

IRB BARCELONA 2010 ANNUAL REPORT

SCIENCE AT IRB BARCELONA

Research Programmes

Chemistry and Molecular Pharmacology

Ernest Giralt: Peptides and proteins



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Highlights

- Mass spectrometry has been applied to study molecular recognition at protein surfaces in gas phase. Five vascular endothelial growth factor (VEGF) peptide ligands have shown reverse affinity when studied in solution (by NMR) and in gas-phase.
- Molecular dynamics is emerging as a key player in protein-protein and ligand-protein molecular recognition events. It has been shown for the first time that the $\beta\gamma$ subunit of the G-protein changes its dynamic behaviour depending on the effector molecule to which it is bound.
- The combined use of ¹⁹F-NMR and fluorinated peptide substrates provides a very efficient method for simultaneous inhibitor screening of proteases.

Publications

- Carulla N, Zhou M, Giralt E, Robinson CV and Dobson CM. Structure and intermolecular dynamics of aggregates populated during amyloid fibril formation studied by hydrogen/deuterium exchange. *Acc Chem Res*, 43 (8), 1072-9 (2010)
- Dyachenko A, Goldflam M, Vilaseca M and Giralt E. Molecular recognition at protein surface in solution and gas phase: Five VEGF peptidic ligands show inverse affinity when studied by NMR and CID-MS. *Biopolymers*, 94 (6), 689-700 (2010)
- Guerrero S, Araya E, Fiedler JL, Arias JI, Adura C, Albericio F, Giralt E, Arias JL, Fernández MS and Kogan MJ. Improving the brain delivery of gold nanoparticles by conjugation with an amphipathic peptide. *Nanomedicine-uk*, 5 (6), 897-913 (2010)
- Hernáez B, Tarragó T, Giralt E, Escribano JM and Alonso C. Small peptide inhibitors disrupt a high-affinity interaction between cytoplasmic dynein and a viral cargo protein. *J Virol*, 84 (20), 10792-801 (2010)
- Kichik N, Tarragó T and Giralt E. Simultaneous (19)F NMR screening of prolyl oligopeptidase and dipeptidyl peptidase IV inhibitors. *Chembiochem*, 11 (8), 1115-9 (2010)
- Llop-Tous I, Madurga S, Giralt E, Marzabal P, Torrent M, Ludevid MD, Relevant elements of a maize γ -zein domain involved in protein body biogenesis. *J Biol Chem*, (285), 35633-3564 (2010)
- Malakoutikhah M, Prades R, Teixidó M and Giralt E. N-methyl phenylalanine-rich peptides as highly versatile blood-brain barrier shuttles. *J Med Chem*, 53 (6), 2354-63 (2010)
- Marques MR, Stüker C, Kichik N, Tarragó T, Giralt E, Morel AF and Dalcol II. Flavonoids with prolyl oligopeptidase inhibitory activity isolated from *Scutellaria racemosa* Pers. *Fitoterapia*, 81 (6), 552-6 (2010)
- Mendieta L, Picó A, Tarragó T, Teixidó M, Castillo M, Rafecas L, Moyano A and Giralt E. Novel peptidyl aryl vinyl sulfones as highly potent and selective inhibitors of cathepsins L and B. *ChemMedChem*, 5 (9), 1556-67 (2010)
- Mzoughi O, Gaston F, Granados GC, Lakhdar-Ghazal F, Giralt E and Bahraoui E. Fusion intermediates of HIV-1 gp41 as targets for antibody production: design, synthesis, and HR1-HR2 complex purification and characterization of generated antibodies. *ChemMedChem*, 5 (11), 1907-18 (2010)
- Sabidó E, Tarragó T and Giralt E. Towards the identification of unknown neuropeptide precursor-processing enzymes: Design and synthesis of a new family of dipeptidyl phosphonate activity probes for substrate-based protease identification. *Bioorgan Med Chem*, 18 (23), 8350-5 (2010)
- Smrcka AV, Kichik N, Tarragó T, Burroughs M, Park MS, Itoga NK, Stern HA, Willardson BM, Giralt E. NMR analysis of G-protein betagamma subunit complexes reveals a dynamic Galpha-Gamma subunit interface and multiple protein recognition modes. *Proc Natl Acad Sci U S A*, 107, 639-644 (2010)

- Torres E, Gorrea E, Burusco KK, Da Silva E, Nolis P, Rúa F, Boussert S, Díez-Pérez I, Dannenberg S, Izquierdo S, Giralt E, Jaime C, Branchadell V and Ortuño RM. Folding and self-assembling with beta-oligomers based on (1R,2S)-2-aminocyclobutane-1-carboxylic acid. *Org Biomol Chem*, 8 (3), 564-75 (2010)

Collaborations

- Amyloid recycling. Christopher M Dobson, Cambridge University (Cambridge, United Kingdom)
- Cell-penetrating peptides. Shiroh Futaki, Kyoto University (Kyoto, Japan)
- Cyclodepsipeptides as potential anticancer agents. Ricardo Pérez-Tomas, Bellvitge Hospital (Barcelona, Spain)
- Remote manipulation of protein aggregation. Marcelo Kogan, University of Chile (Santiago, Chile)

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 proteïns. 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). 2006-2010. 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
- Nanobarras de oro funcionalizadas con péptidos lanzadera para el tratamiento y diagnóstico de enfermedades neurodegenerativas. Programa Cooperación Interuniversitaria e Investigación Científica (A/024489/09). Spanish Agency for International Cooperation AECL. 2010. Principal investigator: Ernest Giralt