

IRB BARCELONA 2011 ANNUAL REPORT

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Ernest Giralt: Peptides and Proteins



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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.
A β 40 and A β 42 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)

- Kichik N, Tarragó T, Claassen B, Gairí M, Millet O, Giralt E.
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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 $\alpha\beta$ 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 proteïnes. 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 $\alpha\beta$ 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



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