome stability.
- We have determined the pattern of post-translational modifications of *Drosophila* linker histone H1.
- We have revealed the role of dKDM5/LID in the regulation of H3K4me3 at the transcriptional start site of developmental genes and its contribution to transcription.

Publications

- Moreno-Moreno O, Medina-Giró S, Torras-Llort M and Azorín F.
  The F box protein partner of paired regulates stability of Drosophila centromeric histone H3, CenH3(CID)
  Curr Biol, **21**, 1488-93 (2011)
- Batlle M, Marsellach FX, Huertas D and Azorín F.
  Drosophila vigilin, DDP1, localises to the cytoplasm and associates to the rough endoplasmic reticulum
  Biochim Biophys Acta, **1809**, 46-55 (2011)

PhD Theses

- *Identificació d' isoformes i modificacions posttraduccionals del factor GAGA de Drosophila melanogaster. (Identificación de isoformas y modificaciones posttraduccionales del factor GAGA de Drosophila melanogaster)*. Aran Guiu, Xavier, University of Barcelona (2010). Thesis director: Jordi Bernués. Honors: Cum Laude

Research projects

- Study of the Determinants of Heterochromatin Formation and Maintenance (HETCHROMPROJECT) 268400 FP7- People- Marie Curie Action: "Reintegration Grants" European Commission (EC) 2011-2015. Principal investigator: Anne Daulny
- Caracterización biológica de inhibidores de metil transferasas PET2007-0319-02 PETRI Spanish Ministry of Science and Innovation (MICINN) 2009-2011. Principal investigator: Ferran Azorín
- Epigenética: Mecanismos y enfermedad CSD2006-49 Consolider Spanish Ministry of Science and Innovation (MICINN) 2006-2010. Principal investigator: Ferran Azorín

- REGULACION EPIGENETICA DE LA ESTRUCTURA Y FUNCION DE LA CROMATINA BFU2009-07111/BMC Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2010-2012. Principal investigator: Ferran Azorín

Collaborations

- *ChIP-seq analysis of histone modifications and chromatin binding proteins*, David Rossell, IRB (Barcelona, Spain)
- *Post-translational modifications of histones*, Ernest Giralt, IRB (Barcelona, Spain)

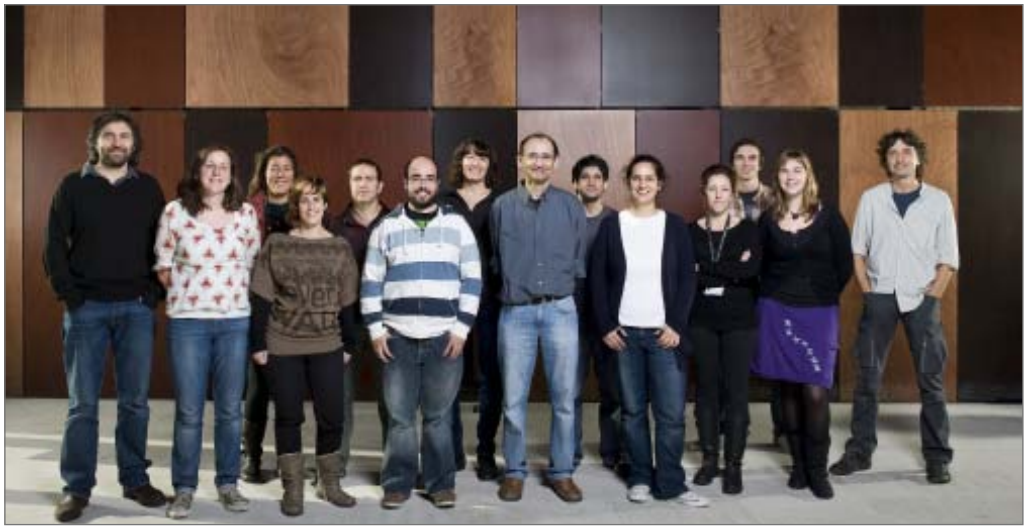
INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

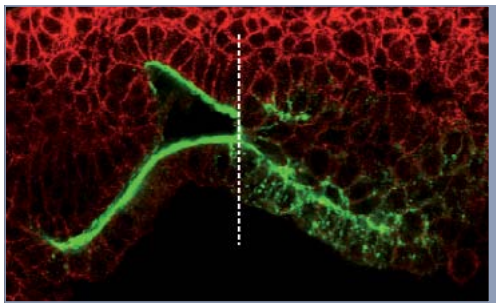
CELL AND DEVELOPMENTAL BIOLOGY

Jordi Casanova: Morphogenesis in Drosophila

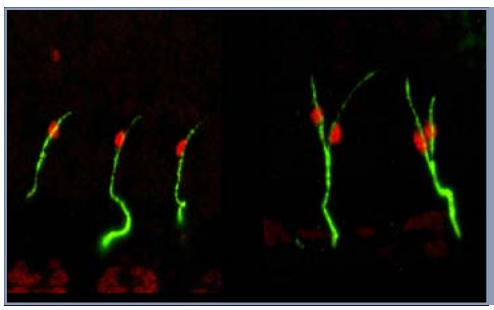


Highlights

- Specific GATA factors trigger an alternate pathway to epithelial-to-mesenchymal transition (EMT) through a downregulation of junctional dE-Cadherin, without a blocking in its transcription, and the direct repression of Crumbs.
- Identification of the Sequoia transcription factor as a repressor of FGF expression allowed us to show that becoming a tip cell does not prevent other cells in the migrating cluster from taking the same position.
- Control of germline *torso* expression by the BTB/POZ domain protein Pipsqueak.
- DSRF acts as a boosting mechanism to sustain FGF-induced terminal branching in the *Drosophila* tracheal system.



Posterior midgut primordium of a Drosophila embryo. Cells at the left of the line remain as epithelial cells (static, highly polarized in the apicobasal axis and arranged in palisade). Cells at the right of the line have begun a transition towards mesenchymal cells (with loss of apicobasal polarity, gain of migratory capacity and more rounded morphology).



Detail of the tracheal ganglionic branches of a wildtype and a sequoia mutant Drosophila embryo. In green, the lumen labelled with the 2A12 antibody. In red, the nucleus of the terminal cells visualised by an anti-DSRF antibody. Note that there is only one terminal cell per ganglionic branch in the wildtype while in the sequoia mutant these branches have two terminal cells.

Group Members

Group Leader

Jordi Casanova

Research Associates

Sofia Araujo
Andreu Casali
Marc Furriols

Postdoctoral Fellows

Kyra Campbell
Nareg Djabrayan
Gael Le Breton

PhD Students

Elisenda Buti
Gaylord Darras
Marco Grillo
Friedemann Linsler
Oscar Martorell
Arzu Ozturk

Research Assistant

Nicolás Martín

Lab Technicians

Esther Fuentes
Maria Yolanda Rivera

Publications

- Grillo M, Furriols M, Casanova J and Luschnig S.
  Control of germline torso expression by the BTB/POZ domain protein pipsqueak is required for embryonic terminal patterning in Drosophila
  Genetics, **187**, 513-21 (2011)
- Gervais L and Casanova J.
  The Drosophila homologue of SRF acts as a boosting mechanism to sustain FGF-induced terminal branching in the tracheal system
  Development, **138**, 1269-74 (2011)
- Araújo SJ and Casanova J.
  Sequoia establishes tip-cell number in Drosophila trachea by regulating FGF levels
  J Cell Sci, **124**, 2335-40 (2011)
- Campbell K, Whissell G, Franch-Marro X, Batlle E and Casanova J.
  Specific GATA factors act as conserved inducers of an endodermal-EMT
  Dev Cell, **21**, 1051-61 (2011)

Research projects

- Cellular properties and morphogenesis. from genes to shape: analysis of morphogenesis in *Drosophila* and vertebrates. Consolider Ingenio-2010 (CSD 2007-008). Spanish Ministry of Science and Innovation (MICINN). 2007-2012. Principal Investigator: Jordi Casanova
- Desenvolupament i morfogènesi a *Drosophila*. Grups de Recerca reconeguts per la generalitat de Catalunya 2009-2013 (2009 SGR 343). Agency for Administration of University and Research Grants (AGAUR). Principal Investigator: Jordi Casanova
- Regulación de los mecanismos celulares en la morfogénesis de *Drosophila*. Proyectos Investigación fundamental (BFU2009-07629). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal Investigator: Jordi Casanova
- Análisis de los mecanismos básicos que regulan la homeostasis de las células madre intestinales adultas de *Drosophila* y su papel en el desarrollo de tumores (BFU2011-23479). Spanish Ministry of Science and Innovation (MICINN). 2012-2014. Principal Investigator: Andreu Casali Taberner

Collaborations

- *Specific GATA factors as conserved inducers of an endodermal-EMT*, Eduard Batlle, IRB Barcelona (Barcelona, Spain)
- *New elements in the Drosophila terminal system*, Stephan Luschnig, University of Zurich (Zurich, Switzerland)
- *On the origin of insect tracheal systems*, Michalis Averof, IMBB (Crete, Greece)

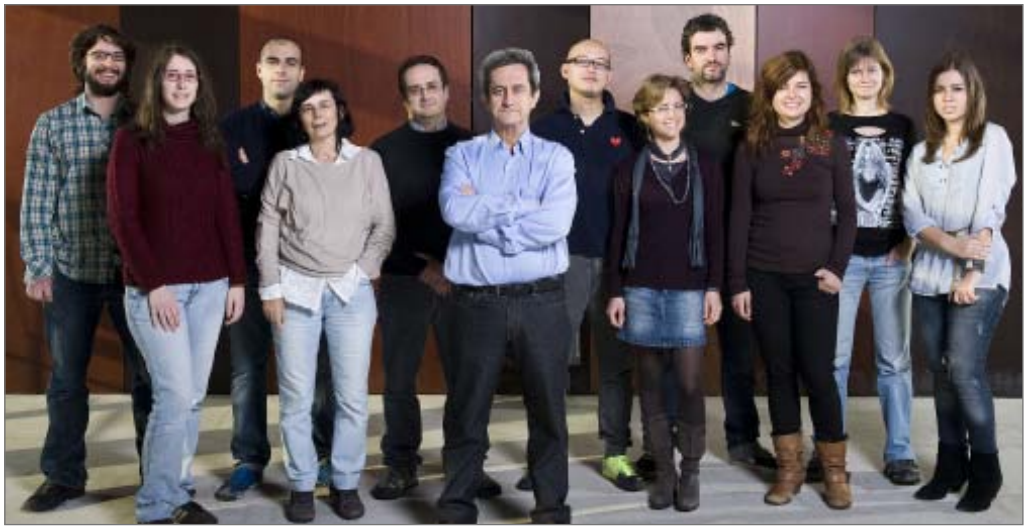
INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CELL AND DEVELOPMENTAL BIOLOGY

Cayetano González: Cell division



Group Members

Group Leader

Cayetano González

Postdoctoral Fellows

Kazuya Hashiyama
Jens Januschke
Judit Pampalona
Giulia Pollarolo
José Reina
Fabrizio Rossi
Zhanna Shcheprova

PhD Student

Eulàlia Scheenaard

Research Assistants

Jan Peter Heinen
Salud Llamazares

Administrative Assistant

Sandra Ricol

Highlights

- In *Drosophila* neuroblasts, asymmetric division is largely driven by cortical polarity.
- Upon asymmetric mitosis in *Drosophila* neuroblasts, the mother centrosome is inherited by the differentiating daughter cell.
- The stemness properties of *Drosophila* neuroblasts are not linked to mother centrosome inheritance.

Publications

- **Drosophila neuroblasts retain the daughter centrosome**
  Januschke J, Llamazares S, Reina J and Gonzalez C.
  Nat Commun **2**, 243 (2011)
- **An ana2/ctp/mud complex regulates spindle orientation in Drosophila neuroblasts**
  Wang C, Li S, Januschke J, Rossi F, Izumi Y, Garcia-Alvarez G, Gwee SS, Soon SB, Sidhu HK, Yu F, Matsuzaki F, Gonzalez C, Wang H.
  Dev Cell, **21**, 520 (2011)

PhD Theses

- A link between loss of developmentally controlled gene silencing and tumour growth. Ana Janic, Universitat de Barcelona (2011). Thesis director: Cayetano González. Honors: Summa Cum Laude

Research projects

- Grupo de división celular, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 938). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Cayetano González
- Nuevas estrategias basadas en biomarcadores para la detección del cáncer, su pronóstico, la predicción de respuesta y el desarrollo de nuevos tratamientos. CEN-20091016 CENIT Centro de Desarrollo tecnológico Industrial (CDTI) . Principal investigator: Cayetano González
- Stem cell polarity, genomic instability and tumor growth in Drosophila. Proyectos Investigación fundamental (BFU2009-07975). Spanish Ministry of Science and Innovation (MICINN), 2010-2012. Principal investigator: Cayetano González
- Hacia la comprensión estructural y funcional del centrosoma. CENTROSOME 3D CSD2006-00023 Consolider Spanish Ministry of Science and Innovation (MICINN) 2006-2011. Principal investigator: Cayetano González

Collaborations

- *Centrosoma 3D*, Luís Serrano Pubull, Center for Genomic Regulation (Barcelona, Spain)
- *Neuroblast polarity and self-renewal*, Dr. Hongyan Wang, National University of Singapore and NUS Graduate School for Integrative Sciences and Engineering (Singapore, Singapore)
- *New strategies for cancer detection and prognosis*, GP Pharm (Gavà (Barcelona), Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CELL AND DEVELOPMENTAL BIOLOGY

Jens Lüders: Microtubule organization

Highlights

- While the role of the γ-tubulin ring complex (γTuRC) as a nucleator of microtubule polymerization is well established, γTuRC regulation is poorly understood. We have identified multiple novel *in vivo* phosphorylation sites in core subunits of γTuRC and have started their functional characterization.
- To study microtubule organization and dynamics *in vivo* markers are needed that allow specific labelling of microtubule ends. We have developed tools and techniques that allow time-lapse imaging of γTuRCs as potential minus end marker in living cells.
- The microtubule cytoskeleton is essential for morphogenesis and neuronal function. Surprisingly, very little is known about the mechanisms that assemble and organize microtubules in neurons. We have performed a genome-wide gene expression screen for candidate proteins that might be involved in microtubule organization in neurons.

Research projects

- Microtubule organizing centers and microtubule nucleation in mitosis (MTOC FUNCTION) 224835 FP7-People- Marie Curie Reintegration Grants European Commission (EC) 2008-2012. Principal investigator: Jens Luders
- MICROTUBULE ORGANIZATION GROUP 2009 SGR 1536 Grup de Recerca reconegut de la Generalitat de Catalunya Agency for Administration of University and Research Grants (AGAUR) 2009-2013. Principal investigator: Jens Luders
- Organización molecular de los sitios de nucleación de microtubulos centrosómicos y no centrosómicos BFU2009-08522 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2010-2012. Principal investigator: Jens Luders

Group Members

Group Leader

Jens Lüders

Postdoctoral Fellows

Roberta Kiffin
Marko Marjanovic*
Carlos Sánchez
Neus Teixidó*
*shared with another lab

PhD Students

Francisco Freixo
Sabine Klischies
Nicolas Lecland

Research Assistant

Cristina Lacasa

Visiting Student

Adrian Baumann

Collaborations

- *Microtubule organization during neuronal differentiation.*, Eduardo Soriano, IRB Barcelona (Barcelona, Spain)
- *Regulation of microtubule nucleation through phosphorylation*, Carme Caelles, IRB Barcelona (Barcelona, Spain); Joan Roig, IRB Barcelona (Barcelona, Spain)
- *The centrosome as an integrator of DNA damage signalling: implications for mitotic spindle assembly and function.*, Travis Stracker, IRB Barcelona (Barcelona, Spain)
- *Composition and regulation of the human γTuRC*, Carme Caelles, IRB Barcelona (Barcelona, Spain); Joan Roig, IRB Barcelona (Barcelona, Spain); Judit Villen, University of Washington (Seattle, United States)
- *Super resolution imaging of mitotic spindles.*, Melike Lakadamyali, ICFO (Castelldefels, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

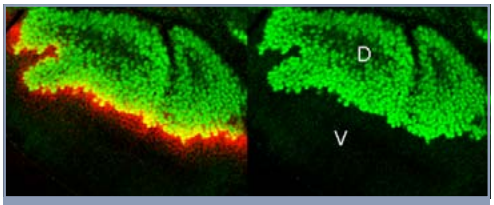
Research Programmes

CELL AND DEVELOPMENTAL BIOLOGY

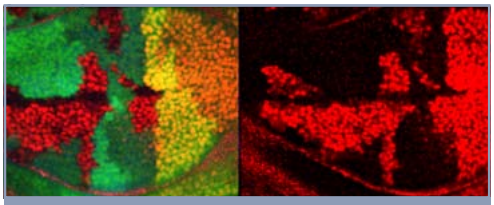
Marco Milán: Development and growth control laboratory

Highlights

- Communication between Enhancers and Polycomb Responsive Elements contributes to the expansion of gene expression domains within highly proliferative primordia.
- Subdivision of proliferating tissues into adjacent cell populations that do not mix plays a key role in animal development, and increased mixing contributes to cancer. We have identified the molecular effectors that link Notch signalling and the actin cytoskeleton and that contribute to the generation of these affinity barriers.



Altered affinity formation between D and V cells upon expression of bantam miRNA in boundary cells



Expression of the hedgehog gene (red) in clones mutant for engrailed and ci (labeled by the absence of GFP in green)

Publications

- Pérez L, Barrio L, Cano D, Fiuza UM, Muzzopappa M and Milán M.
  Enhancer-PRE communication contributes to the expansion of gene expression domains in proliferating primordia
  Development, **138**, 3125-34 (2011)
- Becam I, Rafel N, Hong X, Cohen SM and Milán M.
  Notch-mediated repression of bantam miRNA contributes to boundary formation in the Drosophila wing
  Development, **138**, 3781-9 (2011)
- Dekanty A and Milán M.
  The interplay between morphogens and tissue growth
  Embo Rep, **12**, 1003-10 (2011)

Group Members

Group Leader

Marco Milán

Postdoctoral Fellows

Najate Benhra
Andrés Dekanty
Juan Manuel Murillo
Mariana Muzzopappa
Christopher Sinadinos *
*shared with another lab

PhD Students

Lara Barrio
Laura Boulan
Ana Patricia Ferreira
Carles Recasens

Programme Technician

Ainhoa Olza

Research Assistant

Lidia Pérez

Lab Technician

Mercedes San Miguel

PhD Theses

- Coordination of Growth between territotries within the developing wing primordium of *Drosophila melanogaster*. Duarte Mesquita, University of Barcelona (2011). Thesis director: Marco Milan. Honors: Cum Laude

Research projects

- Development and growth control laboratory. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1536). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Marco Milán
- Compartments, organizing molecules and growth control in *Drosophila*. EMBO Young Investigator Programm. European Molecular Biology Organization (EMBO). 2008-open. Principal investigator: Marco Milán
- EMBO YOUNG INVESTIGATOR PROGRAMME 2007 AWARD. Acciones Complementarias (BFU2008-00104-E). Ministry of Science and Innovation (MICINN). 2008-2011. Principal investigator: Marco Milán
- Bordes de compartimentos en el ala de *Drosophila*. Organizadores de crecimiento y bordes de afinidad. BFU2010-21123 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2011-2013. Principal investigator: Marco Milán
- From genes to shape: analysis of morphogenesis in Drosophila and vertebrates. Consolider Ingenio-2010 (CSD2007-00008). Spanish Ministry of Science and Innovation (MICINN). 2008-2010. Participant IP: Marco Milán

Collaborations

- *Lafora disease in Drosophila*, Joan Guinovart, IRB Barcelona (Barcelona, Spain)
- *p38 signaling in Drosophila*, Angel Nebreda, IRB Barcelona (Barcelona, Spain)
- *miRNAs in compartment boundary formation*, Stephen Cohen, IMCB Singapore (Singapore, Singapore)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CELL AND DEVELOPMENTAL BIOLOGY

Lluis Ribas: Gene Translation

Highlights

- We have described a new non-canonical role for an aminoacyl-tRNA synthetase. These ancient enzymes are preferred scaffolds for the emergence of new signalling activities. In this case we have reported that lysyl-tRNA synthetase in the protozoan *Entamoeba histolytica* plays a role in the modulation of host inflammatory response. In collaboration with other groups we have shown that *Plasmodium falciparum* tryptophanyl-tRNA synthetase also acts as a cell signalling molecule in malaria infections.
- The laboratory has also reported on the mechanisms that allow for mutually exclusive expression of a family of *Plasmodium falciparum* genes unrelated to the VAR family. The formation of heterochromatin in bistable chromatin domains controls the repression of the clonally variant family of Clag genes in *P. falciparum*.

