

# IRB BARCELONA 2010 ANNUAL REPORT

## SCIENCE AT IRB BARCELONA

Research Programmes

## Molecular Medicine

### Manuel Palacín: Heterogenic and multigenic diseases



#### Group Members

##### Group Leader

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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.
- The residue Lys295 of the LAT transporter SteT (serine/threonine exchanger) from *Bacillus sp* limits the substrate specificity of the transporter.

#### Publications

- Bartoccioni P, Del Rio C, Ratera M, Kowalczyk L, Baldwin JM, Zorzano A, Quick M, Baldwin SA, Vázquez-Ibar JL and Palacín M. Role of transmembrane domain 8 in substrate selectivity and translocation of SteT, a member of the L-amino acid transporter (LAT) family. *J Biol Chem*, 285 (37), 28764-76 (2010)
- Chillarón J, Font-Llitjós M, Fort J, Zorzano A, Goldfarb DS, Nunes V and Palacín M. Pathophysiology and treatment of cystinuria. *Nat Rev Nephrol*, 6 (7), 424-34 (2010)
- D'Adamo P, Ulivi S, Beneduci A, Pontoni G, Capasso G, Lanzara C, Andrighetto G, Hladnik U, Nunes V, Palacín M and Gasparini P. Metabonomics and population studies: age-related amino acids excretion and inferring networks through the study of urine samples in two Italian isolated populations. *Amino Acids*, 38 (1), 65-73 (2010)
- Domínguez F, Simón C, Quiñero A, Ramírez MÁ, González-Muñoz E, Burghardt H, Cervero A, Martínez S, Pellicer A, Palacín M, Sánchez-Madrid F and Yáñez-Mó M. Human endometrial CD98 is essential for blastocyst adhesion. *PLoS One*, 5 (10), e13380 (2010)
- Mauvezin C, Orpinell M, Francis VA, Mansilla F, Duran J, Ribas V, Palacín M, Boya P, Teleman AA and Zorzano A. The nuclear cofactor DOR regulates autophagy in mammalian and *Drosophila* cells. *EMBO Rep*, 11 (1), 37-44 (2010)
- Zorzano A, Hernández-Alvarez MI, Palacín M and Mingrone G. Alterations in the mitochondrial regulatory pathways constituted by the nuclear co-factors PGC-1alpha or PGC-1beta and mitofusin 2 in skeletal muscle in type 2 diabetes. *Biochim Biophys Acta*, 1797 (6-7), 1028-33 (2010)
- Zorzano A, Liesa M, Sebastián D, Segalés J and Palacín M. Mitochondrial fusion proteins: dual regulators of morphology and metabolism. *Semin Cell Dev Biol*, 21 (6), 566-74 (2010)

#### Collaborations

- Bioinformatics on amino acid transporters. Modesto Orozco, IRB Barcelona (Barcelona, Spain)
- Crystal structure of membrane proteins. Ignasi Fita, IRB Barcelona (Barcelona, Spain)

- Physiopathology of inherited aminoacidurias cystinuria and lysinuric protein intolerance (LPI). Gianfranco Sebastio, Federico II University (Naples, Italy); Virginia Nunes, Bellvitge Institute for Biomedical Research and University of Barcelona (Barcelona, Spain); Josep Chillarón, University of Barcelona (Barcelona, Spain)
- Role of 4F2hc in tumorigenesis. Pedro Fernández, Department of Pathology, Hospital Clínic de Barcelona (Barcelona, Spain); Joaquín Abian, IDIBAPS-CSIC (Barcelona, Spain); María Antonia Lizarbe, Department of Biochemistry. Universidad Complutense de Madrid (Madrid, Spain)
- Structure-function relationship in heteromeric amino acid transporters (HATs). Steve Baldwin, Astbury Centre for Structural Molecular Biology, University of Leeds (Leeds, United Kingdom); Dimitrios Fotiadis, University of Bern (Bern, Switzerland); Ignasi Fita, IRB Barcelona (Barcelona, Spain); 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)

## Research projects

- Base molecular de la reabsorcion renal de aminoacidos: modelos de raton y estudios de relacion estructura-funcion. Proyectos de investigación fundamental (SAF2009-12606-CO2-01). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Manuel Palacín
- Construcción de una proteína politópica de membrana termoestable apta para cristalización mediante un método 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 and consortium coordinator: 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