

# IRB BARCELONA 2011 ANNUAL REPORT

## Research Programmes

### MOLECULAR MEDICINE

#### Manuel Palacín: Heterogenic and Multigenic Diseases



#### Group Members

##### Group Leader

Manuel Palacín (UB)

##### Postdoctoral Fellows

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Olga Bausà\*  
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#### 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  $\Pi$ -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, Palacín 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

## 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:patologia i terapia moleculars en enfermetats heterogèniques i multigèniques. 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 tumorigenesis*, 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)*, Steve Baldwin, Astbury Centre for Structural Molecular Biology, University of Leeds (Leeds, United Kingdom), Ignacio Fita, IRB Barcelona (Barcelona, Spain); Dimitrios Fotiadis, University of Bern (Bern, Switzerland); Eric Gouaux, Vollum Institute (Portland, United States), Modesto Orozco, IRB Barcelona (Barcelona, Spain), Matthias Quick, Cornell University (New York, United States)
- *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)