Publications

- Bhatt TK, Khan S, Dwivedi VP, Banday MM, Sharma A, Chandele A, Camacho N, Ribas de Pouplana L, Wu Y, Craig AG, Mikkonen AT, Maier AG, Yogavel M and Sharma A.
  Malaria parasite tyrosyl-tRNA synthetase secretion triggers pro-inflammatory responses
  Nat Commun **2**, 530 (2011)
- Castro de Moura M, Miro F, Han JM, Kim S, Celada A and Ribas de Pouplana L.
  Entamoeba lysyl-tRNA synthetase contains a cytokine-like domain with chemokine activity towards human endothelial cells
  Plos Neglect Trop D, **5**, e1398 (2011)
- Krog JS, Español Y, Giessing AM, Dziergowska A, Malkiewicz A, Ribas de Pouplana L, and Kirpekar F.
  3-(3-amino-3-carboxypropyl)-5,6-dihydrouridine is one of two novel post-transcriptional modifications in tRNALys(UUU) from Trypanosoma brucei
  Febs J, **278**, 4782-96 (2011)
- Olmedo-Verd E, Santamaría-Gómez J, Ochoa de Alda JA, Ribas de Pouplana L and Luque I.
  Membrane anchoring of aminoacyl-tRNA synthetases by convergent acquisition of a novel protein domain
  J Biol Chem, **286**, 41057-68 (2011)
- Jackson KE, Habib S, Frugier M, Hoen R, Khan S, Pham JS, Ribas de Pouplana L, Royo M, Santos MA, Sharma A and Ralph SA.
  Protein translation in Plasmodium parasites
  Trends Parasitol, **27**, 467-76 (2011)

Group Members

Group Leader

Lluis Ribas

Postdoctoral Fellows

Valerie Margarita Crowley

Tanit Guitart

Francisco Miguel Torres

PhD Students

Eva Maria Novoa

Daria Picchioni

Lab Technicians

Noelia Camacho

Anna Tor

- Crowley VM, Rovira-Graells N, Ribas de Pouplana L and Cortés A.
Heterochromatin formation in bistable chromatin domains controls the epigenetic repression of clonally variant Plasmodium falciparum genes linked to erythrocyte invasion
Mol Microbiol, **80**, 391-406 (2011)

PhD Theses

- *Epigenetic regulation of clonally variant gene expression in plasmodium falciparum*. Valerie Crowley, Universitat Pompeu Fabra (2011). Thesis director: Lluis Ribas de Pouplana. Honors: Summa Cum Laude

Research projects

- Bases moleculares de la regulación. Epigenética de la expresión génica clonal. Variante en Plasmodium Falciparum. SAF2010-20111 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2011 Principal investigator: Alfred Cortés
- Implicación de componentes del código genético en patologías humanas BIO2009-09776 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2011-2013 Principal investigator: Lluis Ribas de Pouplana
- Síntesis de proteínas en los orgánulos de Plasmodium falciparum PRI-PIBIN-2011-1279 Proyectos Internacionales-Programa Bilateral con India Spanish Ministry of Science and Innovation (MICINN) 2011-2014 Principal investigator: Lluis Ribas de Pouplana
- Targeting protein synthesis in the apicoplast and cytoplasm of plasmodium (MEPHITIS) 223024 FP7-Cooperation-Health-2007 European Commission (EC) 2009-2011 Principal investigator and consortium coordinator: Principal investigator: Lluís Ribas de Pouplana
- BIOLOGIA DE LA TRADUCCIÓ GENÈTICA 2009 SGR 1277 Grup de Recerca reconegut de la Generalitat de Catalunya Agency for Administration of University and Research Grants (AGAUR) 2009-2013 Principal investigator: Lluís Ribas de Pouplana

Collaborations

- *Role of AIMP1 in Entamoeba infections*, Antonio Celada, IRB Barcelona (Barcelona, Spain)
- *Characterisation of antimalarial activities of ARS inhibitors*, José Manuel Bautista, UCM Madrid (Madrid, Spain)
- *Design of new dual ARS inhibitors*, Miriam Royo, Barcelona Science Park (Barcelona, Spain)
- *In vivo activity of inhibitors of Plasmodium ARSs*, José Manuel Bautista, Universidad Complutense de Madrid (Madrid, Spain)
- *Plasmodium TyrRS structure and function*, Amit Sharma, International Centre for Genetic Engineering and Biotechnology (New delhi, India)
- *Solving the crystal structure of Entamoeba EELP*, Osamu Nureki, University of Tokyo (Tokyo, Japan)

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CELL AND DEVELOPMENTAL BIOLOGY

Eduardo Soriano: Neurobiology and regeneration

Group Members

Group Leader

Eduardo Soriano

Research Associates

Ferran Burgay
Marta Pascual
Jesús Ureña

Postdoctoral Fellows

Tiziana Cotrufo
Ramón Martínez
Ashraf Muhaisen
Lluis Pujadas
Catia Teixeira
Alexander Ulloa

PhD Students

Pablo Jose Barrecheguren
Carles Bosch
Beatriz García
Nuria Masachs
Maria Del Mar Masdeu
Serena Mirra
Antoni Parcerisas
Mª Esther Pérez
Oriol Ros
Daniela Rossi
Sara Esmeralda Rubio
Román Serrat

MSc Students

Martí Quevedo
Cristina Roselló

Highlights

- We have shown that the Sytx1/DCC complex associates with the v-SNARE (vesicle SNARE) tetanus neurotoxin-insensitive vesicle-associated membrane protein (TI-VAMP) and that knockdown of TI-VAMP in the commissural pathway in the spinal cord results in aberrant axonal guidance phenotypes. Our data provide evidence of a new signalling mechanism that couples chemotropic Netrin-1/DCC axonal guidance and Sytx1/TI-VAMP SNARE proteins, thus regulating membrane turnover and exocytosis.
- We have found that Reelin overexpression in the mouse forebrain by transgene expression prevents the manifestations of psychiatric disease-related phenotypes, induced by stress and cocaine sensitization. In addition, we demonstrate that while stress increased NMDA NR2B-mediated synaptic transmission, known to be implicated in depression, Reelin overexpression significantly reduced it. Together, these results point to the Reelin signaling pathway as a relevant drug target for the treatment of psychiatric disorders.
- We have discovered that oligodendrocyte precursor cells express Semaphroin 4F receptor and are sensitive to this guidance cue during the migratory process. The present data uncover a novel function of this receptor in the control of oligodendrocyte precursor migration in the developing brain.

Publications

- Armendáriz BG, Bribian A, Pérez-Martínez E, Martínez A, de Castro F, Soriano E and Burgaya F.
  Expression of Semaphorin 4F in neurons and brain oligodendrocytes and the regulation of oligodendrocyte precursor migration in the optic nerve
  Mol Cell Neurosci, **49**, 54-67 (2011)
- Llorens-Martín M, López-Doménech G, Soriano E and Avila J.
  GSK3β is involved in the relief of mitochondria pausing in a Tau-dependent manner
  PLoS One, **6**, e27686 (2011)
- Courtès S, Vernerey J, Pujadas L, Magalon K, Cremer H, Soriano E, Durbec P and Cayre M.
  Reelin controls progenitor cell migration in the healthy and pathological adult mouse brain
  PLoS One, **6**, e20430 (2011)
- Rubio SE, Martínez A, Chauvet S, Mann F, Soriano E and Pascual M.
  Semaphorin 3C is not required for the establishment and target specificity of the GABAergic septohippocampal pathway in vitro
  Eur J Neurosci, **34**, 1923-33 (2011)
- Valles-Ortega J, Duran J, Garcia-Rocha M, Bosch C, Saez I, Pujadas L, Serafin A, Cañas X, Soriano E, Delgado-García JM, Gruart A and Guinovart JJ.
  Neurodegeneration and functional impairments associated with glycogen synthase accumulation in a mouse model of Lafora disease
  EMBO Mol Med, **3**, 667-81 (2011)

- Teixeira CM, Martín ED, Sahún I, Masachs N, Pujadas L, Corvelo A, Bosch C, Rossi D, Martinez A, Maldonado R, Dierssen M and Soriano E.
  Overexpression of Reelin prevents the manifestation of behavioral phenotypes related to schizophrenia and bipolar disorder
  Neuropsychopharmacology, **36**, 2395-405 (2011)
- Cotrufo T, Pérez-Brangulí F, Muhaisen A, Ros O, Andrés R, Baeriswyl T, Fuschini G, Tarrago T, Pascual M, Ureña J, Blasi J, Giralt E, Stoeckli ET and Soriano E.
  A signaling mechanism coupling netrin-1/deleted in colorectal cancer chemoattraction to SNARE-mediated exocytosis in axonal growth cones
  J Neurosci, **31**, 14463-80 (2011)

PhD Theses

- *Papel de la proteina sintaxina1 en el crecimiento axonal mediado por neurotrofinas*. Giulia Fuschini, Universitat de Barcelona (2011). Thesis director: Eduardo Soriano. Honors: Cum Laude

Research projects

- Caixa Catalunya Obra Social 2008-2011 Principal Investigator: Eduardo Soriano
- Protective role of Reelin in addictive disorders 2010/149 Proyectos Investigación sobre drogodependencias Ministerio Sanidad, Servicios Sociales e Igualdad 2010-2013 Principal Investigator: Eduardo Soriano
- Identificación y caracterización de nuevos genes y vías de señalización implicados en desarrollo cortical BFU2008-03980 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2009-2013 Principal Investigator: Eduardo Soriano
- Participación de la tirosina quinasa Ack1 en patologías neurodegenerativas y sinaptogénesis PI10/01750 Proyectos de Investigación en Salud Carlos III Health Institute (ISCIII) 2011-2013 Principal Investigator: Jesús Ureña
- Desarrollo y maduración de la conexión septohipocámpica, implicaciones en la enfermedad de Alzheimer PI08-1891 Proyectos de Investigación en Salud Carlos III Health Institute (ISCIII) 2009-2011 Principal Investigator: Marta Pascual

Collaborations

- *Role of the glycogen synthase enzyme in neuronal function and degeneration*, Joan J Guinovart, IRB Barcelona (Barcelona, Spain)
- *Regulation of A-beta formation by Reelin*, Javier Ávila, Centro de Biología Molecular “Severo Ochoa” (Madrid, Spain); Ernest Giralt, IRB Barcelona (Barcelona, Spain)
- *Anatomical and Physiological changes in the GABEergic septohippocampal pathway in AD models*, Agnés Gruart, Universidad Pablo Olavide (Sevilla, Spain); Joaquín del Rio, CIBERNED (Madrid, Spain); José Delgado García, Universidad Pablo Olavide (Sevilla, Spain)
- *Functions of the novel tyrosin kinase Pyk1 in brain development*, Joseph Schlessinger, Yale University (Yale, Spain)
- *New Mitochondrial proteins in trafficking and neural diseases,* Ramón trullas, IDIBAPS - Unidad de Neurobiologia IIBB-CSIC (Barcelona, Spain)
- *Presenilin-1 modulates Reelin levels through ApoER2 processing.,* J. Nimpf, Medical University of Vienna (Viena, Spain); Javier Sáez Valero, Inst. Neurociencias; Univ. Miguel Hernández-CSIC (Alicante, Spain); J. Herz, University of Texas Southwestern Medical Center (Dallas, United States); Carlos Saura, Universidad. Autònoma de Barcelona (Barcelona, Spain)
- *Role of Alex-3 in mitochondrial biology,* Antoni Andreu, Vall d’Hebron Hospital (Barcelona, Spain); Pablo Villoslada, CIMA (Pamplona, Spain); Ramón Trullás, CSIC-IIBB (Barcelona, Spain); Martin Kerschensteiner, Ludwig Maximilians University (Munich, Spain); José Berciano, Universidad de Santander (Santander, Spain); Jaume Bertranpetit, UPF (Barcelona, Spain)
- *Role of GSK3, TAU and A-Beta in mitochondrial transport.,* Javier Avila, Centro de Biología Molecular “Severo Ochoa” (Madrid, Spain)
- *Role of podocalixin in the adult peripheral nervous system after injury and during regeneration,* Xavier Navarro, Universitat Autonoma de Barcelona (Barcelona, Spain); Isabel Illa, Hospital de la Santa Creu i Sant Pau (Barcelona, Spain)
- *Role of Syntaxin1 and Podocalyxins in axonal guidance and brain development,* Thomas Südhoff, Southwestern University (Dallas, United States); Esther Stoeckli, Zurich University (Zurich, Switzerland); José Rizo-Rey, Southwestern University (Dallas, United States)

Lab Technicians

Maria Rosa Andrés
Lucas Brunso
Natalia Ruiz

Administrative Assistant

Jan Vara

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Patrick Aloy: Structural Bionformatics and Network Biology

Highlights

- We have identified 200 high-confidence interactors directly related to Alzheimer´s disease (AD). Our results point to a putative role of PDCD4 as a neuronal death regulator and ECSIT as a molecular link between oxidative stress, inflammation, and mitochondrial dysfunction in AD.
- Through the analyses of 2090 unique unbound - bound transitions, we have shown that two-thirds of these proteins do not undergo significant structural changes upon binding. Among the remaining proteins, one-third explores the bound conformation in the unbound state (conformational selection model) and, while most transitions are possible from an energetic perspective, a few do require external help to break the thermodynamic barrier (induced fit model).
- We have also found that domains interacting with many partners undergo smaller changes upon association, and are less likely to freely explore larger conformational changes.

Publications

- Soler-López M, Zanzoni A, Lluís R, Stelzl U and Aloy P.
  Interactome mapping suggests new mechanistic details underlying Alzheimer's disease
  Genome Res, **21**, 364-76 (2011)
- Aranda B, Blankenburg H, Kerrien S, Brinkman FS, Ceol A, Chautard E, Dana JM, De Las Rivas J, Dumousseau M, Galeota E, Gaulton A, Goll J, Hancock RE, Isserlin R, Jimenez RC, Kerssemakers J, Khadake J, Lynn DJ, Michaut M, O'Kelly G, Ono K, Orchard S, Prieto C, Razick S, Rigina O, Salwinski L, Simonovic M, Velankar S, Winter A, Wu G, Bader GD, Cesareni G, Donaldson IM, Eisenberg D, Kleywegt GJ, Overington J, Ricard-Blum S, Tyers M, Albrecht M and Hermjakob H.
  PSICQUIC and PSISCORE: accessing and scoring molecular interactions
  Nat Methods, **8**, 528-9 (2011)
- Stein A, Rueda M, Panjkovich A, Orozco M and Aloy P.
  A systematic study of the energetics involved in structural changes upon association and connectivity in protein interaction networks
  Structure, **19**, 881-9 (2011)
- Stein A, Mosca R and Aloy P.
  Three-dimensional modeling of protein interactions and complexes is going 'omics
  Curr Opin Struc Biol, **21**, 200-8 (2011)
- Feliu E, Aloy P and Oliva B.
  On the analysis of protein-protein interactions via knowledge-based potentials for the prediction of protein-protein docking
  Protein Sci, **20**, 529-41 (2011)

Group Members

Group Leader

Patrick Aloy

Research Associates

Roberto Mosca
Andreas Zanzoni

PhD Students

Manuel Alejandro Alonso
Rodrigo Arroyo
Eva Capdevila
Miquel Duran
Samira Jaeger*

*shared with another lab

Postdoctoral Fellows

Nahuai Badiola
Arnaud Ceol
Albert Pujol

Research Assistant

Jose Luis Ruiz

Experimental Bioinformatics Lab Director

Montserrat Soler

Lab Technician

Victor Alcalde

- Zanzoni A, Carbajo D, Diella F, Gherardini PF, Tramontano A, Helmer-Citterich M and Via A.
  Phospho3D 2.0: an enhanced database of three-dimensional structures of phosphorylation sites
  Nucleic Acids Res, **39**, D268-71 (2011)
- Stein A, Céol A and Aloy P.
  3did: identification and classification of domain-based interactions of known three-dimensional structure
  Nucleic Acids Res, **39**, D718-23 (2011)

PhD Theses

- A novel framework for the computational analyses of biological networks. Roland A Pache, University of Barcelona (2011). Thesis director: Patrick Aloy. Honors: Cum Laude

Patents

- *Methods and Systems for identifying molecules or processes of biological interest by using knowledge discovery in biological data*
  Mas JM, Pujol A, Farrés J and Aloy P
  Applicant: Anaxomics Biotech SL
  Publication number/date: WO2011051805 (05/05/2011)

Research projects

- A network medicine approach to colorectal and breast cancer. Proyectos Investigación Fundamental Spanish (BIO2010-22073). Ministry of Science and Innovation (MICINN). 2010-2013. Principal investigator: Patrick Aloy
- Identification and validation of novel drug targets in Gram-negative bacteria by global search: a trans-system approach (ANTIPATHOGN), European Commission (223101). 2009-2013. Principal investigator: Patrick Aloy
- Identification of secondary targets and drug design through the structural and functional analyses of biological networks. Proyectos Singulares Estratégicos (PSE-010000-2009-008 2009). Spanish Ministry of Science and Innovation (MICINN) (MICINN). 2009-2011. Principal investigator: Patrick Aloy
- Structural bioinformatics and network biology, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1519). Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Patrick Aloy

Collaborations

- *Identification of novel genes involved in DNA repair processes*, Travis Stracker, IRB Barcelona (Barcelona, Spain)
- *Identification of novel substrates for p53.* , Angel R. Nebreda, IRB Barcelona (Barcelona, Spain)
- *Network medicine approaches to Alzheimer´s disease*, Ulrich Stelzl, MPI for Molecular Genetics (Berlin, Germany)
- *Novel strategy for network-based therapeutics*, Modesto Orozco, IRB Barcelona (Barcelona, Spain); José Manuel Mas, Infociencia & Anaxomics Biotech (Barcelona, Spain)
- *Novel ways of assessing protein-DNA interactions*, Anastassis Perrakis, Nederlands Kanker Instituut (Amsterdam, Netherlands)
- *Structural systems biology*. B Oliva, Pompeu Fabra University (Barcelona, Spain); M Madan Babu, LMB-MRC (Cambridge, United Kingdom); Miquel Pons, IRB Barcelona (Barcelona, Spain); J Fernández-Recio, Barcelona Supercomputing Center (BSC) (Barcelona, Spain)

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

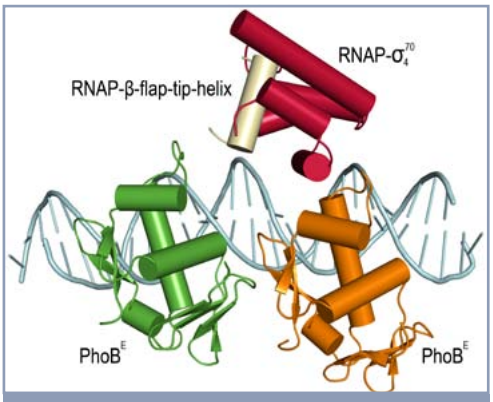
Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Miquel Coll: Proteins, Nucleic Acids and Molecular Machines

Highlights

- Transcription factors modulate gene expression by several mechanisms. PhoB is a two-component response regulator that activates transcription by interacting with the σ^{70} subunit of the *E. coli* RNA polymerase in promoters where the -35 σ^{70}-recognition element has been replaced by the *pho box* sequence. The 3D structure of a transcription initiation sub-complex that includes the σ_4 domain of σ^{70} fused to the RNA polymerase β subunit flap tip-helix, the PhoB effector domain and the *pho box* DNA unveils the mechanism for polymerase recruitment to these non-canonical promoters.
- The crystal structure of human mitochondrial transcription factor A in complex with a DNA oligonucleotide containing the mitochondrial light-strand promoter reveals two HMG domains attached to the DNA, inducing a dramatic U-turn in the double helix.
- In Picornaviridae the RNA genome directs the synthesis of a polyprotein that is processed into mature proteins by the viral protease $3C^{pro}$, thus making it an excellent antiviral target. We have solved the crystal structures of the $3C^{pro}$ from EV-93, a recently identified pathogen, in complex with several inhibitors. Our findings provide the framework for further structure-guided development of antiviral molecules.



3D structure of a transcription activation sub-complex (Blanco et al., (2011) EMBO J. 30, 3776–3785).

Publications

- Blanco AG, Canals A, Bernués J, Solà M and Coll M.
  The structure of a transcription activation subcomplex reveals how σ(70) is recruited to PhoB promoters
  EMBO J, **30**, 3776-3785 (2011)

Group Members

Group Leader

Miquel Coll

Research Associate

Albert Canals

Postdoctoral Fellows

Roeland Boer
Salvatore Bongarzone*
Robert Janowski
Cristina Machón
Marta Nadal
Joan Pous
Fabio Sessa
*shared with another lab

PhD Students

Juliana Amodio
Zuzanna Kaczmarska
Simone Pieretti
Radoslaw Pluta
Anna Rubio

Research Assistants

Nayibe Guarin
Rosa Maria Pérez

Lab Technician

Esther Ferrando

- Rubio-Cosials A, Sidow JF, Jiménez-Menéndez N, Fernández-Millán P, Montoya J, Jacobs HT, Coll M, Bernadó P and Solà M.
Human mitochondrial transcription factor A induces a U-turn structure in the light strand promoter
Nat Struct Mol Biol, **18**, 1281-9 (2011)
- Costenaro L, Kaczmarska Z, Arnan C, Janowski R, Coutard B, Solà M, Gorbalenya AE, Norder H, Canard B and Coll M.
Structural basis for antiviral inhibition of the main protease, 3C, from human enterovirus 93
J Virol, **85**, 10764-73 (2011)
- Fernandez FJ, Garces F, Lopez-Estepa M, Aguilar J, Baldoma L, Coll M, Badia J and Vega MC.
The UlaG protein family defines novel structural and functional motifs grafted on an ancient RNase fold
BMC Evol Biol, **11**, 273 (2011)
- McManus G, Costa M, Canals A, Coll M and Mantle TJ.
Site-directed mutagenesis of mouse glutathione transferase P1-1 unlocks masked cooperativity, introduces a novel mechanism for 'ping pong' kinetic behaviour, and provides further structural evidence for participation of a water molecule in proton abstraction from glutathione
FEBS J, **278**, 273-81 (2011)
- Berger I, Blanco AG, Boelens R, Cavarelli J, Coll M, Folkers GE, Nie Y, Pogenberg V, Schultz P, Wilmanns M, Moras D and Poterszman A.
Structural insights into transcription complexes
J Struct Biol, **175**, 135-46 (2011)
- Lorenzo-Díaz F, Dostál L, Coll M, Schildbach JF, Menéndez M and Espinosa M.
The MobM relaxase domain of plasmid pMV158: thermal stability and activity upon Mn2+ and specific DNA binding
Nucleic Acids Res, **39**, 4315-29 (2011)
- Norder H, De Palma AM, Selisko B, Costenaro L, Papageorgiou N, Arnan C, Coutard B, Lantez V, De Lamballerie X, Baronti C, Solà M, Tan J, Neyts J, Canard B, Coll M, Gorbalenya AE and Hilgenfeld R.
Picornavirus non-structural proteins as targets for new anti-virals with broad activity
Antiviral Res, **89**, 204-18 (2011)

PhD Theses

- Estructura tridimensional del factor de terminación mitocondrial humano mTERF en complejo con DNA. Nereida Jiménez Menéndez, Universitat Autònoma de Barcelona (2011). Thesis directors: Maria Solà and Miquel Coll. Honors: Cum Laude

Research projects

- Centrosoma 3D: Hacia la comprensión estructural y funcional del centrosoma. Consolider Ingenio-2010 (CSD2006- 23). Spanish Ministry of Science and Innovation (MICINN). 2006-2010. Principal investigator: Miquel Coll
- Estructura de proteínas y complejos de unión al ADN. Proyectos de investigación fundamental (BFU2008-02372/BMC). Spanish Ministry of Science and Innovation (MICINN). 2009-2011. Principal investigator: Miquel Coll
- Grup de cristal.lografia de proteïnes, Grups de Recerca reconeguts per la generalitat de Catalunya 2009-2013 (2009 SGR 1309). Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Miquel Coll
- Small-molecule Inhibitor Leads Versus emerging and neglected RNA viruses (SILVER), European Commission (260644). 2010-2014. Principal investigator: Miquel Coll

Collaborations

- *Fragment screening*, Ernest Giralt, IRB Barcelona (Barcelona, Spain)
- *Bacterial conjugation*, Fernando de la Cruz, Universidad de Cantabria (Cantabria, Spain)
- *Centrosomal proteins*, Cayetano González, IRB Barcelona (Barcelona, Spain); Juan Carlos Zabala, Universidad de Cantabria (Santander, Spain); José María Carazo, Centro Nacional de Biotecnología-CSIC (Madrid, Spain)
- *Chromatin-modifying proteins*, Ferran Azorín, IRB Barcelona (Barcelona, Spain)
- *Chromatin-modifying proteins*, Ferran Azorín, IRB Barcelona (Barcelona, Spain); Xavier Barril, University of Barcelona (Barcelona, Spain)
- *DNA drug complexes*, Joan Aymamí, Universitat Politècnica de Catalunya (Barcelona, Spain); Per Lincoln, Chalmers University of Technology (Göteborg, Sweden); Fernando Albericio, IRB Barcelona (Barcelona, Spain); Michael Hannon, University of Birmingham (Birmingham, United Kingdom)
- *Gram+ plasmid replication and transfer*, Manuel Espinosa and Gloria del Solar, Centro de

Investigaciones Biológicas-CSIC (Madrid, Spain)

- *Horizontal gene transfer and plasmid biology*, Gloria del Solar, Centro de Investigaciones Biológicas-CSIC (Madrid, Spain); Fernando de la Cruz, Universidad de Cantabria (Cantabria, Spain); Manuel Espinosa, Centro de Investigaciones Biológicas-CSIC (Madrid, Spain)
- *HTP protein expression*, Darren J Hart, European Molecular Biology Laboratory (Heidelberg, Germany)
- *Transcription regulation*, Barry L Wanner, Purdue University (Purdue, United States); Konstantin Severinov, Rutgers University (Piscataway, United States); Margarita Salas, Centro de Biología Molecular-CSIC (Madrid, Spain); Juan Aguilar, University of Barcelona (Barcelona, Spain); Ramón Diaz, CIB (Madrid, Spain); Dolf Weijers, Wageningen University (Wageningen, Netherlands); Antonia Herrero, Instituto de Bioquímica Vegetal y Fotosíntesis-CSIC (Seville, Spain)
- *Tubulin folding co-factors*, Juan Carlos Zabala, University of Cantabria (Cantabria, Spain)
- *Viral proteins*, Bruno Canard, Architecture et Function des Macromolécules Biologiques (Marseille, France); Alexander Gorbalenya, Leiden University Medical Center (Leiden, Netherlands); Nuria Verdaguer, IBMB (Barcelona, Spain); Frank van Kuppeveld, Radboud University Nijmegen Medical Centre (Nijmegen, Netherlands)

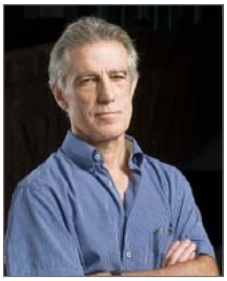
INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Ignasi Fita: Macromolecular Aggregates



Group Members

Group Leader

Ignasi Fita

Postdoctoral Fellows

Xavi Carpena
Barbara Machado
Maria Mercè Ratera

PhD Students

Maria Adell
David Aparicio
Luca Martinelli

Lab Technician

Mª Queralt García

Publications

- Vidossich P, Carpena X, Loewen PC, Fita I and Rovira C
  Oxygen Binding to Catalase-Peroxidase
  J Phys Chem Lett, **3**, 196-200 (2011)
- Díaz A, Loewen PC, Fita I and Carpena X.
  Thirty years of heme catalases structural biology
  Arch Biochem Biophys (2011)
- Díaz A, Martínez-Pons C, Fita I, Ferrer JC and Guinovart JJ.
  Processivity and subcellular localization of glycogen synthase depend on a non-catalytic high affinity glycogen-binding site
  J Biol Chem, **286**, 18505-14 (2011)
- Jha V, Louis S, Chelikani P, Carpena X, Donald LJ, Fita I and Loewen PC.
  Modulation of heme orientation and binding by a single residue in catalase HPII of Escherichia coli
  Biochemistry, **50**, 2101-10 (2011)
- Kowalczyk L, Ratera M, Paladino A, Bartoccioni P, Errasti-Murugarren E, Valencia E, Portella G, Bial S, Zorzano A, Fita I, Orozco M, Carpena X, Vázquez-Ibar JL and Palacín M.
  Molecular basis of substrate-induced permeation by an amino acid antiporter
  Proc Natl Acad Sci U S A, **108**, 3935-40 (2011)
- Addington T, Calisto B, Alfonso-Prieto M, Rovira C, Fita I and Planas A.
  Re-engineering specificity in 1,3-1, 4-?-glucanase to accept branched xyloglucan substrates
  Proteins, **79**, 365-75 (2011)

Research projects

- Análisis estructural de las proteínas peroxisomales: Enzimas metabólicos y peroxinas. Proyectos de investigación fundamental (BFU2009-09268). Spanish Ministry of Science and Innovation (MICINN). 2009-2012. Principal investigator: Ignasi Fita
- Grup de cristal.lografia de proteïnes, Grups de Recerca reconeguts per la generalitat de Catalunya 2009-2013 (2009-SGR-1309). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Miquel Coll
- Unraveling the molecular mechanism of nitrosative stress resistance in tuberculosis (NOSTRESS), European Commission, 223335, (2008-2011). Principal investigator: Ignasi Fita

INSTITUTE FOR RESEARCH IN BIOMEDICINE

IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain

Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14

info@irbbarcelona.org

Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Maria Jesus Macias: Protein NMR Spectroscopy

Group Members

Group Leader

Maria Jesus Macias

Postdoctoral Fellow

James Gordon

PhD Students

Eric Aragón
Albert Escobedo
Constanze Schelhorn

Lab Technicians

Tiago Lopes
Lidia Ruiz

Research Assistant

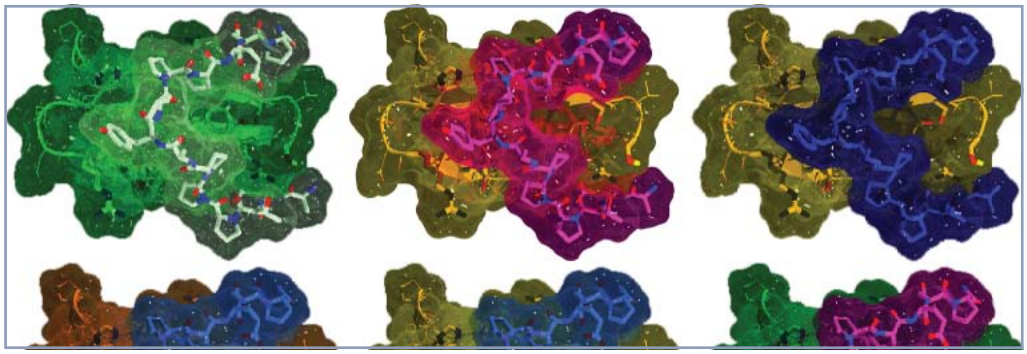
Pau Martín

Visiting Scientist

Carlos Alberto Areche

Highlights

- SMAD binding proteins.
- Inter- and intra-molecular interactions in E3 ubiquitin ligases.
- Molecular and structural analysis of ribonucleoprotein complexes.



Publications

- Aragón E, Goerner N, Zaromytidou AI, Xi Q, Escobedo A, Massagué J and Macias MJ.
  A Smad action turnover switch operated by WW domain readers of a phosphoserine code
  Genes Dev, **25**, 1275-88 (2011)
- Ramón R, Martín-Gago P, Verdaguer X, Macias MJ, Martin-Malpartida P, Fernández-Carneado J, Gomez-Caminals M, Ponsati B, López-Ruiz P, Cortés MA, Colás B and Riera A.
  SSTR1- and SSTR3-Selective Somatostatin Analogues
  Chembiochem, **12**, 625-32 (2011)

PhD Theses

- Interactions of Smads and WW domains of proteins involved in TGF-signaling, Nina Goerner, Freie Universität Berlin. Thesis director: Maria J. Macias, honors: (Magna cum laude)

Research projects

- Estudio estructural de los cambios conformacionales en las ubiquitin ligasas ITCH y RSP5 por RMN . Proyectos de investigación fundamental (BFU2008-02795). Spanish Ministry of Science and Innovation (MICINN). 2009-2011. Principal investigator: Maria Macias
- Integrated approach to post-transcriptional regulation of gene expression and its role in human disease, RNAREG. Consolider-Ingenio-2010 (CSD2009-00080). Spanish Ministry of Science and Innovation (MICINN). 2010-2014. Principal investigator: Maria Macias
- Unitat de recerca en síntesi asimètrica. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 901). Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Antoni Riera
- BCN PEPTIDES S.A. 2009-2014 María Macías

Collaborations

- *NMR studies of somatostatin and derivatives*, Antoni Riera, IRB Barcelona (Barcelona, Spain)
- *Protein and Peptide ligations*, Miriam Royo, Barcelona Science Park (Barcelona, Spain)
- *Protein-protein and protein-RNA complexes*, Juan Valcárcel, Center for Genomic Regulation (Barcelona, Spain); Raul Mendez, IRB Barcelona (Barcelona, Spain)
- *SMAD proteins*, Joan Massagué, Memorial-Sloan Kettering Cancer Center (New York, United States)

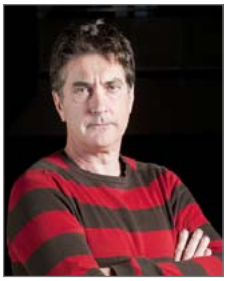
INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Modesto Orozco: Molecular modelling and bioinformatics



Highlights

- We have determined the conformational nature of a prototypical molten-globule moonlighting protein and advanced in the description of the unfolded state of proteins.
- We have gained ground in the description of chromatin structure using both experimental and theoretical approaches.
- We have progressed in describing the connection between changes in DNA sequence and structure and genetic pathologies such as cancer.

Publications

- Kowalczyk L, Ratera M, Paladino A, Bartoccioni P, Errasti-Murugarren E, Valencia E, Portella G, Bial S, Zorzano A, Fita I, Orozco M, Carpena X, Vázquez-Ibar JL and Palacín M.
  Molecular basis of substrate-induced permeation by an amino acid antiporter
  Proc Natl Acad Sci U S A, **108**, 3935-40 (2011)
- Luque FJ, Dehez F, Chipot C and Orozco M
  Polarization effects in molecular interactions
  WIREs Comput Mol Sci **1**, 844-854 (2011)
- Orozco M, Orellana L, Hospital A, Naganathan AN, Emperador A, Carrillo O and Gelpí JL.
  Coarse-grained representation of protein flexibility. Foundations, successes, and shortcomings
  Adv Protein Chem Struct Bio **85**, 183-215 (2011)
- Blas JR, Huertas O, Tabares C, Sumpter BG, Fuentes-Cabrera M, Orozco M, Ordejón P and Luque FJ.
  Structural, dynamical, and electronic transport properties of modified DNA duplexes containing size-expanded nucleobases
  J Phys Chem A, **115**, 11344-54 (2011)
- Deniz O, Flores O, Battistini F, Pérez A, Soler-López M and Orozco M.
  Physical properties of naked DNA influence nucleosome positioning and correlate with transcription start and termination sites in yeast
  Bmc Genomics **12**, 489 (2011)
- Naganathan AN and Orozco M.
  The protein folding transition-state ensemble from a G?-like model
  Phys Chem Chem Phys, **13**, 15166-74 (2011)
- Naganathan AN and Orozco M.
  The native ensemble and folding of a protein molten-globule: functional consequence of downhill folding
  J Am Chem Soc, **133**, 12154-61 (2011)

Group Members

Group Leader

Modesto Orozco

Research Associates

Agustí Emperador
Josep Ll. Gelpí
Manuel Rueda

Postdoctoral Fellows

Andreu Alibés
Federica Battistini
Rima Chaudhuri
Rosana Collepardo

Pablo Ignacio Daniel Dans

Guillem Portella
Robert Soliva
Nadine Simone Utz

PhD Students

Annalisa Arcella
Michela Candotti
Ozgen Deniz
Elisa Durán
Ignacio Faustino
Oscar Flores
Ivan Ivani
Samira Jaeger*
Laura Orellana
Pedro Sfriso

*shared with another lab

Research Assistants

José Antonio Alcántara
Chiara Lara Castellazzi
Adam Hospital
Floriane Montanari

- Flores O and Orozco M.
  nucleR: a package for non-parametric nucleosome positioning
  Bioinformatics, **27**, 2149-50 (2011)
- Stein A, Rueda M, Panjkovich A, Orozco M and Aloy P.
  A systematic study of the energetics involved in structural changes upon association and connectivity in protein interaction networks
  Structure, **19**, 881-9 (2011)
- Puente XS, Pinyol M, Quesada V, Conde L, Ordóñez GR, Villamor N, Escaramis G, Jares P, Beà S, González-Díaz M, Bassaganyas L, Baumann T, Juan M, López-Guerra M, Colomer D, Tubío JM, López C, Navarro A, Tornador C, Aymerich M, Rozman M, Hernández JM, Puente DA, Freije JM, Velasco G, Gutiérrez-Fernández A, Costa D, Carrió A, Guijarro S, Enjuanes A, Hernández L, Yagüe J, Nicolás P, Romeo-Casabona CM, Himmelbauer H, Castillo E, Dohm JC, de Sanjosé S, Piris MA, de Alava E, San Miguel J, Royo R, Gelpí
  Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukaemia
  Nature, **475**, 101-5 (2011)
- D'Abramo M, Orozco M and Amadei A.
  Effects of local electric fields on the redox free energy of single stranded DNA
  Chem Commun, **47**, 2646-8 (2011)
- Ayuso-Tejedor S, García-Fandiño R, Orozco M, Sancho J and Bernadó P.
  Structural analysis of an equilibrium folding intermediate in the apoflavodoxin native ensemble by small-angle X-ray scattering
  J Mol Biol, **406**, 604-19 (2011)
- Raimondi F, Portella G, Orozco M and Fanelli F.
  Nucleotide binding switches the information flow in ras GTPases
  Plos Comput Biol, **7**, e1001098 (2011)
- Pons C, Talavera D, de la Cruz X, Orozco M and Fernandez-Recio J.
  Scoring by intermolecular pairwise propensities of exposed residues (SIPPER): a new efficient potential for protein-protein docking
  J Chem Inf Model, **51**, 370-7 (2011)

Research projects

- Desarrollo de nuevas etiquetas peptídicas (EpiTag). INNPACTO (IPT-010000-2010-19). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Modesto Orozco
- European life-science infrastructure for biological information, European Commission (214227), 2007-2011. Principal investigator: Modesto Orozco
- Modelització molecular i bioinformàtica, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1348). Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Modesto Orozco
- Molecular recognition, Fundación Marcelino Botín, (2007-2010). Principal investigator: Modesto Orozco
- Red temática de investigación cooperativa en biomedicina computacional "COMBIOMED". (RD07/0067/0009). Carlos III Health Institute (ISCIII). 2008-2012. Principal investigator: Modesto Orozco
- Scalable Software Services for Life Science (ScalaLife), European Commission (261523). 2010-2013. Principal investigator: Modesto Orozco
- Simulaciones de formas inusuales o tensionadas de los ácidos nucleicos de potencial interés biotecnológico o biomédico. Proyectos de investigación fundamental (BIO2009-10964). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Modesto Orozco
- Supercomputación y e-ciencia. Consolider Ingenio-2010 (CSD2007-00050). Spanish Ministry of Science and Innovation (MICINN). 2007-2012. Principal investigator: Modesto Orozco.
- Plataforma en Red de Bioinformática (INB-ISCIII). Carlos III Health Institute (ISCIII). 2004-2011. Principal investigator: Modesto Orozco
- Spanish Ministry of Science and Innovation (MICINN). 2010. Principal investigator: Modesto Orozco
- Pfizer Research and Technology Center. 2010. Principal investigator: Modesto Orozco
- Palau Pharma 2011-2012 Modesto Orozco

MSc Student

Marco Paulo Seco

Visiting Scientist

Athi Narayanan Naganathan

Administrative Assistant

Margarita Pedro

Collaborations

- *Definition of new generation simulation methods*, Department of Physical Chemistry. Pharmacy School., University of Barcelona (Barcelona, Spain)
- *Essential deformation patterns in protein recognition*, University of California (San Diego, United States)
- *Genotyping of chronic lymphocytic leukemia*, University of Oviedo (Oviedo, Spain)
- *Representation of DNA conductivity*, Department of Chemistry, University La Sapienza of Rome (Rome, Italy)
- *Representation of partially folded proteins*. Department of Chemistry, University of Zaragoza (Zaragoza, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Miquel Pons: Biomolecular NMR

Group Members

Group Leader

Miquel Pons

Research Associate

Jesús García

Postdoctoral Fellows

Irene Amata*
Ildefonso Marín
Daniel Valverde
*shared with another lab

PhD Students

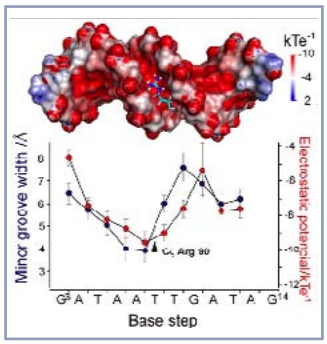
Tiago Cordeiro
Carles Fernández
Anabel-Lise Le Roux
Mariano Maffei
Oriol Marimón
Yandi Naranjo

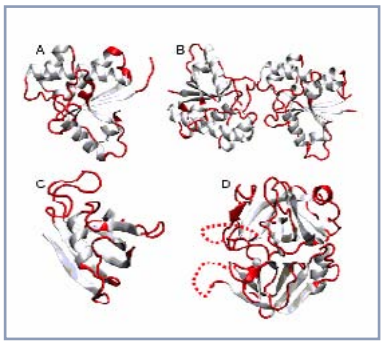
Visiting Scientists

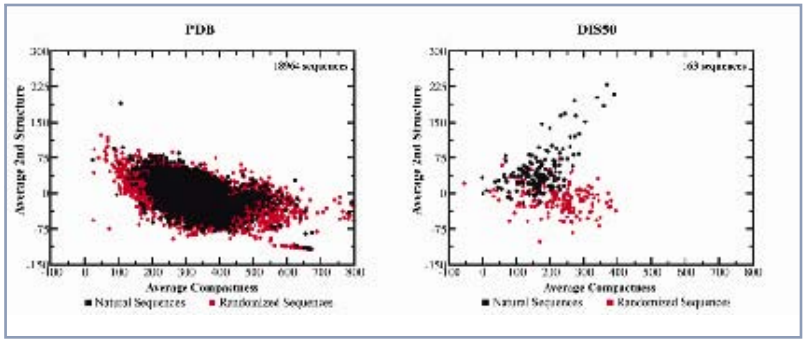
Pau Bernadó
Isis Figueiredo

Highlights

- Using NMR, we have resolved the 3D structure of the first DNA complex of a member of the H-NS family of proteins. The structure reveals an indirect minor-groove readout mechanism (Fig. 1).
- Metastructure correlation maps show distinct features for folded and intrinsically disordered proteins, thereby pointing to varoious strategies to prevent amyloid formation (Fig 2).
- Loop compaction has been identified as the mechanism by which proteins are stabilized by arginine and glutamic acid mixtures. This is a general mechanism for protein stabilization by polyelectrolite mixtures (Fig 3).







Publications

- Blobel J, Brath U, Bernadó P, Diehl C, Ballester L, Sornosa A, Akke M and Pons M.
  Protein loop compaction and the origin of the effect of arginine and glutamic acid mixtures on solubility, stability and transient oligomerization of proteins
  Eur Biophys J Biophy (2011)
- Cordeiro TN, Schmidt H, Madrid C, Juárez A, Bernadó P, Griesinger C, García J and Pons M.
  Indirect DNA readout by an H-NS related protein: structure of the DNA complex of the C-terminal domain of Ler
  Plos Pathog, **11** (7), e1002380 (2011)
- Banerjee D, Paniagua JC, Mugnaini V, Veciana J, Feintuch A, Pons M and Goldfarb D.
  Correlation of the EPR properties of perchlorotriphenylmethyl radicals and their efficiency as DNP polarizers
  Phys Chem Chem Phys, **41** (13), 18626-37 (2011)
- Alba CF, Solórzano C, Paytubi S, Madrid C, Juarez A, García J and Pons M.
  Essential residues in the H-NS binding site of Hha, a co-regulator of horizontally acquired genes in Enterobacteria
  Febs Lett, **12** (585), 1765-70 (2011)

Research projects

- Nuevos metodos de RMN y nuevos conceptos para el estudio de biomoléculas con interaccipones dinámicas implicadas en la señalización (BIO2010-15683). Spanish Ministry of Science and Innovation (MICINN). 2011-2013. Principal investigator: Miquel Pons
- NMR for Structural Biology (Bio-NMR) 7th FP (Contract 261863) 2010-2014. Principal investigator: Ivano Bertini.
- European Network for Hyperpolarization Physics and Methodology in NMR and MRI (COST action TD1103). 2011-2015. Principal investigator: Walter Köckenberger .
- Resonància magnètica nuclear de biomolècules (BIO-RMN) 2009 SGR 1352 Grup de Recerca reconegut de la Generalitat de Catalunya Agency for Administration of University and Research Grants (AGAUR) 2009-2013. Principal investigator: Miquel Pons
- 081510 Projectes Recerca Fundació la Marató de TV3. Principal investigator: Miquel Pons
- Descubrimiento de compuestos de interés terapéutico (leads) mediante tecnologías computacionales y estructurales TRA2009_0254_03 TRACE Spanish Ministry of Science and Innovation (MICINN) 2010-2012. Principal investigator: Miquel Pons
- PCI2006-A9-0690 Acciones Complementarias Internacionales Spanish Ministry of Science and Innovation (MICINN) 2007-2012. Principal investigator: Miquel Pons
- Multidisciplinary Frontiers of Magnetic Resonance 05-PGM-022 ESF Research Networking Program European Science Foundation (ESF) 2007-2012. Principal investigator: Miquel Pons

Collaborations

- *Computational studies in nucleoid-associated proteins,* Modesto Orozco, IRB Barcelona (Barcelona, Spain)
- *in vivo NMR in Xenopus oocytes,* Angel Nebreda, IRB (Barcelona, Spain)
- *Bacterial nucleoid-associated proteins,* Antonio Juarez, University of Barcelona & Institute for Bioengineering of Catalonia (Barcelona, Spain)
- *Chlorinated radicals for DNP,* Jaume Veciana, Institut de Ciencias dels Materials Barcelona (Bellaterra, Spain)
- *DNP ,* Daniella Goldfarb, Weizmann Institute (Rehovolt, Israel)
- *Drug Discovery,* Jordi Quintana, Parc Científic de Barcelona (Barcelona, Spain)
- *Drug discovery,* Ismael Zamora, Lead Molecular Design (Sant Cugat del Valles, Spain)
- *Drug Discovery, Phosphatases,* Lydia Tabernero, Manchester University (Manchester, United Kingdom)
- *Intrinsically disordered regions and ubiquitination,* Bernat Crosas, CSIC (Barcelona, Spain)
- *Ler structure,* Christian Griesinger, Max-Planck Institute (Göttingen, Germany)
- *Metastructures, LINGO and NMR,* Robert Konrat, University of Vienna (Vienna, Austria)
- *New radicals for Dynamic Nuclear Polarization (DNP),* Anita Marsaioli, UNICAMP (Campinas, Brazil); Antoni Riera, IRB Barcelona (Barcelona, Spain); Jaume Veciana, Institute of Material Sciences (Barcelona, Spain)
- *NMR studies of coagulation factors with unfolded regions,* Pablo Fuentes, Hospital de la Santa Creu i Sant Pau (Barcelona, Spain)
- *Polyelectrolyte based stabilization of proteins,* Enrique García España, Universitat de Valencia (Valencia, Spain)
- *Protein-protein docking,* Juan Recio, Barcelona Supercomputing Center (Barcelona, Spain)
- *Relaxation dispersion,* Oscar Millet, CIC bioGUNE (Bilbao, Spain)
- *Ribosomal proteins,* Mikael Akke, University of Lund (Lund, Sweden)

- *SAXS,* Dmitri Svergun, European Molecular Biology Laboratory (Hamburg, Germany)
- *Solid-state NMR studies of H-NS,* Marc Baldus, Bijvoet Center for Biomolecular Research, Utrecht University (Utrecht, Netherlands)
- *Target characterization in drug design,* Andrew Marsh, University of Warwick (Coventry, United Kingdom)
- *Topological analysis of unfolded protein space,* Federico Thomas, Insitut de Robòtica Industrial CSIC (Barcelona, Spain)
- *Unfolded proteins and residual dipolar couplings,* Martin Blackledge, Institute de Biologie Structurale (Grenoble, France)

Awards and honours

- *Board of Trustees member*
  EUROMAR (2008-2012)
  Awardee: Miquel Pons
- *Council member*
  International Society for Magnetic Resonance (ISMAR) (2007-2014)
  Awardee: Miquel Pons
- *Executive officer*
  AMPERE society (2009-2012)
  Awardee: Miquel Pons
- *Treasurer*
  EUROMAR (2010-2012)
  Awardee: Miquel Pons

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

MOLECULAR MEDICINE

Carme Caelles: Cell signalling

Group Members

Group Leader

Carme Caelles

Research Associate

Joan Roig

Postdoctoral Fellows

Neus Teixidó *
Johan Tisserand
*shared with another lab

PhD Students

Mª Teresa Bertrán
Kader Cavusoglu
Jordi Lanuza
Giuseppe Pulice
Sara Sdelci

MSc Student

Susana Eibes

Lab Technician

Cristina Vila

Highlights

- Pro-inflammatory SAPK pathways are inhibited by ligand-activated LXR.
- Treatment with rosiglitazone reverts the glucose intolerance caused by the in vivo selective activation of JNK in pancreatic β cells.
- DYNLL/LC8 protein controls signal transduction through the Nek9/Nek6 signaling module by regulating Nek6 binding to Nek9.
- Nek9 is a Plk1-activated kinase that regulates prophase centrosome separation through Nek6/7 and the mitotic kinesin Eg5.

Publications

- Regué L, Sdelci S, Bertran MT, Caelles C, Reverter D and Roig J.
  DYNLL/LC8 Protein Controls Signal Transduction through the Nek9/Nek6 Signaling Module by Regulating Nek6 Binding to Nek9.
  J Biol Chem, **286**, 18118-29 (2011)
- Bertran MT, Sdelci S, Regué L, Avruch J, Caelles C and Roig J.
  Nek9 is a Plk1-activated kinase that controls early centrosome separation through Nek6/7 and Eg5
  Embo J (2011)
- Carulla P, Bribián A, Rangel A, Gavín R, Ferrer I, Caelles C, Del Río JA and Llorens F.
  Neuroprotective role of PrPC against kainate-induced epileptic seizures and cell death depends on the modulation of JNK3 activation by GluR6/7-PSD-95 binding
  Mol Biol Cell, **22**, 3041-54 (2011)
- Perdiguero E, Sousa-Victor P, Ruiz-Bonilla V, Jardí M, Caelles C, Serrano AL and Muñoz-Cánoves P.
  p38/MKP-1-regulated AKT coordinates macrophage transitions and resolution of inflammation during tissue repair
  J Cell Biol, **195**, 307-22 (2011)

PhD Theses

- Identification and characterization of NERCC1/NEK9-interacting proteins. Laura Regué, University of Barcelona (2011). Thesis director: Joan Roig. Honors: Cum Laude

Research projects

- Inhibición de las rutas de SAPKs por GR, PPARs y LXRs como un mecanismo responsable de sus acciones farmacológicas (antiinflamatorias, antidiabéticas y antiateroscleróticas), SAF2010-21682, (2011-2013) Principal investigator: Carme Caelles
- El módulo de señalización NERCC1/NEK6/7. Regulación y funciones, BFU2008-03441, (2009-2011) Principal investigator: Joan Roig
- Senyalització cel.lular, Grups de Recerca reconeguts per la Generalitat de Catalunya, 2009-SGR-163 (2009-2013). Principal investigator: Diego Haro

Collaborations

- *Regulation of MAPK pathways in macrophage,* Antonio Celada, IRB Barcelona (Barcelona, Spain)
- *Regulation of microtubule nucleation through phosphorylation,* Jens Lüders, IRB Barcelona (Barcelona, Spain)
- *Functional analysis of JNK activation in pancreatic β-cells,* Ramón Gomis, IDIBAPS (Barcelona, Spain)
- *LXR-MAPK pathways cross talk,* Annabel F Valledor, University of Barcelona (Barcelona, Spain)
- *MAPK signalling pathways in myogenesis,* Pura Muñoz-Cánoves, Pompeu Fabra University (Barcelona, Spain)
- *Mechanisms of glucocorticoid resistance,* Cesar Picado, Hospital Clínic (Barcelona, Spain)
- *Structural basis for the mechanism of Nercc1 autoinhibition,* David Reverter, Institute of Biotechnology and Biomedicine, Autonomous University of Barcelona (Barcelona, Spain)
- *Study of the regulation and function of the Nercc1/Nek6/7 signalling module in the Xenopus egg extra,* Isabelle Vernos, Centre for Genomic Regulation (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

MOLECULAR MEDICINE

Antonio Celada: Gene expression

Group Members

Group Leader

Antonio Celada

Research Associates

Mònica Comalada
Jorge Lloberas
Luis Francisco Santamaria

Postdoctoral Fellow

Maria Glòria Sans

PhD Students

Erika Barboza
Selma Patricia Pereira
Milos Tatarski
Juan Tur
Lorena Valverde
Catrin Youssif
Fatemeh Zare

MSc Students

Pol Barbarroja
Juan Antonio Calatayud
Ester Ruiz

Lab Technicians

Gemma López
Judith Rodríguez

Highlights

- The damage produced during macrophage activation includes breakage of single -and double- stranded DNA. To be protected against this damage, activated macrophages induce the exonuclease Trex1, RnasH, SAMHD1 and the polymerase μ.
- We have developed and *in vitro* method capable of producing an unlimited number of macrophages that express Ly6 and move specifically to the inflammatory loci. This breakthrough is the first cellular therapy directed to inflammation.
- A mutation in the CAT2 promoter in a mouse strain produces deficient arginine transport in macrophages. This effect correlates with impaired macrophage activation *in vitro* and with decreased inflammation *in vivo*.

Publications

- Serra M, Forcales SV, Pereira-Lopes S, Lloberas J and Celada A.
  Characterization of Trex1 induction by IFN-γ in murine macrophages
  J Immunol, **186**, 2299-308 (2011)
- Pascual-García M, Carbó JM, León T, Matalonga J, Out R, Van Berkel T, Sarrias MR, Lozano F, Celada A and Valledor AF.
  Liver X receptors inhibit macrophage proliferation through downregulation of cyclins D1 and B1 and cyclin-dependent kinases 2 and 4
  J Immunol, **186**, 4656-67 (2011)
- Bailón E, Cueto-Sola M, Utrilla P, Nieto A, Garrido-Mesa N, Celada A, Zarzuelo A, Xaus J, Gálvez J and Comalada M.
  DNFB-DNS hapten-induced colitis in mice should not be considered a model of inflammatory bowel disease
  Inflamm Bowel Dis, **17**, 2087-101 (2011)
- Castro de Moura M, Miro F, Han JM, Kim S, Celada A and Ribas de Pouplana L.
  ***Entamoeba* lysyl-tRNA synthetase contains a cytokine-like domain with chemokine activity towards human endothelial cells**
  Plos Neglect Trop D, **5**, e1398 (2011)
- Garrido-Mesa N, Utrilla P, Comalada M, Zorrilla P, Garrido-Mesa J, Zarzuelo A, Rodríguez-Cabezas ME and Gálvez J.
  The association of minocycline and the probiotic Escherichia coli Nissle 1917 results in an additive beneficial effect in a DSS model of reactivated colitis in mice
  Biochem Pharmacol, **82**, 1891-900 (2011)

- Garrido-Mesa N, Camuesco D, Arribas B, Comalada M, Bailón E, Cueto-Sola M, Utrilla P, Nieto A, Zarzuelo A, Rodríguez-Cabezas ME and Gálvez J.
  The intestinal anti-inflammatory effect of minocycline in experimental colitis involves both its immunomodulatory and antimicrobial properties
  Pharmacol Res, **63**, 308-19 (2011)

PhD Theses

- Mecanismos moleculares de la activación del macrófago por el IFN-g" Consol Farreras, University of Barcelona (2011). Thesis director: Antonio Celada and Jorge Lloberas. Honors: Cum Laude

Research projects

- Grup de biologia del macròfag. Regulació de l'expressió gènica, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 856). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Antonio Celada
- Inmunopatología de la psoriasis. Estudio mediante un nuevo modelo ex vivo. Proyectos de investigación en Salud (PI09/2222). Carlos III Health Institute (ISCIII). 2009-2011. Principal investigator: Luis Santamaría
- Mecanismos moleculares y celulares en enfermedades inflamatorias crónicas y autoinmunes (MEICA). Fundación para el desarrollo de la investigación en Genómica y Proteómica. 2009-2011. Principal investigator: Antonio Celada
- Nuclease Immune Mediated Brain and Lupus-like conditions: natural history, pathophysiology, diagnostic and therapeutic modalities with application to other disorders of autoimmunity (NIMBL). European Commission, FP7-HEALTH-F2-2010- (241779). 2010-2013. Principal investigator: Antonio Celada
- Regulation of the expression of genes involved in the proliferation, differentiation, activation and apoptosis of macrophages and dendritic cells. Proyectos de investigación fundamental (BFU2007-63712/BMC). Spanish Ministry of Science and Innovation (MICINN). 2007-2011. Principal investigator: Antonio Celada
- Molecular mechanisms involved in lxr-and rxr-mediated prevention of a atherosclerosis Research Projects La Marató TV3 2009-2011. Principal investigator: Annabel Fernández-Valledor
- Janus Developments S.L. 2011-2012. Principal investigator: Luis Santamaría
- Función de la Inmunidad Innata en la toleranci iIntestinal: papel de los TIRS y la Microbiota SAF2010-16755 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2011-2013. Principal investigator: Mònica Comalada

Collaborations

- *Arginine transport systems,* Manuel Palacín , IRB Barcelona (Barcelona, Spain)
- *Cytokines and parasites,* Lluís Ribas de Pouplana, IRB Barcelona (Barcelona, Spain)
- *Role of mytofusine on macrophages,* Antonio Zorzano, IRB Barcelona (Barcelona, Spain)
- *Tumor associated macrophages,* Roger Gomis, IRB Barcelona (Barcelona, Spain)
- *Inflammation and polymerases,* Antonio Bernard, Spanish National Centre for Cardiovascular Research (Madrid, Spain)
- *Telomerase and macrophaging*. María Blasco, Spanish National Cancer Research Centre (Madrid, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

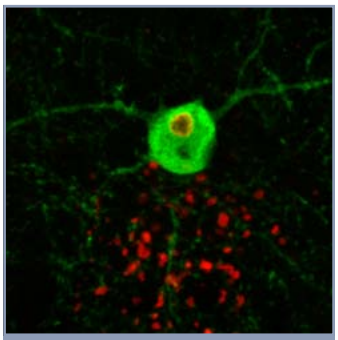
Research Programmes

MOLECULAR MEDICINE

Joan J. Guinovart: Metabolic Engineering and Diabetes

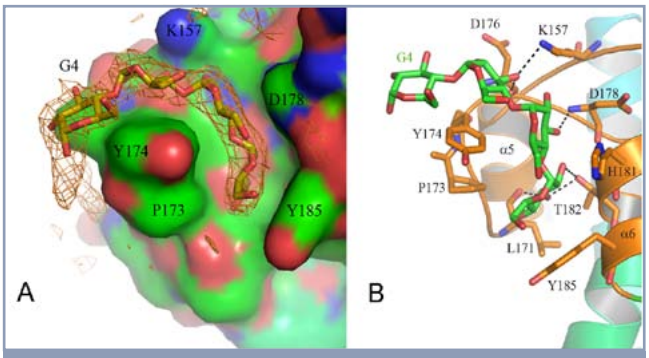
Highlights

- Mice lacking the malin gene show progressive accumulation of Lafora bodies, loss of parvalbumin-positive hippocampal neurons and brain function deficits.
- We have generated new mouse and *Drosophila* transgenic models in order to study the impact of glycogen over-accumulation or glycogen depletion on specific tissues. The role of glycogen as a metabolic sensor and glycogen-mediated neurodegeneration are currently being studied using these models.



Author: Jordi Vallès Ortega, PhD

Caption: Interneuron obtained from an engineered mouse lacking the malin gene (in green) and showing the accumulation of Lafora bodies (in red). Note the presence of a large polyglucosan body in the soma of the neuron and of several other aggregates associated to the neuronal processes.



Author: Adelaida Díaz Vilchis, PhD

Caption: In the search for potential modulators of glycogen synthase, the crystal structure of monomeric PaGS has been obtained. This structure reveals the existence of a high affinity glycogen binding site, shown in the figure with surface (A) or ribbon (B) representations. Maltotetraose (shown as sticks) occupies the glycogen binding site by curling around the Y174 residue, and makes hydrogen bonds with K157, L171, D178 and T182.

Group Members

Group Leader

Joan J. Guinovart

Research Associates

Joaquim Calbó
Maria Del Mar García

Postdoctoral Fellows

Adelaida Díaz Vilchis
Jordi Duran
Carlos Rodríguez
Christopher Sinadinos
Flor Tevi
Delia Zafra

PhD Students

Óscar Blanco
Mireia Díaz
Carles Martínez
Laura Nocito
Isabel Sáez
Juan Felipe Slebe
Giorgia Testoni
Jordi Vallès

Research Assistant

Anna Adrover

Lab Technicians

Manuel Gris
Emma Veza

Administrative Assistants

Carolina Sánchez

- Restoration of hepatic glycogen deposition by transduction of a constitutively active liver glycogen synthase mutant reduces hyperglycemia, hyperphagia and the expression of gluconeogenic enzymes in STZ-diabetic rats.
- The processivity and subcellular localization of glycogen synthase depend on a non-catalytic high affinity glycogen-binding site. We have structurally and biochemically characterized a novel glycogen-binding motif in glycogen synthase.

Publications

- Valles-Ortega J, Duran J, Garcia-Rocha M, Bosch C, Saez I, Pujadas L, Serafin A, Cañas X, Soriano E, Delgado-García JM, Gruart A and Guinovart JJ.
  Neurodegeneration and functional impairments associated with glycogen synthase accumulation in a mouse model of Lafora disease
  EMBO Mol Med, **3**, 1-15 (2011)
- Ros S, García-Rocha M, Calbó J and Guinovart JJ.
  Restoration of hepatic glycogen deposition reduces hyperglycaemia, hyperphagia and gluconeogenic enzymes in a streptozotocin-induced model of diabetes in rats
  Diabetologia, **54**, 2639-48 (2011)
- Fernández-Novell JM, Ballester J, Altirriba J, Ramió-Lluch L, Barberà A, Gomis R, Guinovart JJ and Rodríguez-Gil JE.
  Glucose and fructose as functional modulators of overall dog, but not boar sperm function
  Reprod Fert Develop, **23**, 468-80 (2011)
- Borg J, Campos A, Diema C, Omeñaca N, de Oliveira E, Guinovart J and Vilaseca M.
  Spectral counting assessment of protein dynamic range in cerebrospinal fluid following depletion with plasma-designed immunoaffinity columns
  Clin Proteomics, **8**, 6 (2011)
- Gómez-Gómez MM, Rodríguez-Fariñas N, Cañas-Montalvo B, Domínguez J, Guinovart J and Cámara-Rica C.
  Biospeciation of tungsten in the serum of diabetic and healthy rats treated with the antidiabetic agent sodium tungstate
  Talanta, **84**, 1011-8 (2011)
- Díaz A, Martínez-Pons C, Fita I, Ferrer JC and Guinovart JJ.
  Processivity and subcellular localization of glycogen synthase depend on a non-catalytic high affinity glycogen-binding site
  J Biol Chem, **286**, 18505-14 (2011)

PhD Theses

- Determinants de la unió a glicogen i translocació de la glicogen sintasa. Carles Martinez, Universitat de Barcelona (2011). Thesis director: Joan Guinovart. Honors: Cum Laude
- Estudio de la regulación de la glucógeno sintasa hepática por modificación postraduccional. Oscar Blanco Presas, Universitat de Barcelona (2011). Thesis director: Joan J. Guinovart. Honors: Cum Laude
- Modulació transcripcional del metabolisme hepàtic per tungstat de sodi. Laura Nocito Labad, Universitat de Barcelona (2011). Thesis director: Joan J. Guinovart. Honors: Cum Laude

Research projects

- The dark side of a bright molecule: Determinants of glycogen-induced cell dysfunction. Human HFSP Program Grants, RGP0027/2011 (2011-2014). Principal investigator: Joan J. Guinovart
- Estudio de un nuevo mecanismo de regulación del metabolismo del glucogeno. Análisis de las implicaciones patológicas de la acumulación anómala de polímeros de glucosa. Proyectos de investigación fundamental (BFU2008-00769). Spanish Ministry of Science and Innovation (MICINN). 2009-2011. Principal investigator: Joan J Guinovart
- Centro de Investigación Biomédica en Red de Diabetes y enfermedades metabólicas asociadas (CIBERDEM), Carlos III Health Institute, CB07-08-0045 (since 2008). Principal investigator: Joan J Guinovart.
- Enginyeria metabòlica i teràpia de la diabetis, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1176). Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Joan J Guinovart

Collaborations

- *The use of Drosophila melanogaster as model system for the study of Lafora disease,* Marco Milán, IRB Barcelona (Barcelona, Spain)
- *Electrophysiological effects of the modulation of brain glycogen metabolism,* JM Delgado-Garcia, Universidad Pablo de Olavide (Sevilla, Spain)
- *Glycogen-induced dysfunctions in pancreas and retina and their involvement in the ethiogenesis of diabetes mellitus,* Rafael Simó, Institut de Recerca Hospital Vall d'Hebrón (Barcelona, Spain); Ramon Gomis, IDIBAPS-Hospital Clínic (Barcelona, Spain)
- *Impact of GBE1 defficiency on energy metabolism,* Jerzy Duszynski , Nencki Institute of Experimental Biology (Warsaw, Poland); Adam Godzik, Sanford - Burnham Medical Research Institute (La Jolla, United States)
- *Metabolomic analysis of animal models with deregulated glycogen metabolism,* Xavier Correig, Metabolomics Platform - CIBERDEM (Tarragona, Spain)
- *Molecular dissection of the mechanisms of action of the antidiabetic agent sodium tungstate in skeleton muscle,* Mª Dolores Girón, Rafael Salto, University of Granada (Granada, Spain)
- *Relation between the diabetic syndrome and the key glucose homeostasis enzymes, fructose-1,6-Biphosphatase and glycogen synthase,* Juan Carlos Slebe, Instituto de Bioquímica, Universidad Austral de Chile (Valdivia, Chile)
- *Study of glycogen accumulation in Alzheimer disease,* Isidre Ferrer, Institute of Neuropathology, IDIBELL, Bellvitge University Hospital-ICS (L'Hospitalet de Llobregat, Spain)
- *Study of the actions of sodium tungstate on the ionic homeostasis,* Miguel A Valverde, Pompeu Fabra University (Barcelona, Spain)
- *Study of the alterations of glycogen metabolism in animal models with neurological diseases,* Martí Pumarola, Autonomous University of Barcelona (Barcelona, Spain)
- *Study of the molecular targets and biological actions of sodium tungstate,* José Ramón Murguia, Universidad Politécnica de Valencia (Valencia, Spain)
- *Structural determinants of the activity and regulation of Glycogen Synthase,* Joan Carles Ferrer, University of Barcelona (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

MOLECULAR MEDICINE

Raúl Méndez: Translational control of cell cycle and differentiation

Highlights

- We have identified a new function for CPEB1 in nuclear processing of pre-mRNAs. CPEB-1 regulates in this manner hundreds of transcript enriched in genes related to proliferation and differentiation, thus providing coordinated gene regulation at the translational and pre-mRNA processing levels.
- We have determined that CPEB4 is ectopically expressed in pancreatic tumors and gliomas. We have shown that CPEB4 is essential for tumoral growth and vascularization and performed a genome-wide identification of CPEB4 targets in pancreatic tumours.

Publications

- Ortiz-Zapater E, Pineda D, Martínez-Bosch N, Fernández-Miranda G, Iglesias M, Alameda F, Moreno M, Eliscovich C, Eyras E, Real FX, Méndez R and Navarro P.
  Key contribution of CPEB4-mediated translational control to cancer progression
  Nat Med, **18**, 83-90 (2011)

Research projects

- Translational reprogramming of gene expression in Pancreatic Cancer: from mechanisms to therapy AICR Research Grants Association for International Cancer Research (AICR) 2011-2013. Principal investigator: Raúl Méndez
- Desvelando los circuitos de regulación génica definidos por la familia CPEB de proteínas de unión a RNA: de los mecanismos a las funciones biológicas. BFU2008-02373 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2010-2011. Principal investigator: Raúl Méndez
- RNAREG (Integrated approach to post-transcriptional regulation of gene expression and its role in human disease). CSD2009-00080 Consolider Spanish Ministry of Science and Innovation (MICINN) 2011-2014. Principal investigator: Raúl Méndez
- Control traduccional de l'expresió gènica SGR 2009 1436 Grup de Recerca reconegut de la Generalitat de Catalunya Agency for Administration of University and Research Grants (AGAUR) 2010-2013. Principal investigator: Raúl Méndez

Group Members

Group Leader

Raúl Méndez

Research Associates

Eulàlia Belloc

Gonzalo Fernández-Miranda

Postdoctoral Fellows

Carolina Segura
Laure Weill

PhD Students

Vittorio Calderone
Valeria Giangarra
Carlos Maíllo

Visiting Student

Felice Alessio Bava

Lab Technicians

Verónica Chanes
Judit Martín

Collaborations

- *An integrated approach to post-transcriptional regulation of gene expression and its role in human disease,* RNAREG consortium (Barcelona, Spain)
- *Role of CPEBs in angiogenesis,* Mercedes Fernandez , August Pi i Sunyer Biomedical Research Institute (IDIBAPS) (Barcelona, Spain)
- *Role of CPEBs in tumor development*. Pilar Navarro , IMIM (Hospital del Mar Research Institute) (Barcelona, Spain); Francisco X. Real , Spanish National Cancer Research Centre (Madrid, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

MOLECULAR MEDICINE

Manuel Palacín: Heterogenic and multigenic diseases

Highlights

- The crystal structure of the mutant Asn101Ala of AdiC (arginine/agmatine exchanger) from *E. coli* represents the first structure of the open-to-out substrate-bound state in transporters with the LeuT-fold.
- Proper Π-cation interaction of the guanidium group of the substrate L-arginine with the AdiC residue Trp293 is required to occlude the substrate in the outward-facing state.
- Proof of principle of the assessment of membrane protein expression and stability using a split green fluorescent protein reporter.

Publications

- Kowalczyk L, Ratera M, Paladino A, Bartoccioni P, Errasti-Murugarren E, Valencia E, Portella G, Bial S, Zorzano A, Fita I, Orozco M, Carpena X, Vázquez-Ibar JL and Palacín M.
  Molecular basis of substrate-induced permeation by an amino acid antiporter
  Proc Natl Acad Sci U S A, **108**, 3935-40 (2011).
- Bröer S and Palacín M.
  The role of amino acid transporters in inherited and acquired diseases
  Biochem J, **436**, 193-211 (2011)
- Turnay J, Fort J, Olmo N, Santiago-Gómez A, Palacín M and Lizarbe MA.
  Structural characterization and unfolding mechanism of human 4F2hc ectodomain
  Biochim Biophys Acta, **1814**, 536-44 (2011)
- Jeckelmann JM, Palacin M and Fotiadis D.
  A tool for the qualitative comparison of membrane-embedded and detergent-solubilized membrane protein structures in projection
  J Struct Biol, **173**, 375-81 (2011)

PhD Theses

- *Characterization of the multifunctional protein 4F2hc.* Laura Rodriguez, University of Barcelona (2011). Thesis director: Manuel Palacín. Honors: Cum Laude

Group Members

Group Leader

Manuel Palacín

Postdoctoral Fellows

Paola Chiara Bartoccioni
Susanna Bodoy
Ekaitz Errasti
Joana Fort
Albert Rossell

PhD Students

Maria Elena Álvarez
Gonzalo Delgado
Ana Zuleima Obando
Arturo Rodríguez

Lab Technicians

Susanna Bial
Jorge Manuel Seco

Project Manager

Olga Bausà*

*shared with another lab

Research projects

- Base molecular de la reabsorcion renal de aminoacidos: modelos de ratón y estudios de relacion estructura-funcion. Proyectos de investigación fundamental (SAF2009-12606-C02-01). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Manuel Palacín
- Construccion de una proteina politopica de membrana termoestable apta para cristalizacion mediante un metodo aleatorio. Proyectos de investigación fundamental (BFU2008-04637). Spanish Ministry of Science and Innovation (MICINN). 2009-2011. Principal investigator: Jose Luis Vázquez
- European drug initiative on channels and transporters (EDICT), European Commission, HEALTH-F4-2007 (201924). 2008-2012. Principal investigator: Manuel Palacín
- Grup d'estudi de les bases moleculars de patologies associades a transportadors de membrana (genexartis:patología i terapia moleculars en enfermetats heterogéniques i multigéniques. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1355). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Manuel Palacín
- Centro de Investigación Biomédica en Red de enfermedades raras (CIBERER), Medicina Metabólica Hereditaria. Carlos III Health Institute (ISCIII). 2006-open. Principal investigator: Manuel Palacín

Collaborations

- *Bioinformatics on Amino acid Transporters,* Modesto Orozco, IRB-Barcelona (Barcelona, Spain)
- *Crystal structure and structure-function relationship of amino acid transporters,* Ignasi Fita, IRB Barcelona (Barcelona, Spain); Lucy R Forrest, Max Planck Institute for Biophysics (Frankfurt, Germany); María Antonia Lizarbe, Universidad Complutense de Madrid (Madrid, Spain); Dimitrios Fotiadis, University of Bern (Bern, Switzerland); Eric Gouaux, Vollum institute (Oregon, United States)
- *Crystal structure of eukaryotic amino acid transporters,* Eric Gouaux, Vollum Institute (Portland, Oregon, United States)
- *Physiopathology of inherited aminoacidurias cystinuria and lysinuric protein intolerance (LPI),* Virginia Nunes, Bellvitge Institute for Biomedical Research and University of Barcelona (Barcelona, Spain); Josep Chillarón, University of Barcelona (Barcelona, Spain); Gianfranco Sebastio, Federico II University (Naples, Italy)
- *Role of 4F2hc in integrin signaling and amino acid transport,* Chloé Feral, Université de Nice (Nice, France)
- *Role of 4F2hc in tumourigenesis,* María Antonia Lizarbe, Department of Biochemistry. Universidad Complutense de Madrid (Madrid, Spain); Pedro Fernández, Department of Pathology, Hospital Clínic de Barcelona (Barcelona, Spain); Joaquín Abian, IDIBAPS-CSIC (Barcelona, Spain)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Ignacio Fita, IRB Barcelona (Barcelona, Spain); Dimitrios Fotiadis, University of Bern (Bern, Switzerland); Eric Gouaux, Vollum Institute (Portland, United States)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Dimitrios Fotiadis, University of Bern (Bern, Switzerland)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Modesto Orozco, IRB Barcelona (Barcelona, Spain)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Ignasi Fita, IRB Barcelona (Barcelona, Spain)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Matthias Quick, Cornell University (New York, United States)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Modesto Orozco, IRB Barcelona (Barcelona, Spain)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Matthias Quick, Cornell University (New York, United States)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Steve Baldwin, Astbury Centre for Structural Molecular Biology, University of Leeds (Leeds, United Kingdom); Matthias Quick, Weill Medical College (Cornell University, Spain)
- *Structure-function relationship in heteromeric amino acid transporters (HATs),* Steve Baldwin, University of Leeds (Leeds, United Kingdom)
- *Symmetry in LeuT fold transporters,* Lucy R Forrest, The Max Planck Institute for Biophysics (Frankfurt, Germany)
- *The molecular bases of renal reabsorption of amino acids,* Virginia Nunes, Idibell and University of Barcelona (Barcelona, Spain); Paolo Gasparini, Institute for Maternal and Child Health IRCCS-Burlo Garofolo (Trieste, Italy)

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

MOLECULAR MEDICINE

Antonio Zorzano: Heterogenic and polygenic diseases

Highlights

- The nuclear cofactor DOR participates in osteoblast differentiation through the activation of thyroid hormones.
- Endoplastic Reticulum (ER) stress induces an early increase in mitochondrial metabolism that is critically dependent on mitochondria-ER coupling and Ca^{2+} transfer.
- The macrophage molecule CD14 modulates the inflammatory activity and insulin resistance of adipose tissue.

Publications

- Resmini E, Morte B, Sorianello E, Gallardo E, de Luna N, Illa I, Zorzano A, Bernal J and Webb SM.
  Identification of novel GH-regulated genes in C2C12 cells
  Horm Metab Res, **43**, 919-30 (2011)
- Fernández-Real JM, Pérez del Pulgar S, Luche E, Moreno-Navarrete JM, Waget A, Serino M, Sorianello E, Sánchez-Pla A, Pontaque FC, Vendrell J, Chacón MR, Ricart W, Burcelin R and Zorzano A.
  14 modulates inflammation-driven insulin resistance
  Diabetes, **60**, 2179-86 (2011)
- Muñoz JP and Zorzano A.
  Endoplasmic reticulum stress enters a Nogo zone
  Sci Transl Med, **3**, 88ps26 (2011)
- Bravo R, Vicencio JM, Parra V, Troncoso R, Munoz JP, Bui M, Quiroga C, Rodriguez AE, Verdejo HE, Ferreira J, Iglewski M, Chiong M, Simmen T, Zorzano A, Hill JA, Rothermel BA, Szabadkai G and Lavandero S.
  Increased ER-mitochondrial coupling promotes mitochondrial respiration and bioenergetics during early phases of ER stress
  J Cell Sci, **124**, 2143-52 (2011)
- Linares GR, Xing W, Burghardt H, Baumgartner B, Chen ST, Ricart W, Fernández-Real JM, Zorzano A, Mohan S.
  Role of diabetes- and obesity-related protein in the regulation of osteoblast differentiation
  Am J Physiol Endocrinol Metab, **301**, E40-8 (2011)
- Kowalczyk L, Ratera M, Paladino A, Bartoccioni P, Errasti-Murugarren E, Valencia E, Portella G, Bial S, Zorzano A, Fita I, Orozco M, Carpena X, Vázquez-Ibar JL and Palacín M.
  Molecular basis of substrate-induced permeation by an amino acid antiporter
  Proc Natl Acad Sci U S A, **108**, 3935-40 (2011)

Group Members

Group Leader

Antonio Zorzano

Postdoctoral Fellows

Mª Àngels Díaz
Saska Ivanova
Juan Pablo Muñoz
Montserrat Romero
Manuela Sánchez
Jana Sánchez
David Sebastián
Eleonora Mariana Sorianello

PhD Students

Hilda Yuliana Enciso
Maria Isabel Hernández
Eduard Noguera
Sonia Pereira Da Veiga
David Sala
Ana Sancho

Visiting Scientists

Francesc Xavier Duran
Saadet Turkseven

Lab Technicians

Ignacio Castrillón
Juan Carlos Monasterio

Programme Technician

Natàlia Plana

Project Manager

Olga Bausà*

*shared with another lab

PhD Theses

- Effects of protein mitofusin 2 on muscle metabolism. Jessica Segalés, University of Barcelona (2011). Thesis Director: Antonio Zorzano. Honors: Cum Laude
- Role Mitofusin 2 and mitochondrial metabolism in obesity and type 2 diabetes. Maria Isabel Hernández Álvarez, University of Barcelona (2011). Thesis Director: Antonio Zorzano. Honors: Cum Laude
- Rol of DOR in autophagy. Caroline Mauvezin, University of Barcelona (2011). Thesis Director: Antonio Zorzano. Honors: Cum Laude
- Unraveling the metabolic significance of the nuclear receptor co-activator RAP250. Sonia Pereira da Veiga, University of Barcelona (2011). Thesis Director Antonio Zorzano. Honors: Cum Laude.
- DOR and Tp53inp1 are dual regulators of autophagy and transcription. Ana Sancho, University of Barcelona (2011). Thesis Director: Antonio Zorzano. Honors: Cum Laude.

Research projects

- Determinantes genéticos de las alteraciones metabólicas de la obesidad y diabetes de tipo 2. Proyectos de investigación fundamental (SAF2008-03803). Spanish Ministry of Science and Innovation (MICINN). 2009-2013. Principal investigator: Antonio Zorzano
- Grup d'estudi de les bases moleculars de patologies associades a transportadors de membrana (Genexartis: patología i terapia molecular en enfermetats heterogénicas y poligénicas). Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 915) Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Antonio Zorzano
- Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Heterogenic and polygenic disease- Genexartis. Carlos III Health Institute (ISCIII). 2007-open. Principal investigator: Antonio Zorzano
- Integration of the system models of insulin signalling and of mitochondrial function and its application in the study of complex diseases (MITIN). FP7- Cooperation-Health-2007. European Commission (223450). 2008-2011. Principal investigator and consortium coordinator: Antonio Zorzano
- Rol potencial dels components de la dieta mediterrània en els tractaments de l'obesitat, la diabetis i les hiperlipidèmies. Accions de cooperació en el marc de la Comunitat de Treball dels Pirineus-CTP-DGR (2009 CTP 00003). Agency for Administration of University and Research Grants (AGAUR). 2010-2011. Principal investigator: Antonio Zorzano
- Transnational cooperation for technological innovation in the development of molecules for the treatment of diabetes and obesity. Research Project Interreg IV-SUDOE (SOE/P1/E178). SUDOE-FEDER. 2009-2011. Principal investigator and consortium coordinator: Antonio Zorzano

Collaborations

- *Expression of genes in human adipose tissue,* Joan Vendrell, Hospital Joan XXIII (Tarragona, Spain)
- *Functional analysis of adipose cell proteins,* José Manuel Fernández-Real, Hospital Trueta (Girona, Spain)
- *Generation of a screening platform,* Fernando Albericio, IRB Barcelona (Barcelona, Spain); Mabel Loza, Univesidad Santiago de Compostela (Santiago de Compostela, Spain)
- *Molecular and physiological effects of lifestyle factors on diabetes/obesity,* John Nolan, Steno Diabetes Center (Gentofte, Denmark)
- *Structural analysis of DOR protein,* Sandra Macedo Ribeiro, Institute for Molecular and Cell Biology (Porto, Portugal)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Fernando Albericio: Combinatorial Chemistry

Highlights

- The conjugation of a LPS-neutralizer to a novel trivalent PEGylated platform has produced improved LPS-neutralizing activity and a reduced toxicity profile over the parent compound. This finding thus proves the efficacy of this platform as a multivalent ligand scaffold for biological applications.
- We have performed the first total synthesis of aeruginazole A, a macrocyclic dodecapeptide that inhibits activity toward *Bacillus subtilis*, via a convergent strategy. This approach has allowed conservation of the stereochemistry of the intermediates, has been carried out.
- The derivatization of two ergopeptides showing high affinity at dopamine receptors has been optimized using a combinatorial chemistry approach in order to develop a novel biotin ergopeptide that maintains both nanomolar binding affinities and an agonistic behaviour against dopamine receptors.

Publications

- Bruno P, Peña S, Just-Baringo X, Albericio F, Alvarez M.
  Total Synthesis of Aeruginazole A
  Org Lett, **13**, 4648-4651 (2011)
- Torres A, Mas-Moruno C, Pérez-Payá E, Albericio F, Royo M.
  Trivalent PEGylated Platform for the Conjugation of Bioactive Compounds.
  Bioconjugate Chem 22, 2172-2178 (2011)
- Rodríguez H, Copro J, Suárez M, Martínez-Álvarez R, Martín N, Albericio F.
  Methodology to Prepare N-Heterocycles Related to Dihydropyridines: Microwave-Assisted Synthesis of Alkyl 4-Arylsubstituted-6-chloro-5-formyl-2-methyl-1,4-dihydropyridine-3-carboxylate and 4-Arylsubstituted-4,7-dihydrofuro[3,4-b]pyridine-2,5(1H,3H)-di
  Molecules 16, 9620-9635 (2011)
- Narayanaswamy VK, Albericio F, Coodavia YM, Kruger HG, Maguire GEM, Pillaym M, Govender T.
  Total synthesis of a Depsidomycin analogue by convergent solid phase peptide synthesis and macrolactonization Strategy for antitubercular activity
  J Pept Sci 17, 683-689 (2011)
- Prats-Alfonso E, Albericio F.
  Functionalization of Gold Surfaces: Recent Developments and Applications.
  J Mater Sci 46, 7643-7648 (2011)

Group Members

Group Leader

Fernando Albericio

Research Associates

Mercedes Álvarez
Jan Spengler

Postdoctoral Fellows

Salvatore Bongarzone *
Markus Muttenthaler

Hortensia María Rodríguez

Judit Tulla

*shared with another lab

PhD Students

Vida De La Paz Del Mar Castro

Anna-Iris Fernández-Llamazares

Peter Fransen
Xavier Just
Janire Lamariano
Adriana Lorente
Laia Miret
Marta Pelay
Tobias Maria Postma
Ramón Subirós
Rubí Zamudio

MSc Students

Iván Ramos
Clàudia Roca

Research Assistants

Gerardo Acosta
Miriam Góngora
Marta Paradís

- Subirós-Funosas R, El-Faham A, Albericio F.
  Aspartimide formation in peptide chemistry: occurrence, prevention strategies and the role of N-hydroxylamines.
  Tetrahedron 67, 8595-8606 (2011)
- Bruno P, Peña S, Just-Baringo X, Albericio F, Álvarez M.
  Highly Efficient, Multigram and Enantiopure Synthesis of 2-(2,4?-bithiazol-2-yl) pyrrolidine.
  Org Lett 13, 4648-4651 (2011)
- Just-Baringo X, Bruno P, Albericio F, Álvarez M.
  Highly Efficient, Multigram and Enantiopure Synthesis of 2-(2,4?-bithiazol-2-yl) pyrrolidine.
  Tetrahedron Lett 52, 5435-5437 (2011)
- Martins-Santos MES, Resende RR, Pinto FCH, Soares AM, Marangoni S, Oliveira E, Albericio F, Da Silva SL.
  Effect of a Pool of Peptides Isolated from Crotalus durissus terrificus (South American Rattlesnake) Venom on Glucose Levels of Mice Fed on a High-Fat Diet
  Int J Pept Res Ther 17, 225-230 (2011)
- El-Faham A, Albericio F.
  Peptide Coupling Reagents, More than a Letter Soup.
  Chem Rev 111, 6557-6602 (2011)
- Custodio L, Fernandes E, Escapa AL, Fajardo A, Aligué R, Albericio F, Neng N, Nogueira JM, Romano A.
  Antioxidant and Cytotoxic Activities of Carob Tree Fruit Pulps are Strongly Influenced by Gender and Cultivar.
  J Agr Food Chem, **59** (2011)
- Ferreira R, Artali R, Farrera-Sinfreu J, Albericio F, Royo M, Eritja E, Mazzini S.
  Acridine and quindoline oligomers linked through a 4-aminoproline backbone prefer G-quadruplex structures.
  Biochim Biophys Acta 1810, 769-776 (2011)
- Zaccaro L, Garcia-Lopez MT, Gonzalez-Muñiz R, Garcia-Martinez C, Ferrer-Montiel A, Albericio F, Royo M.
  TRPV1 modulators: Structure-activity relationship using a rational combinatorial approach
  Bioorgan Med Chem 21, 3541-3545 (2011)
- Khattab SN, Hamed EZ, Albericio F, El-Faham A.
  Synthesis and Aminolysis of 2,4-Dinitro Phenyl and 5-Nitro Pyridine N-Hydroxy Oxime Derivatives,
  B Chem Soc Jpn 84, 633-639 (2011)
- Pla D, Albericio F, Álvarez M.
  Progress on Lamellarins
  Med Chem Commun 2, 689-697 (2011)
- Jofré C, Guzmán F, Cárdenas C, Albericio F, Marshall SH.
  A natural peptide and its variants from the processing of Infectious Pancreatic Necrosis Virus (IPNV) display enhanced antimicrobial activity: A novel alternative to control bacterial diseases
  Peptides 32, 852-858 (2011)
- Rodriguez H, Coro J, Martin O, Lam A, Salfrán E, Rodríguez-Salarichs J, Suárez M, Albericio F, Martín N.
  Efficient preparation of alkyl 4-aryl substituted-2-methyl-6-thioxo-1,4,5,6-tetrahydropyridine-3-carboxylates under microwave irradiation conditions
  Arkivoc, 125-141 (2011)
- Custodio L, Fernandes E, Escapa AL, Fajardo A, Aligué R, Albericio F, Neng N, Nogueira JM, Romano A.
  Phytochemical profile, antioxidant and cytotoxic activities of carob tree (Ceratonia siliqua L.) germ flour extracts.
  Plant Food Hum Nutr 66, 78-84 (2011)
- Jastrząbek KG, Subiros R, Albericio F, Kamiński ZJ
  . 4-(4,6-[2,2,2-Trifluoroethoxy]-1,3,5-triazin-2-yl)-4-methylomorpholinium tetrafluoroborate (DFET/ NMM/BF4). Triazine based coupling reagents designed for coupling sterically hindered substrates.
  J Org Chem 76, 4506-4513 (2011)
- Gómez-Arreaza A, Acosta H, Barros-Álvarez X, Concepcion JL, Albericio F, Avilan L.
  Leishmania mexicana: LACK (Leishmania homologue of receptors for activated C-kinase) is a plasminogen binding protein.
  Exp Parasitol 127, 752-761 (2011)
- Vendrell M, Molero A, Gonzalez S, Pérez-Capote K, Lluis C, McCormick PJ, Franco R, Cortés A, Casadó V, Albericio F, Royo M.
  Biotin Ergopeptide Probes for Dopamine Receptors
  J Med Chem 54, 1080-1090 (2011)
- Gongora M, Tulla-Puche J, Paradis M, Werbitzky O, Giraud M, Albericio F.
  Optimized Fmoc Solid-Phase Synthesis of the Cysteine-Rich Peptide Linaclotide.
  Biopolymers 96, 69-80 (2011)

- Cruz LJ, Rueda F, Cordobilla B, Simon L, Hosta L, Albericio F, Domingo JC.
  Targeting nanosystems to human DCs via Fc receptor as an effective strategy to deliver antigen for immunotherapy.
  Mol Pharmacol 8, 104-116 (2011)
- Ruiz P, Savina S, Albericio F, Álvarez M.
  Structure, Synthesis, and Bioactivity of Natural Products with Hexahydropyrrolo[2,3-b] indole.
  Chem-eur J 17, 1388-1408 (2011)
- Garay H, Menéndez T, Cruz-Leal Y, Coizeau E, Noda J, Morera V, Guillén G, Albericio F, Reyes O.
  Study of various presentation forms for a peptide mimetic of Neisseria meningitidis sero-group capsular polysaccharide.
  Bioconjugate Chem 22, 33-41 (2011)
- Gerona-Navarro G, González-Muñiz R, Fernández-Carvajal A, González-Ros JM, Ferrer-Montiel A, Carreño C, Albericio F and Royo M.
  Solid-phase synthesis of a library of amphipatic hydantoins. Discovery of new hits for TRPV1 blockade
  Acs Comb Sci, **13**, 458-65 (2011)
- Martínez-Ceron MC, Marani MM, Taulés M, Etcheverrigaray M, Albericio F, Cascone O and Camperi SA.
  Affinity chromatography based on a combinatorial strategy for rerythropoietin purification
  Acs Comb Sci, **13**, 251-8 (2011)

PhD Theses

- Solid-phase chemical tools for biomedical applications on gold surfaces. Elisabet Prats, University of Barcelona (2011). Thesis director: Fernando Albericio. Honors: Excellent Cum Laude
- Combinatorial strategies for cancer drug delivery. Tommaso Cupido, University of Barcelona (2011). Thesis director: Fernando Albericio. Honors: Excellent Cum Laude
- Polímers reticulats de PEG. Alliberació de fàrmacs. Gemma Vilar, University of Barcelona (2011). Thesis director: Fernando Albericio. Honors: Excellent Cum Laude
- New coupling reagents for peptide synthesis based on ethyl 2-cyano-2-(hydroxymino) acetate (Oxyma) as additive. Ramon Subirós, University of Barcelona (2011). Thesis director: Fernando Albericio. Honors: Excellent Cum Laude
- Síntesi total de productes marins amb l'estructura triptòfan-pirroloindole. Pau Ruiz, University of Barcelona (2011). Thesis directors: Fernando Albericio and Mercedes Álvarez. Honors: Excellent Cum Laude
- Desarrollo de nanoconjugados como transportadores de fármacos anticancerígenos: dendrímeros multifuncionales basados en polietilenglicol y polimersomas del copolímero PMPC-PDPA. Lorena Simón, University of Barcelona (2011). Thesis directors: Fernando Albericio and Miriam Royo. Honors: Excellent Cum Laude
- New multicomponent reactions based into isonitrile activation. Application to biomedicine. Nicola Kielland, University of Barcelona (2011). Thesis directors: Fernando Albericio and Rodolfo Lavilla. Honors: Excellent Cum Laude

Research projects

- Laboratorio de nanobiotecnología para el desarrollo de nuevas herramientas para el diagnóstico y terapia de engermedades de interés regional con la Universidad de Santiago de Chile. Programa Cooperación Interuniversitaria e Investigación Científica (D/030482/10). Spanish Agency for International Cooperation (AECI). 2011. Principal investigator: Fernando Albericio
- Plataforma quimica basada en productos naturales: descubrimiento y administracion de fármacos. Proyectos de investigación fundamental (CTQ2009-07758). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Fernando Albericio
- Polysfera - Nanocápsulas poliméricas para liberación controlada y dirigida de fármacos antitumorales INNPACTO (IPT-090000-2010-1) Spanish Ministry of Science and Innovation (MICINN). 2010-2013. Principal investigator: Fernando Albericio
- Química combinatòria per al desenvolupament de nous compostos. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1024). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Fernando Albericio
- MEMTIDE—Membrane Enhanced Tide Synthesis - A New Paradigm Peptide/ Oligonucleotide Synthesis Technology 2009-2013 (FP7-PEOPLE-ITN-2008). Marie Curie Actions—Networks for Initial Training (ITN). Principal Investigator: Fernando Albericio

Collaborations

- *Delivery systems for si RNA,* Ramon Eritja, IRB Barcelona (Barcelona, Spain)
- *Synthesis and conformational analysis of cyclodepsipeptides from marine origin,* Ernest Giralt, IRB Barcelona (Barcelona, Spain)
- *Anti-leishmania compounds,* Luís Rivas, Centro Nacional de Biología-CSIC (Madrid, Spain)
- *Antiinflamatory compounds,* Enrique Pérez-Payá, Centro de Investigación Príncipe Felipe (Valencia, Spain)
- *Combinatorial chemistry for purification of proteins,* Osvaldo Cascone, Universidad de Buenos Aires (Buenos Aires, Argentina)
- *Commodities for peptide synthesis,* Ayman El-Faham , Alexandria University (Alexandria , Egypt)
- *Coupling reagents,* Luxembourg Ind (Tel Aviv, Israel)
- *Development of nanoparticles as vehicles for the treatment of metastatic colorectal cancer,* Ramon Mangues, Hospital Sant Pau (Barcelona, Spain)
- *Drug delivery systems,* Miriam Royo, Combinatorial Chemistry Platform, Barcelona Science Park (PCB) (Barcelona, Spain)
- *Nanoparticles for therapy,* Marcelo Kogan, Universidad de Chile (Santiago de Chile, Chile)
- *Natural cyclic peptides,* Gert Krueger, University Kwala-Zulu (Durbam, South Africa)
- *Natural Products from marine origin,* PharmaMar SA (Madrid, Spain)
- *Natural toxin peptides,* Saulo Luis da Silva, Federal University of São João Del Rei (Divianopolis, Brazil)
- *Peptide Methodology,* IRIS BIOTEC (Germany, Germany)
- *Plant natural products,* Luisa Custodio, University of Algarve (Portugal, Portugal)
- *Synthesis of natural products of marine origin,* Instituto BioMar (León, Spain)
- *Synthesis of new therapeutic agents,* Carmen Cuevas, PharmaMar SA (Madrid, Spain)
- *Synthesis of peptides,* Lonza AG (Visp, Switzerland)

Awards and honours

- Vincent du Vigneaud Award (2011) from the American Peptide Society (USA). Awardee: Fernando Albericio.
- Magistral Lecture (2011) at the University of Chile. Honoured: Fernando Albericio.

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Ramon Eritja: Nucleic Acidic Chemistry

Highlights

- Development of modified siRNA with powerful anti-inflammatory activity in a mouse model of the inflammatory bowel disease (IBD).
- Synthesis and properties of siRNA carrying bicyclohexane pseudosugars with a *North*-conformation. These modifications have a strong stabilizing effect against nuclease degradation without decreasing the inhibitory properties of siRNA.
- Quindoline and acridine oligomers produced by a novel solid-phase method have a remarkable affinity for biologically relevant quadruplex, such as telomeric sequences and oncogene promoters, thus resulting in compounds with antiproliferative activity.

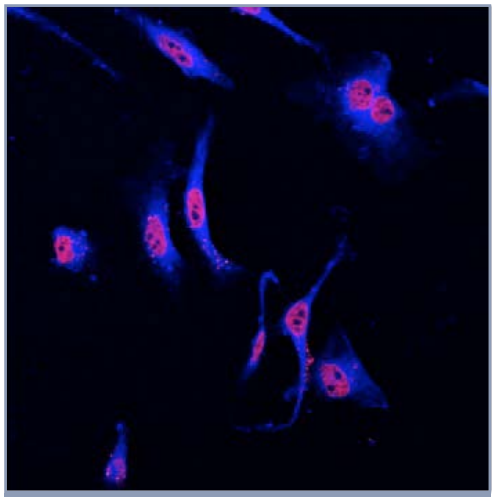


Figure1. Hela cells treated with fluorescent siRNA. The blue-violet colour is due to transfection of cells with siRNA.

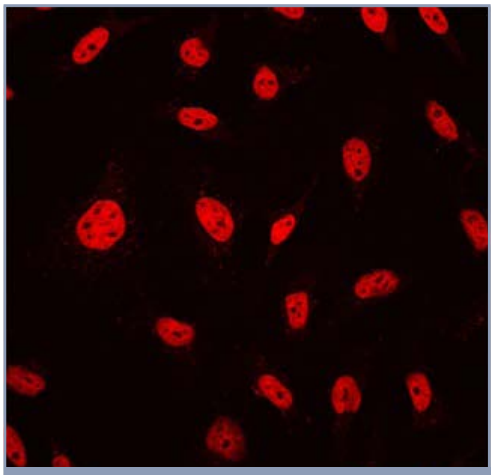


Figure2. The same cells in the presence of fluorescent siRNA without transfecting agent. The red colour of the nuclei is a stain to show the location of the nucleic.

Group Members

Group Leader

Ramon Eritja

Research Associates

Anna Maria Aviñó
Maria Carme Fàbrega

Postdoctoral Fellows

Isaac Gallego
Alejandra Victoria Garibotti
Santiago Grijalvo
Sandra Milena Ocampo
Sonia Pérez
Montserrat Terrazas

PhD Students

Adele Alagia
Ruben Ferreira
Maria Tintoré

Visiting Scientist

Nicholas Hud

Publications

- Terrazas M, Aviñó A, Siddiqui MA, Marquez VE and Eritja R.
  A Direct, Efficient Method for the Preparation of siRNAs Containing Ribo-like North Bicyclo[3.1.0]hexane Pseudosugars
  Org Lett, **13**, 2888-2891 (2011)
- Terrazas M, Ocampo SM, Perales JC, Marquez VE and Eritja R.
  Effect of North Bicyclo[3.1.0]hexane 2'-Deoxy-pseudosugars on RNA Interference: A Novel Class of siRNA Modification
  Chembiochem, **12**, 1056-65 (2011)
- Manning, B., Gállego, I., Tintoré, M., Fàbrega, C., Aviñó, A., Eritja, R.
  Preparation and AFM-characterization of self-assembled monolayers functionalized with a thrombin binding aptamer
  Int Rev Phys Chem, **2**, 74-77 (2011)
- Manning B and Eritja R.
  Use of oligonucleotides carrying photolabile groups for the control of the deposition of nanoparticles in surfaces and nanoparticle association
  Int J Mol Sci, **12**, 7238-49 (2011)
- Garibotti AV, Pérez-Rentero S and Eritja R.
  Functionalization and self-assembly of DNA bidimensional arrays
  Int J Mol Sci, **12**, 5641-51 (2011)
- Aviñó A, Grijalvo S, Pérez-Rentero S, Garibotti A, Terrazas M and Eritja R.
  Synthesis of oligonucleotide-peptide conjugates for biomedical and technological applications
  Methods Mol Biol 751, 223-38 (2011)
- Diculescu, VC, Chiorcea-Paquim, AM, Eritja, R, and Oliveira-Brett, AM
  Evaluation of the structure-activity relationship of thrombin binding aptamers by voltammetry and atomic force microscopy
  J Electroanal Chem, **656**, 159-166 (2011)
- Fernández S, Eritja R, Aviñó A, Jaumot J and Gargallo R.
  Influence of pH, temperature and the cationic porphyrin TMPyP4 on the stability of the i-motif formed by the 5'-(C(3)TA(2))(4)-3' sequence of the human telomere
  Int J Biol Macromol, **49**, 729-36 (2011)
- Ferreira R, Artali R, Farrera-Sinfreu J, Albericio F, Royo M, Eritja R and Mazzini S.
  Acridine and quindoline oligomers linked through a 4-aminoproline backbone prefer G-quadruplex structures
  Biochim Biophys Acta, **1810**, 769-776 (2011)
- Aviñó A, Ocampo SM, Lucas R, Reina JJ, Morales JC, Perales JC and Eritja R.
  Synthesis and in vitro inhibition properties of siRNA conjugates carrying glucose and galactose with different presentations
  Mol Divers, **15**, 751-757 (2011)
- Terrazas M and Eritja R.
  Synthesis and properties of small interfering RNA duplexes carrying 5-ethyluridine residues
  Mol Divers, **15**, 677-686 (2011)
- Aviñó A, Ocampo SM, Perales JC and Eritja R.
  Branched RNA: A New Architecture for RNA Interference
  J Nucleic Acids, **2011**, 586935 (2011)
- Grijalvo S, Ocampo SM, Perales JC and Eritja R.
  Synthesis of lipid-oligonucleotide conjugates for RNA interference studies
  Chem Biodivers, **8**, 287-99 (2011)
- Jaumot J, Eritja R and Gargallo R.
  Chemical equilibria studies using multivariate analysis methods
  Anal Bioanal Chem, **399**, 1983-97 (2011)
- Lucas R, Gómez-Pinto I, Aviñó A, Reina JJ, Eritja R, González C and Morales JC.
  Highly Polar Carbohydrates Stack onto DNA Duplexes via CH/? Interactions
  J Am Chem Soc, **133**, 1909-1916 (2011)

Research projects

- Diseño de inhibidores de los mecanismos de reparación del ADN como coadyuvantes en quimoterapia CTQ2010-20541. Proyectos de Investigación Fundamental. Spanish Ministry of Science and Innovation (MICINN). 2011-2013. Principal investigator: Carme Fàbrega
- Self-assembly guanosine structures for molecular electronic devices "G4NET". MP0802 (OC-2007-2-1520). COST Actions European Commission (EC). 2008-2012. Principal investigator: Ramon Eritja
- Multi-scale formation of functional nanocrystal-molecule assemblies and architectures. (FUNMOL) 213382 FP7- Cooperation-NMP-2007 European Commission (EC). 2008-2011. Principal investigator: Ramon Eritja

- Multifunctional Nanotechnology for selective detection and Treatment of cancer. (MULTIFUN) 262943-2 FP7- Cooperation-NMP European Commission (EC). 2011-2015. Principal investigator: Ramon Eritja
- Gruo de síntes i estructura de biomolècules. 2009 SGR 208 Grup de Recerca reconegut de la Generalitat de Catalunya. Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Ramon Eritja
- Synthesis of RNA interference linked to lipids. Sylentis SAU. Principal investigator: Ramon Eritja
- Nucleic Acid Chemistry Group. Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CiberBBN). Carlos III Health Institute (ISCIII). 2006-open. Principal investigator: Ramon Eritja
- Estudio estructural de dominios peptídicos del GB virus C con capacidad inhibitoria del HIV-1 y de aptameros de RNA que se unen a la proteína PrP IT2009-0067. Acciones Integradas. Spanish Ministry of Science and Innovation (MICINN). 2010-2011. Principal investigator: Ramon Eritja
- Structural Studies of biomolecules of biomedical and technological. CTQ2010-20541-C03-01. Proyectos de Investigación Fundamental. Spanish Ministry of Science and Innovation (MICINN) 2011-2013. Principal investigator: Ramon Eritja

Collaborations

- *Synthesis and characterization of DNA quadruplex structures,* Stefania Mazzini, University of Milan (Milan, Spain)
- *Synthesis and evaluation of modified siRNA,* José Carlos Perales, University of Barcelona (Barcelona, Spain)
- *Synthesis and NMR characterization of oligonucleotides,* Carlos González, Institute of Structure of Matter, CSIC (Madrid, Spain)
- *Synthesis of new RNA derivatives,* Ana Isabel Jiménez, Sylentis SAU (Madrid, Spain)
- *Synthesis of oligonucleotide-carbohydrate conjugates,* Juan Carlos Morales, Institute of Chemical Research (Seville, Spain)
- *Synthesis of oligonucleotides carrying DNA-methyltransferase inhibitors and conformationally-restricted nucleosides,* Víctor Márquez, National Institutes of Health (Frederick, United States)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Ernest Giralt: Peptides and proteins

Highlights

- Design, synthesis and characterization of a new anionic cell-penetrating peptide: SAP(E). This new compound internalizes into a range of cell lines with low toxicity. The discovery of this new class of cell penetratin protein (CPP) opens the way to the intracellular delivery of new molecular cargoes.
- Molecular recycling of Alzheimer's disease related β-amyloid fibrils have been demonstrated for the first time. The more toxic Ab 1-42 variant recycles much slower than the less toxic Ab 1-40.
- Prolyl oligopeptidase (POP) is a serine protease whose biological function has been related to cognitive processes. Using advanced NMR spectroscopy we have found that POP is highly dynamic and that inhibition of catalytic activity shifts this conformational equilibrium towards a less dynamic state.

Publications

- Malakoutikhah M, Teixidó M, Giralt E.
  Shuttle-Mediated Drug Delivery to the Brain.
  Angew Chem Int Edit **50**, 7998-8014 (2011)
- Martin I, Teixido M, Giralt E.
  Design, synthesis and characterization of a new anionic cell-penetrating peptide: SAP(E).
  Chem Biochem Eng Q **12**, 896-903 (2011)
- Sanchez L, Madurga S, Pukala T, Vilaseca M, Lopez-Iglesias C, Robinson C, Giralt E, Carulla N.
  Aβ40 and Aβ42 amyloid fibrils exhibit distinct molecular recycling properties
  J Am Chem Soc **133**, 6505-6508 (2011)
- Mendieta L, Tarrago T, Giralt E.
  Recent patents of dipeptidyl peptidase IV inhibitors
  Expert Opin Ther Pat **21**, 1693-1741 (2011)
- López A, Tarragó T, Giralt E.
  Low molecular weight inhibitors of Prolyl Oligopeptidase: a review of compounds patented from 2003 to 2010
  Expert Opin Ther Pat, 1-22 (2011)
- Martínez J, Lisa S, Sánchez R, Kowalczyk W, Zurita E, Teixidó M, Giralt E, Andreu D, Avila J, Gasset M.
  Selenomethionine incorporation into amyloid sequences regulates fibrillogenesis and toxicity.
  PLoS One **6**, e27999 (2011)

Group Members

Group Leader

Ernest Giralt

Research Associates

Natàlia Carulla
Mª Teresa Tarragó
Meritxell Teixidó

Postdoctoral Fellows

Martin Ivanov
Miguel Moreno
Laura Nevola
Soledad Royo
Montserrat Serra

PhD Students

Xavier Arroyo
Andrey Dyachenko
Josep Garcia
Júlia García
Michael Goldflam
Bernat Guixer
Abraham López
Irene Martín
Laura Mendieta
Benjamí Oller
Roger Prades
Bernat Serra
Xavier Vila
Silvia Vilaprinyó

Lab Technicians

Marta Mena
Albert Puigpinós

Research Assistant

Esther Zurita

- Kichik N, Tarragó T, Claasen B, Gairí M, Millet O, Giralt E.
  15N relaxation NMR studies of prolyl oligopeptidase, an 80 kDa enzyme, reveal a pre-existing equilibrium between different conformational states.
  Chembiochem **12**, 2737-2739 (2011)
- Cotrufo T, Pérez-Brangulí F, Muhaisen A, Ros O, Andrés R, Baeriswyl T, Fuschini G, Tarrago T, Pascual M, Ureña J, Blasi J, Giralt E, Stoeckli ET, Soriano E.
  A signaling mechanism coupling netrin-1/deleted in colorectal cancer chemoattraction to SNARE-mediated exocytosis in axonal growth cones.
  J Neurosci **31**, 14463-80 (2011)
- Seneviratne AM, Burroughs M, Giralt E, Smrcka AV.
  Direct-reversible binding of small molecules to G protein ?? subunits.
  Biochim Biophys Acta **1814**, 1210-1218 (2011)
- Vila-Farres X, Garcia de la Maria C, López-Rojas R, Pachón J, Giralt E and Vila J.
  In vitro activity of several antimicrobial peptides against colistin-susceptible and colistin-resistant Acinetobacter baumannii
  Clin Microbiol Infect **4**, 383-7 (2011)
- Gordo S, Martos V, Vilaseca M, Menéndez M, Mendoza J, Giralt E.
  On the role of flexibility in protein?ligand interactions: the example of p53 tetramerization domain.
  Chem-asian J **6**, 1463-1469 (2011)
- Marin S, Pujals S, Giralt E, Merkoci A.
  Electrochemical investigation of cellular uptake of quantum dots decorated with a proline-rich cell penetrating peptide.
  Bioconjugate Chem **22**, 180-185 (2011)
- Dessal AL, Prades R, Giralt E, Smrcka AV
  Rational design of a selective covalent modifier of G protein ?? subunits.
  Mol Pharmacol **79**, 24-33 (2011)

PhD Theses

- Inhibitor screening and NMR'based structural studies of the enzyme prolyl oligopeptidase. Nessim Kichik, University of Barcelona (2011). Thesis directors: Ernest Giralt and Teresa Tarragó. Honors: Excellent Cum Laude

Research projects

- Estudio del proceso de agregación de la proteína Beta-amiloide asociado a la enfermedad de Alzheimer. Evaluación de moléculas pequeñas de importancia farmacéutica (ABAGIN). Proyectos de investigación fundamental (SAF2009-07600). Spanish Ministry of Science and Innovation (MICINN), 2010-2012. Principal investigator: Natàlia Carulla
- Examination of αβ aggregation peptide inhibitors. TRACE (TRA2009_0234). Spanish Ministry of Science and Innovation (MICINN). 2009-2011. Principal investigator: Ernest Giralt
- Disseny, síntesi i estructura de pèptids i proteins. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1005). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Ernest Giralt
- Identificación de compuestos activos en plantas de la medicina tradicional brasileña. Proyectos Cooperación con Brasil (PIB2010BZ-00530). Spanish Ministry of Science and Innovation (MICINN). 2010-2013. Principal investigator: Ernest Giralt
- Nanotechnologies in biomedicine (Nanobiomed). Consolider Ingenio-2010 (CSD2006-12). Spanish Ministry of Science and Innovation (MICINN). 2006-2011. Principal investigator: Ernest Giralt
- Structural and dynamic characterization of ab aggregation, La Marató de TV3 Foundation, 90610. Principal investigator: Teresa Tarragó
- Structure-Toxicity Relationship of Abeta Oligomers. New Investigator Research Grant (NIRG-10-133418). Alzheimer´s Association. 2010-2011. Principal investigator: Natàlia Carulla
- Studies of neurosecretion by remote control of exocytosis and endocytosis (OpticalBullet), European Commission, ERC-2007 StG -210355 (2008-2012). Principal investigator: Ernest Giralt
- Suzuki peptides. Marie Curie Reintegration Grants. European Commission, PERG05-GA-2009-(248668). 2010-2012. Principal investigator: Soledad Royo
- Reconocimiento molecular de superficies proteicas. Proyectos de investigación fundamental (BIO2008-00799). Spanish Ministry of Science and Innovation (MICINN). 2009-2013. Principal investigator: Ernest Giralt

Collaborations

- *Amyloid recycling,* Christopher M Dobson, Cambridge University (Cambridge, United Kingdom)
- *Cell-penetrating peptides,* Shiroh Futaki, Kyoto University (Kyoto, Japan)
- *Remote manipulation of protein aggregation,* Marcelo Kogan, University of Chile (Santiago, Chile)

Awards and honours

- National Research Award (2011) from the Ministerio de Ciencia e Innovación (Spain).
  Awardee: Ernest Giralt
- Novartis Chemistry Lectureship. Novartis (2011-2012)
  Awardee: Ernest Giralt

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Antoni Riera: Asymmetric Synthesis

Group Members

Group Leader

Antoni Riera

Research Associate

Xavier Verdaguer

Postdoctoral Fellow

Agustí Lledó

PhD Students

Núria Aiguabella
Edgar Cristobal
Àlex De La Fuente
Sean Doran
Helea Khaizourane
Thierry Leon
Pablo Antonio Martín
Silvia Orgué

Lab Technician

Daniel Byrom

MSc Student

Aida Fuster

Highlights

- Design and synthesis of new somatostatin analogues with high selectivity towards SSTR1 and SSTR3 receptors.
- Enantioselective synthesis of sphingadienines and aromatic ceramide analogues.
- Improved procedure for the synthesis of P-stereogenic ligands based on the ring opening of bulky oxazaphospholidines.
- Pauson-Khand chemistry: novel reaction using propargylamine salts and a study of the photochemistry of norbornadiene-diarylacetylene adducts.
- Study of the coordination chemistry of PNSO ligands with several transition metals (Ir, Cu, Pd, and Pt)

Publications

- León T, Riera A and Verdaguer X.
  Stereoselective synthesis of P-stereogenic aminophosphines: ring opening of bulky oxazaphospholidines
  J Am Chem Soc, **133**, 5740-3 (2011)
- Ramón R, Martín-Gago P, Verdaguer X, Macias MJ, Martin-Malpartida P, Fernández-Carneado J, Gomez-Caminals M, Ponsati B, López-Ruiz P, Cortés MA, Colás B and Riera A.
  SSTR1- and SSTR3-Selective Somatostatin Analogues
  Chembiochem, **12**, 625-32 (2011)
- Achard, T, Benet-Buchholz, J, Escudero-Adan, E. C, Riera, A, Verdaguer, X
  N-Benzyl-N-phosphino-tert-butylsulfinamide and Its Coordination Modes with Ir(I), Cu(I), Pd(II), and Pt(II): P,S or P,O?
  Organometallics, **30**, 3119-3130 (2011)
- Ji, Y, Riera, A, Verdaguer, X
  Saline intermolecular Pauson-Khand reactions of propargyl amine
  Eur J Org Chem, **2011**, 1438-1442 (2011)
- Moreno M, Murruzzu C and Riera A.
  Enantioselective synthesis of sphingadienines and aromatic ceramide analogs
  Org Lett, **33**, 5184-7 (2011)
- Ji Y, Verdaguer X and Riera A.
  Solvent and substituent effects on the photochemistry of norbornadiene-diarylacetylene Pauson-Khand adducts
  Chemistry, **17**, 3942-8 (2011)

PhD Theses

- Lligands N-fosfinosulfinamida i aminodifosfina: Síntesi i aplicacions en la reacció de Pauson-Khand i la hidrogenació asimétrica. Marc Revés Vilaplana, University of Barcelona (2011). Thesis director: Xavier Verdaguer Espaulella. Honors: Summa Cum Laude
- Nuevas aproximaciones sintéticas a bases esfingoides y ácidos pipecólicos. María Moreno Díaz-Alejo, University of Barcelona (2011). Thesis director: Antoni Riera. Honors: Summa Cum Laude
- Obtención de compuestos biológicamente activos mediante reacciones intermoleculares de Pauson-Khand. Ana Vázquez Romero, University of Barcelona (2011). Thesis director: Antoni Riera. Honors: Summa Cum Laude

Patents

- *A process for the preparation of Trans-(2R)-4-Substituted-Pipecolic Acids and Esthers thereof, and intermediate compounds used therein.* Antoni Riera, Alexander Comely, Xavier Ginesta. Publication number/date: WO2011039290 (07/04/2011). Status: Pre-grant publication
- *Enantiomerically enriched aminodiphosphines as ligands for the preparation of catalysts for asymmetric synthesis.* Mónica Alonso Xalma, Xavier Verdaguer Espaulella, Marc Reves Vilaplana, Antoni Riera Escalé . Publication number/date: WO2011098160 (18/08/2011). Status: Pre-grant publication

Research projects

- Ligand Engineering for Pauson-Khand Reactions (LE-PKR) 294045 FP7- People-CIG Marie-Curie Action: "Career Integration Grants" European Commission (EC) 2010-2013. Principal investigator: Agustí Lledó
- UNITAT DE RECERCA EN SÍNTESI ASIMÈTRICA 2009 SGR 901 Grup de Recerca reconegut de la Generalitat de Catalunya Agency for Administration of University and Research Grants (AGAUR) 2009-2013. Principal investigator: Antoni Riera
- Síntesis enantioselectiva de compuestos biológicamente activos y desarrollo de nueva metodología sintética CTQ2008-00763 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2009-2011. Principal investigator: Antoni Riera

Collaborations

- *NMR studies of peptide structures,* Maria Macias, IRB Barcelona (Barcelona, Spain)
- *Synthesis of pharmaceutically active compounds,* Llorenç Rafecas, Alex Comely and Nicolas Tesson, Enantia SL (Barcelona, Spain)
- *Synthesis of Somatostatin analogues,* Berta Ponsati, Jimena Fernández-Carneado and Marc Gómez, BCN Peptides SL (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Xavier Salvatella: Laboratory of molecular biophysics

Group Members

Group Leader

Xavier Salvatella

Research Assistant

Jordi Silvestre

Postdoctoral Fellows

Carlos Walter Bertoncini

Robert Brynmor Fenwick

Marianela Masin

PhD Students

Giulio Chiesa
Eva De Mol
Bahareh Eftekharzadeh
Anna Montaner

Research Associate

Santiago Esteban

Lab Technician

Joan Miquel Valverde

Highlights

- We have identified in a model protein weak long-range correlated motions such as those responsible for allostery using NMR in combination with molecular simulations.
- In a model protein, we have discovered that disulfide bonds can decrease the entropic cost of forming well-ordered and relatively innocuous amyloid fibrils.
- We have found that disulfide bonds are likely to have evolved in secreted proteins to minimize toxic aggregation by promoting the formation of inert fibrils.

Publications

- Fenwick RB, Esteban-Martín S, Richter B, Lee D, Walter KF, Milovanovic D, Becker S, Lakomek NA, Griesinger C and Salvatella X.
  Weak long-range correlated motions in a surface patch of ubiquitin involved in molecular recognition
  J Am Chem Soc, **133**, 10336-9 (2011)
- Mossuto MF, Bolognesi B, Guixer B, Dhulesia A, Agostini F, Kumita JR, Tartaglia GG, Dumoulin M, Dobson CM and Salvatella X.
  Disulfide bonds reduce the toxicity of the amyloid fibrils formed by an extracellular protein
  Angew Chem Int Edit, **50**, 7048-51 (2011)
- Fenwick RB, Esteban-Martín S and Salvatella X.
  Understanding biomolecular motion, recognition, and allostery by use of conformational ensembles
  Eur Biophys J Biophy, **40**, 1339-55 (2011)
- Ban D, Funk M, Gulich R, Egger D, Sabo TM, Walter KF, Fenwick RB, Giller K, Pichierri F, de Groot BL, Lange OF, Grubmüller H, Salvatella X, Wolf M, Loidl A, Kree R, Becker S, Lakomek NA, Lee D, Lunkenheimer P and Griesinger C.
  Kinetics of conformational sampling in ubiquitin
  Angew Chem Int Edit, **50**, 11437-40 (2011)
- Lamberto GR, Torres-Monserrat V, Bertoncini CW, Salvatella X, Zweckstetter M, Griesinger C and Fernández CO.
  Toward the discovery of effective polycyclic inhibitors of alpha-synuclein amyloid assembly
  J Biol Chem, **286**, 32036-44 (2011)

- Buell AK, Dhulesia A, Mossuto MF, Cremades N, Kumita JR, Dumoulin M, Welland ME, Knowles TP, Salvatella X and Dobson CM.
Population of nonnative states of lysozyme variants drives amyloid fibril formation
J Am Chem Soc, **133**, 7737-43 (2011)

Research projects

- Laboratori de biofísica molecular, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1514). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Xavier Salvatella
- Structural characterization of key conformational transitions in protein deposition diseases. Proyectos de investigación fundamental (CTQ2009-08850-BQU). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Xavier Salvatella
- Identification of the aggregates of Androgen Receptor that cause Spinal Bulbar Muscular Atrophy (102030) Fundació Marató de TV3 (2011-2013) Principal Investigator and coordinator: Xavier Salvatella

Collaborations

- *Correlated motions in globular proteins,* Donghan Lee , Max Planck Institute for Biophysical Chemistry (Göttingen, Germany); Christian Griesinger , Max Planck Institute for Biophysical Chemistry (Göttingen, Germany); Modesto Orozco, IRB Barcelona (Barcelona, Spain)
- *Correlated motions in multi-domain proteins,* Victor Guallar , Barcelona Supercomputing Centre (Barcelona, Spain); Magnus Wolf-Watz , Umeå University (Umeå, Sweden)
- *Methods for the simultaneous determination of the structure and dynamics of native proteins using residual dipolar couplings,* Christian Griesinger, Max Planck Institute for Biophysical Chemistry (Göttingen, Germany)
- *Structure-activity relationships in androgen receptor aggregates involved in spinal bulbar muscular atrophy,* Eva Estébanez-Perpiñá , University of Barcelona (Barcelona, Spain); Leila Luheshi , University of Cambridge (Cambridge, United Kingdom)
- *Structure-activity relationships in protein aggregates,* Christopher Dobson, University of Cambridge (Cambridge, United Kingdom)
- *Use of protein native ensembles in protein-protein docking,* Juan Fernández-Recio, Barcelona Supercomputing Centre (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

ONCOLOGY

Eduard Batlle: Colorectal cancer

Group Members

Group Leader

Eduard Batlle

Research Associate

Elena Sancho

Postdoctoral Fellows

Alexandre Calon
Elisa Espinet
Peter Jung
Anna Merlos
Guiomar Solanas
Daniele Tauriello

PhD Students

Francisco Barriga
Elisa Montagni
Gavin Whissell

Research Assistants

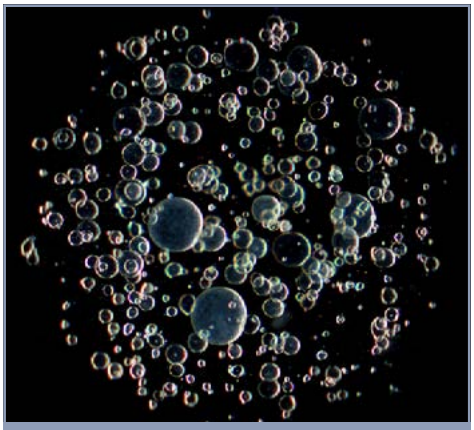
Isabella Dotti
Sergio Palomo

Lab Technicians

Javier Hernando
Marta Sevillano

Highlights

- Normal intestinal stem cells (ISCs) continuously repopulate the epithelium. We have purified and profiled ISCs, crypt proliferative progenitors and late transient amplifying cells from mouse and human intestine. These data have paved the way to unequivocally identify ISC-like tumour cells in colorectal cancer (CRC) samples.
- A frequent complication in CRC is the regeneration of the tumour upon therapy. We have shown that CRC relapse is associated with the presence of ISC-like cells in aggressive tumours.
- For the first time we have established robust *in vitro* culturing conditions for human colon stem cells. This is an important development for adult stem cell research that may allow their use for regenerative medicine.
- The formation and maintenance of complex organs requires the segregation of distinct cell populations into defined territories and the establishment of cell boundaries. EphB receptors interact with E-cadherin and with ADAM10 metalloproteinase at adhesion sites and their activation induces shedding of E-cadherin by ADAM10 at interfaces with ephrin-B1-expressing cells. This results in asymmetric localization of E-cadherin and thus in differences in cell affinity between EphB+ and ephrin-B+ cells.



3D organoids derived from human colon intestinal stem cells expanded in vitro

Publications

- Campbell K, Whissell G, Franch-Marro X, Batlle E and Casanova J
  Specific GATA factors act as conserved inducers of an endodermal-EMT
  Dev Cell, 21, 1051-61 (2011)
- Janich P, Pascual G, Merlos-Suárez A, Batlle E, Ripperger J, Albrecht U, Cheng HY, Obrietan K, Di Croce L and Benitah SA.
  The circadian molecular clock creates epidermal stem cell heterogeneity
  Nature, 480, 209-14 (2011)
- Jung P, Sato T, Merlos-Suárez A, Barriga FM, Iglesias M, Rossell D, Auer H, Gallardo M, Blasco MA, Sancho E, Clevers H and Batlle E.
  Isolation and in vitro expansion of human colonic stem cells
  Nat Med, **17**, 1225-7 (2011)
- Solanas G, Cortina C, Sevillano M and Batlle E.
  Cleavage of E-cadherin by ADAM10 mediates epithelial cell sorting downstream of EphB signalling
  Nat Cell Biol, **13**, 1100-7 (2011)
- Merlos-Suárez A, Barriga FM, Jung P, Iglesias M, Céspedes MV, Rossell D, Sevillano M, Hernando-Momblona X, da Silva-Diz V, Muñoz P, Clevers H, Sancho E, Mangues R and Batlle E.
  The intestinal stem cell signature identifies colorectal cancer stem cells and predicts disease relapse
  Cell Stem Cell, **8**, 511-24 (2011)
- Solanas G and Batlle E.
  Control of cell adhesion and compartmentalization in the intestinal epithelium
  Exp Cell Res, **317**, 2695-701 (2011)

PhD Theses

- *Molecular mechanisms involved in the initiation and progression of colorectal cancer*. Elisa Espinet Hernández, University of Barcelona (2011). Thesis director: Helena Sancho, Eduard Batlle. Honors: Summa Cum Laude

Patents

- Methods and kits for the prognosis of colorectal cancer. Batlle E; Sancho E; Rosell D; Palomo S; Espinet E; Calon A. Publication number/date: EP11382368.6 (28/11/2011). Status: Pre-grant publication

Other

- Member of the Scientific Advisory Committee for the Association for International Cancer Research (AICR)
- Member of the jury for the 2011 Banc de Sabadell Award

Research projects

- Biología del cáncer (ONCOBIO). Consolider Ingenio-2010 (CSD2007-00017). Spanish Ministry of Science and Innovation (MICINN). 2007-2012. Principal investigator: Eduard Batlle
- Dissecting the roles of the beta-catenin and Tcf genetic programmes during colorectal cancer progression, European Commission, ERC-2007STG-208488, (2008-2012). Principal investigator: Eduard Batlle
- Laboratori de cancer colorrectal i biologia del epiteli intestinal. Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 989). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Eduard Batlle
- Señalización por Wnt, receptores Eph y cáncer de colon: un análisis funcional del inicio de la tumorigénesis intestinal. Proyectos de investigación fundamental (SAF2008-01512). Spanish Ministry of Science and Innovation (MICINN). 2009-2011. Principal investigator: Eduard Batlle
- Êcole Polytechnique Fédérale de Lausanne, EPFL-DLSA, (2006-open). Principal investigator: Eduard Batlle

Collaborations

- *A role for TGB-beta in CRC progression*. Elena Sancho, IRB Barcelona (Barcelona, Spain)
- *Antibodies against Intestinal Stem Cell genes involved in CRC*. Francesc Mitjans, Leitat (Barcelona, Spain)
- *Common genes in pancreas cancer and CRC and Eph signalling in pancreas development*. Francisco X Real, Spanish National Cancer Research Center (CNIO)(Madrid, Spain)

- *Development of metastatic models of CRC.* Ramon Mangues and Maria Virtudes Céspedes, Hospital de la Santa Creu i Sant Pau (Barcelona, Spain)
- *Drosophila gut as a model for CRC development*. Andreu Casali, IRB Barcelona (Barcelona, Spain)
- *Intestinal stem cells in CRC.* Hans Clevers, Hubrecht Laboratory (Utrecht, Netherlands)
- *Mediators of EMT in Drosophila and CRC.* Jordi Casanova, IRB Barcelona (Barcelona, Spain)
- *Role of cdk6 in intestinal development*. Mariano Barbacid and Marcos Malumbres, Spanish National Cancer Research Center (CNIO) (Madrid, Spain); Esther Stoeckl, University of Zurich (Zurich, Switzerland)
- *Telomerase length in intestinal Stem Cells.* Maria A. Blasco, Spanish National Cancer Research Center (CNIO) (Madrid, Spain)
- *TGF-beta signaling in Inflammatory Bowel Disease*. Azucena Salas, Institut d'Investigacions Biomèdicas August Pi i Sunyer (IDIBAPS) (Barcelona, Spain)
- *TGF-beta target genes in CRC.* Joan Massagué, Memorial Sloan-Kettering Cancer Center (New York, United States)
- *The circadian molecular clock and stem cell niches*. Salvador Aznar-Benitah. Center for Genomic Regulation (CRG) (Barcelona, Spain)
- *Control of intestinal stem cell positioning,* Hans Clevers, Hubretch Laboratorium (Utrecht, Netherlands)
- *Stem cell gene expression signatures in the prediction of CRC outcome*. José Baselga, Vall d'Hebrón Hospital (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

ONCOLOGY

Roger Gomis: Growth control and cancer metastasis

Group Members

Group Leader

Roger Gomis

Research Associate

Mònica Morales

Postdoctoral Fellow

Jelena Urosevic

PhD Students

Sylwia Gawrzak
Milica Pavlovic

Lab Manager

Marc Guiu

Lab Technician

Esther Fernández

Highlights

- Over the last two years, we have identified a unique *in vivo* model that mimics dormant metastasis in ER(+) breast cancer (BC) human patients. By combining our experimental mouse model of dormant BC metastasis and a genome-wide short-hairpin (shRNA) library, we aim to identify dormant metastasis genes.
- We test the hypothesis that ER+ breast cancer metastasis to the bone selects mediators for homing, survival and colonization of the bone. Interestingly, this process is, in part, led by a recurrent DNA copy number alteration that has been observed specifically to occur ER+ breast cancer primary tumours.
- Colorectal tumours progress slowly to invasive carcinomas, which can then disseminate and colonize the liver and, less frequently, the lungs. The mechanisms that allow colon cancer cells to form liver metastasis are unknown. We shed light on the molecular bases of these processes.

Publications

- Morales M, Planet E, Arnal-Estape A, Pavlovic M, Tarragona M and Gomis RR.
  Tumor-stroma interactions a trademark for metastasis
  Breast, **20 Suppl 3**, S50-5 (2011)

PhD Theses

- Study of new mechanisms of breast cancer tumor progression and metastasis: Characterization of the role of C/EBPβ in TGFβ cytostatic response; definition of an estrogen receptor positive bone metastasis signature. Anna Arnal-Estapé, University of Barcelona (2010). Thesis director: Roger R. Gomis. Honors: Cum Laude
- Study of the TGFβ function in tumoral proliferation and in the metastatic processes. Maria Tarragona, University of Barcelona (2010). Thesis director: Roger R. Gomis. Honors: Cum Laude

Research projects

- Grup de recerca de metàstasi tumoral 2009 SGR 1429 Grup de Recerca reconegut de la Generalitat de Catalunya Agency for Administration of University and Research Grants (AGAUR) 2009-2013. Principal investigator: Roger Gomis
- Estudio de los mecanismos moleculares de la metástasis del cáncer de mama a pulmón: función y potencial terapéutico de genes supresores de metástasis Fundación Asociación Española contra el cáncer (AECC) 2008-2011 Roger Gomis

- Fundación BBVA. Principal investigator: Roger Gomis
- Mechanism of ER positive breast cancer metastasis SAF2010-21171 Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2011-2013. Principal investigator: Roger Gomis
- Prous Institute for Biomedical Research, S.A 2011-2012. Principal investigator: Roger Gomis

Collaborations

- *Breast Cancer Metastasis Suppressors,* Joan Massagué, Memorial Sloan-Kettering Cancer Center (New York, United States)
- *Colon Cancer Metastasis,* Eduard Batlle, IRB Barcelona (Barcelona, Spain)
- *Identification of Breast cancer metastasis mechanisms,* Cristina Nadal, Hospital Clínic (Barcelona, Spain)
- *Identification of colon cancer metastasis mechanisms,* Ramon Mangues, Hospital de Sant Pau (Barcelona, Spain)
- *Mechanisms of metastasis,* Angel Nebreda, IRB Barcelona (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

ONCOLOGY

Angel R. Nebreda: Signalling and cell cycle

Group Members

Group Leader

Angel R. Nebreda

Research Associates

Ivan Del Barco
Ana Igea

Postdoctoral Fellows

Irene Amata*
Sandra Colié
Juan Manuel Murillo*
Sebastian Martin Real
Elisa Isabel Rivas
Marianna Tedesco
*shared with another lab

PhD students

Begoña Cánovas
Jalaj Gupta
Carmen Lorena Pereira
Natalia Trempolec
Jessica Vitos

Research Assistants

Antonio Núñez
Lorena Ramírez

Lab technician

Elisabet Llonch

Highlights

- We have described new essential roles of the p38 MAPK signalling pathway during mouse development. For example, cooperation between p38α and p38β is required for embryonic heart development.
- A collection of genes whose expression is controlled by p38 MAPK signalling in Ras-transformed cells has been identified. Approximately 10% of the genes that are negatively regulated by p38 MAPK contribute to EGF receptor signalling.
- We have established mouse models to study the role of p38 MAPK signalling in tumour development *in vivo*.

Publications

- Del Barco Barrantes I, Coya JM, Maina F, Arthur JS and Nebreda AR ,
  Genetic analysis of specific and redundant roles for p38 α and p38 β MAPKs during mouse development
  Proc Natl Acad Sci U S A, **108**, 12764-9 (2011)
- Swat A, Dolado I, Igea A, Gomez-Lopez G, Pisano DG, Cuadrado A and Nebreda AR,
  Expression and functional validation of new p38 α transcriptional targets in tumorigenesis
  Biochem J, **434**, 549-58 (2011)

Research projects

- Understanding inflammation-associated tumorigenesis for the rational design of novel anti-cancer therapeutic strategies. (INFLA-CARE) 223151 FP7- Cooperation-Health 2009. European Commission (EC) 2009-2012. Principal investigator: Ángel R Nebreda
- La disfunción cerebral durante el envejecimiento, y su relevancia para la enfermedad de Alzheimer (BrainAge). CDS2010-00045 Consolider Spanish Ministry of Science and Innovation (MICINN) 2011-2015. Principal investigator: Ángel R Nebreda
- Regulación celular por la p38a. MAPK BFU2010-17850. Proyectos Investigación Fundamental Spanish Ministry of Science and Innovation (MICINN) 2011-2013. Principal investigator: Ángel R Nebreda
- Fundación BBVA 2011-2015. Principal investigator: Ángel R Nebreda

Collaborations

- *Molecular mechanisms of metastasis*. Roger Gomis, IRB Barcelona (Barcelona, Spain)
- *Stress-induced p38 MAPK signalling*. Francesc Posas, Universitat Pompeu Fabra (Barcelona, Spain)
- *Signalling by p38 MAPKs in Drosophila*. Marco Milan, IRB Barcelona (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

ONCOLOGY

Travis Stracker: Genomic instability and cancer

Group Members

Group Leader

Travis Stracker

Postdoctoral Fellows

Philip Knobel
Marko Marjanovic*
*shared with another lab

PhD Students

Suvi Marjaana Aivio
Helena González
Katrin Rein
Irena Stevanovic

Lab Manager

Lluís Palenzuela

Highlights

- Identification of checkpoint and repair pathway defects that synergize with apoptosis deficiency in tumor suppression.
- Generation of new genetic tools to analyze the regulation of DNA resection after DNA damage.
- Functional characterization of putative DNA damage response factors *in vitro* and *in vivo*.

Publications

- Stracker TH and Petrini JH.,
  The MRE11 complex: starting from the ends
  Nat Rev Mol Cell Bio, **12**, 90-103 (2011)

Research projects

- The role of the Mre11 complex in apoptosis and tumor suppression, Leukemia & Lymphoma Society. 2008-2011. Principal investigator: Travis Stracker
- The regulation of apoptosis and chromosome integrity by the cellular DNA damage response. Proyectos de investigación fundamental (SAF2009-10023). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Travis Stracker

Collaborations

- *Genetic analysis of tumor predisposition*. John H.J. Petrini, Memorial Sloan-Kettering Cancer Center (New York, USA)
- *Characterization of novel DNA repair enzymes*. Aidan Doherty, Genome Damage and Stability Centre (Sussex, United Kingdom)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CORE FACILITIES

Julien Colombelli: Advanced Digital Microscopy

Group Members

Core facility manager

Julien Colombelli

Senior Research Officer

Sébastien Tosi

Research Officers

Lídia Bardia
Anna Lladó

Highlights

- Cruise Speed: Since the opening of the facility, usage of its instruments has increased continuously (17,000 hours in 2009, 22,000 hours in 2010). In 2011, we reached cruise speed with almost 22,000 hours of booking on 12 instruments and 2 workstations.
- Intelligent High Content Screening: In collaboration with Leica Microsistemas (Spain), IRB Barcelona has developed an open software application to perform intelligent screening with ImageJ. The application automates Confocal Microscopy to the next level where ImageJ recognizes targets of interest: High Throughput becomes efficient as the system records only high resolution images of relevant samples, and it can be trained to detect live events automatically.
- Teaching: The facility now organizes yearly courses on ImageJ, Image Processing and Analysis, and programming language for Image processing, open to the IRB Barcelona community and external scientists.
- Networking: The facility is an active member of the newly created Spanish network of advanced light microscopy (REMOA, Red Española de Microscopia óptica avanzada: 51 imaging units in 17 cities), which aims to promote the transfer of knowledge and information in Microscopy to the Spanish scientific community. The facility, through IRB Barcelona, is also stakeholder in the pan-European network research infrastructure project EuroBioImaging (>200 associated partners in 26 European Member States) which seeks to deploy a distributed biological and biomedical imaging infrastructure in Europe in a coordinated and harmonized manner. The facility is a selected site of EuroBioImaging Proof-of-Concept Studies for 2012.

Services offered during 2011

- Core Instrumentation. 24/7 access to 12 light microscopy instruments and 2 image processing workstations: Spectral Confocal Microscopy, Multiphoton Imaging, Spinning Disk Confocal, Automated High Content Imaging, TIRF, Microdissection, Photoactivation, FRAP/FRET, Conventional wide-field fluorescence and Bright-field Imaging, Fluorescence Macroscopy, and combinations thereof.
- Special Instruments: Pulsed Laser Nanosurgery in living cells with confocal spinning disk, Lightsheet Fluorescence Macroscopy for tumour and whole organ imaging.
- Technical expertise throughout the whole experimental process, from design to instrument assistance and image processing/analysis. Special focus on custom image processing, analysis and modelling.

Publications

- Besser, J, Colombelli, J, Stelzer, EHK, Schwarz, U.
  Viscoelastic response of contractile filaments bundles.
  Phys. Rev. E 83: 051902 (2011).
- Roukos V, Kinkhabwala A, Colombelli J, Kotsantis P, Taraviras S, Nishitani H, Stelzer EHK, Bastiaens P, Lygerou Z.
  Dynamic recruitment of licensing factor Cdt1 to sites of DNA damage.
  J Cell Sci, 124, 422-434 (2011)
- Taengemo C, Ronchi P, Colombelli J, Haselman U, Antony C, Stelzer EHK, Pepperkok R, Reynaud EG.
  A novel laser nanosurgery approach supports de novo Golgi biogenesis in mammalian cells.
  J Cell Sci, 124, 978-987 (2011)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CORE FACILITIES

David Rossell: Biostatistics

Group Members

Core Facility Manager

David Rossell

Senior Research Officer

Camille Stephan

Research Officers

Evarist Planet
Oscar Reina

Highlights

- Development of novel methodology for quality control and analysis of high-throughput sequencing data.
- Development of Bayesian statistical theory and applications for model selection in high-throughput setups, in collaboration with the M.D. Anderson Cancer Center and U.C. Los Angeles.
- Contributions to a number of biomedical studies, including publications in cancer stem cell, metastasis and single nucleotide polymorphism research.

Services offered during 2011

- Analysis of high-throughput genomics data.
- Analysis of quantitative proteomics data.
- Statistical methodology consultation.
- Software development for customized analysis needs.
- Statistical analysis of public datasets for the use by IRB Barcelona community.

Publications

- Planet E, Stephan-Otto Attolini C, Reina O, Flores O and Rossell D.,
  htSeqTools: High-Throughput Sequencing Quality Control, Processing and Visualization in R.,
  Bioinformatics (2011)
- Jung P, Sato T, Merlos-Suárez A, Barriga FM, Iglesias M, Rossell D, Auer H, Gallardo M, Blasco MA, Sancho E, Clevers H and Batlle E.
  Isolation and in vitro expansion of human colonic stem cells
  Nat Med, **17**, 1225-7 (2011)
- Morales M, Planet E, Arnal-Estape A, Pavlovic M, Tarragona M and Gomis RR.
  Tumor-stroma interactions a trademark for metastasis
  Breast, **3**, s50-5 (2011)
- Merlos-Suárez A, Barriga FM, Jung P, Iglesias M, Céspedes MV, Rossell D, Sevillano M, Hernando-Momblona X, da Silva-Diz V, Muñoz P, Clevers H, Sancho E, Mangues R and Batlle E.
  The intestinal stem cell signature identifies colorectal cancer stem cells and predicts disease relapse
  Cell Stem Cell, **5**, 511-24 (2011)

- Casabonne D, Reina O, Benavente Y, Becker N, Maynadié M, Foretová L, Cocco P, González-Neira A, Nieters A, Boffetta P, Middeldorp JM and de Sanjose S.
  Single nucleotide polymorphisms of matrix metalloproteinase 9 (MMP9) and tumor protein 73 (TP73) interact with Epstein-Barr virus in chronic lymphocytic leukemia: results from the European case-control study EpiLymph
  Haematol-hematol J, **2**, 323-7 (2011)

Collaborations

- *Consistent model selection in the p>>n setting*. Telesca, D., University of California at Los Angeles (Los Angeles, United States); Hu, J., M.D. Anderson Cancer Center (Houston, United States); Johnson, V.E., M.D. Anderson Cancer Center (Houston, United States)
- *Non-local prior for sequential clinical trial design*. Josep Ginebra, Universitat Politècnica de Catalunya (Barcelona, Spain); Valentí Navarro, Institut Català d'Oncologia (Hospitalet de Llobregat, Spain)
- *Sequential sample size calculation for high-throughput experiments*. Peter Mueller, University of Texas at Austin (Austin, United States)
- *Validation of Alternative Splicing Predictions*. Krishna Kalari, Mayo Clinic (Rochester, United States)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CORE FACILITIES

Herbert Auer: Functional genomics

Group Members

Core Facility Manager

Herbert Auer

Senior Research Officer

Annie Rodolosse

Technical Officer

David Fernández

Highlights

- 300% increase in revenue from IRB Barcelona researchers due to increased productivity.
- 100% increase in revenue from external researchers due to increased productivity.
- New microarray platforms (GeneAtlas from Affymetrix, H2D from Roche NimbleGen) providing more information for less money.

Services offered

- DNA/RNA quantification and quality control.
- Microarray services (Gene arrays and 3' biased arrays containing one probeset per gene, on Exon arrays, tiling arrays and miRNA arrays).
- DNA polymorphism analysis for copy number variation (CNV) and single nucleotide polymorphisms (SNPs).
- Next Generation Sequencing service (ChIP-Seq, mRNA-Seq, miRNA-Seq, Genomic DNA).
- Validation of results by real-time PCR.
- Alteration of gene expression.

Publications

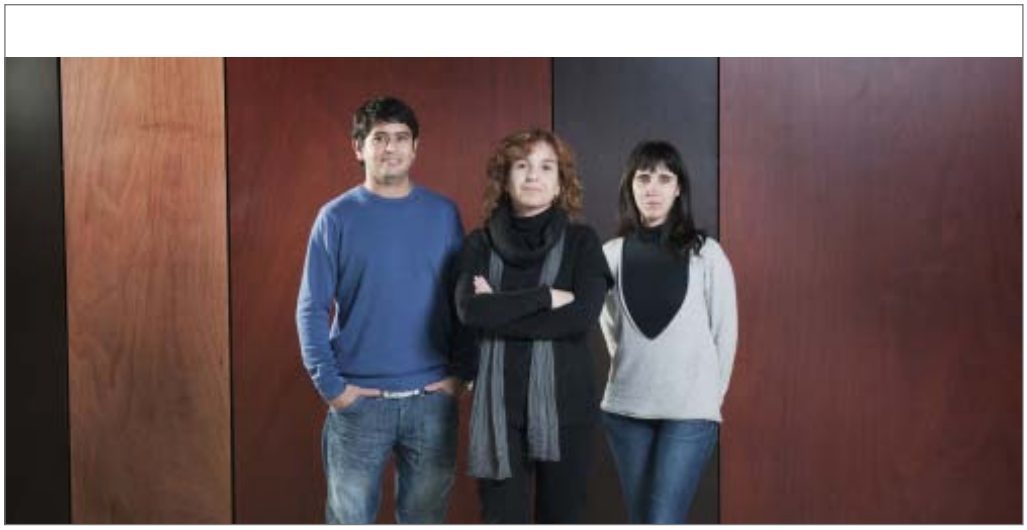
- Jung P, Sato T, Merlos-Suárez A, Barriga FM, Iglesias M, Rossell D, Auer H, Gallardo M, Blasco MA, Sancho E, Clevers H and Batlle E.
  Isolation and in vitro expansion of human colonic stem cells
  Nat Med, **17**, 1225-7 (2011)
- Vassena R, Boué S, González-Roca E, Aran B, Auer H, Veiga A and Izpisua Belmonte JC.
  Waves of early transcriptional activation and pluripotency program initiation during human preimplantation development
  Development, **17**, 3699-709 (2011)

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CORE FACILITIES

Marta Vilaseca: Mass spectrometry



Group Members

Core Facility Manager

Marta Vilaseca

Research Officers

Claudio Diema
Mª Del Mar Vilanova

Highlights

- Ion mobility-MS measurements in our Synapt HDMS mass spectrometer are used to study the topology of proteins, protein oligomers, protein-ligand complexes and nucleic acids in order to obtain structural data directed to new drug design.
- Intact protein analysis by top-down MS strategies performed in our LTQ-FT mass spectrometer is contributing to providing an integrated view of the PTM occupancy at the intact level.
- Implementation of phosphopeptide analysis is allowing quantitative proteomic studies aimed to understand the enzymatic pathways that regulate tumorigenesis. This implementation has been done in conjunction with the PCB Proteomics Platform.

Services offered during 2011

- The services offered include MS, MS/MS and IM-MS analysis of biomolecules using atmospheric pressure ionization techniques (nanoelectrospray and electrospray) coupled to LC, nanoLC or infusion inlets.
- The facility provides consultancy services and analytical method development for specific applications.
- Samples are analyzed either directly by the service or by researchers (previously trained by facility members), who can use mass spectrometers through an open-access system.

Publications

- Jacques Borg, Alex Campos, Claudio Diema, Nuria Omenaca, Eliandre DE Oliveira, Joan Guinovart and Marta Vilaseca,
  Spectral counting assessment of protein dynamic range in cerebrospinal fluid following depletion with plasma-designed immunoaffinity columns
  Clin Proteomics, **8** (2011)
- Susana Gordo, Vera Matos, Marta Vilaseca, Margarita Mendez, Javier de Mendoza and Ernest Giralt,
  On the role of flexibility in protein-ligand interactions: the example of p53 tetramerization ,domain
  Chem-asian J, **6**, 1463-1469 (2011)
- Laia Sanchez, Sergio Madurga, Tara Pukala, Marta Vilaseca, Carmen Lopez-Iglesias, Carol V. Robinson, Ernest Giralt, and Natalia Carulla,
  Aβ40 and Aβ42 Amyloid Fibrils Exhibit Distinct Molecular Recycling Properties
  J Am Chem Soc **133**, 6505-6508 (2011)

- Casado-Vela J, Cebrián A, del Pulgar MT, Sánchez-López E, Vilaseca M, Menchén L, Diema C, Sellés-Marchart S, Martínez-Esteso MJ, Yubero N, Bru-Martínez R and Lacal JC.,
  Lights and shadows of proteomic technologies for the study of protein species including isoforms, splicing variants and protein post-translational modifications
  Proteomics, **11**, 590-603 (2011)
- Flores-Morales P, Diema C, Vilaseca M, Estelrich J, Luque FJ, Gutiérrez-Oliva S, Toro-Labbé A and Silva E.,
  Enhanced reactivity of Lys182 explains the limited efficacy of biogenic amines in preventing the inactivation of glucose-6-phosphate dehydrogenase by methylglyoxal
  Bioorgan Med Chem, **19**, 1613-22 (2011)

Collaborations

- *Combined top-down and bottom-up MS analysis to identify multiple post-translational modifications in Drosophila melanogaster linker histone H1*. Ferran Azorín, IRBB / CSIC (Barcelona, Spain); Carles Bonet, IRBB/CSIC (Barcelona, Spain); Ernest Giralt, IRBB /UB (Barcelona, Spain)
- *Cerebrospinal Fluid quantitative proteomic analysis of patients with Amyotrophic Lateral Sclerosis (ALS)*. Jacques Borg, Jean Monet University (Saint-Étienne, France); David Rossell, IRBB (Barcelona, Spain); Alex Campos, PCB (Barcelona, Spain); Eliandre de Oliveira, PCB (Barcelona, Spain)
- *H/D exchange determined by ESI to study molecular Recycling in Ab(1-42) amyloid fibrils*. Ernest Giralt, IRBB (Barcelona, Spain); Carol Robinson, University of Oxford (Oxford, United Kingdom); Natàlia Carulla, IRBB (Barcelona, Spain)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CORE FACILITIES

Mouse mutant

Highlights

- Generation of several novel gene-targeted and transgenic mouse lines.
- Incorporation of 2 new replacement staff members.
- Introduction of novel technologies and strategies for generating genetically modified mice.

Services offered during 2011

- Project and construct design for gene-targeting and transgenesis.
- Gene targeting vector production by recombineering.
- Production of transgenic mice by pro-nuclear injection of single cell embryos.
- Production of gene-targeted mice by 8-cell/morulae/blastocyst injection.
- Gene targeting in mouse embryonic stem (ES) cells.
- Genotyping of gene-targeted ES clones by long-range PCR.

Collaborations

- *ROSA26 targeted zinc finger nucleases for insertional transgenesis*. Keith Joung, Massachusetts General Hospital (Boston, United States)

INSTITUTE FOR RESEARCH IN BIOMEDICINE
IRB BARCELONA

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org

Research Programmes

CORE FACILITIES

Nick Berrow: Protein expression

Group Members

Core Facility Manager

Nick Berrow

Senior Research Officer

Raquel García

Research Officer

Carles Martínez Pons

Technical Officer

Mª Carmen Romero

Highlights

- Adaptation of a number of our pPEU vectors to encode the high affinity 'One-Strep' tag. This allows simpler purifications of proteins from cells or culture media and also the purification of proteins expressed at low levels.
- Introduction and testing of the MultiBac system from EMBL which allows the cloning of multiple gene cassettes, each with their own promoters, into the baculoviral genome. This system simplifies the expression of multi-meric complexes from a single recombinant baculovirus in insect cells.
- Planned introduction of the 293-6E human cell line in serum- free suspension culture in concert with the episomally replicating pTT expression vector suite. This host-vector combination gives unprecedented levels of recombinant proteins from mammalian cells in a serum-free media that improves stability and simplifies the purification of secreted proteins. A small number of the pTT vectors have been modified to mirror the functionality of the pOPIN/pPEU vectors suites.

Services offered during 2011

- Production of expression constructs for use in vectors *E. coli*, insect or mammalian cells.
- Production of 15N-labelled proteins or peptides in *E. coli* using auto-induction methods.
- Production of secreted, glycosylated proteins in mammalian cells.
- Production of seleno-methionine-labelled proteins in *E. coli* (in prototrophic or auxotrophic strains) for crystallographic structure determination.
- Production of multiple chimeric or mutant expression constructs for comparative function/phenotype studies.
- High-throughput expression screening in *E. coli*, HEK or *Sf9* cells .
- Custom protein expression and purification of intracellular or secreted proteins.
- Production of recombinant baculo-viruses either via the pOPIN or pPEU vector suites
- Recombinant his-tagged 3C (Pre-Scission), TEV and SUMO proteases are available to IRB Barelona researchers.
- Custom cloning of genes or gene fragments into any vector.

Research Networks

- The facility is a member of the P4EU (Protein Production and Purification Partnership in Europe) network initiative. This network was founded in 2010 to establish a platform for the exchange of information, know-how and materials between core facilities in the field of protein expression and purification. There are over 40 laboratories from almost every European country represented in this network. At the autumn 2011 meeting held in The Novo Nordisk Foundation Center for Protein Research (Copenhagen) it was decided that IRB Barcelona would host the next workshop, which will take place in June 2012.

Other News

- Carles Martínez Pons, a member of Joan J. Guinovart's group, joined the facility staff at the end of 2011.

Collaborations

- *High Through Put investigation of the structures of horizontal gene transfer proteins.* Miquel Coll, Albert Canals, IRB (Barcelona, Spain)
- *Production of secreted human signalling proteins for the development of cancer cell models.* Eduard Batlle, IRB (Barcelona, Spain)

Awards and honours

- *HPTA MICINN*
  MICINN (2009-2012)
  Awardee: Raquel Garcia

Parc Científic de Barcelona. C/ Baldiri Reixac 10. 08028 Barcelona - Spain
Tel: +34 93 402 02 50 | Fax: +34 93 403 71 14
info@irbbarcelona.org