

Fecha del CVA	14/10/2020
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## Parte A. DATOS PERSONALES

Nombre y Apellidos	M <sup>a</sup> Mar Orzáez Calatayud		
DNI/NIE/Pasaporte		Edad	
Núm. identificación del investigador	Researcher ID	B-4992-2014	
	Scopus Author ID		
	* Código ORCID	000-0003-3231-5835	

### A.1. Situación profesional actual

Organismo	Centro de Investigación Príncipe Felipe		
Dpto. / Centro	Terapias Avanzadas (Targeted Therapies on Cancer and Inflammation Lab) / Centro de Investigación Príncipe Felipe Terapias Avanzadas (Targeted Therapies on Cancer and Inflammation Lab)		
Dirección			
Teléfono		Correo electrónico	
Categoría profesional	Investigadora	Fecha inicio	2012
Palabras clave			

### A.2. Formación académica (título, institución, fecha)

Licenciatura/Grado/Doctorado	Universidad	Año
Doctor en Ciencias Biológicas	Universitat de València	2003
Licenciado en Ciencias Biológicas Especialidad Bioquímica	Universitat de València	1996

### A.3. Indicadores generales de calidad de la producción científica

#### Parte B. RESUMEN LIBRE DEL CURRÍCULUM

Ph.D. at the Biochemistry Department (University of Valencia, 2003) on the membrane protein folding field. Postdoctoral with ten years of research experience developing modulators of protein-protein interactions relevant for the control of apoptosis and inflammation disorders (2004-2012). Principal Investigator of the group of "Peptides and Proteins Chemistry" of the Advanced therapies department at the Centro de Investigación Príncipe Felipe.

Dr. Orzáez has published more than 65 articles in international journals, has an h index of 22 and a number of citations of 1299. She is also the editor of the book "Cyclin-dependent kinase inhibitors" by Springer protocols of Humana Press, with more of 14,000 downloads. Principal Investigator of the Ministry Projects SAF2017-84689-R-SAF-2014-52614R, SAF2010/15512, Researcher of the Prometeo Excellence program (PROMETEO II / 2014/061\_PROMETEO/2019/065). Member of an H2020 RISE program (H2020-MSCA-RISE-2015; 690939 EPIC) in which we participated with some of the most relevant members of the apoptosis field (i.e. Prof. Peter Vandenabeele).

Member of the ERIC EU-OPENSSCREEN and of the CIPF Drug Discovery platform that leads the "Valencian Community Strategy for Innovative and Precision Drug Development." Member of the joint units of "Disease Mechanisms and Nanomedicine" (CIPF/Polytechnic University of Valencia); and of the "Joint FIVO Cancer Unit".

Over the course of my research career:

- Contributed to the development of a family of Apaf-1 inhibitors. The results obtained from this research line have been patented and successfully transferred to the pharmacological industry (laboratories Salvat S.A). (9 research papers and two patents) . Recently derivative compounds reached clinical trials (ACTRN126180014601280p)

- Developed a new ATP non-competitive cdk2/cyclin A inhibitor (NBI1) that binds to the cyclin A surface inducing cell cycle arrest in S phase and apoptosis. The results of this investigation led to a patent and a publication in JBC journal.

- Implicated on the development of a new drug for the treatment of Myotonic Dystrophy. The results of this investigation were published a high impact factor publication (PNAS 9.7) and one patent that was transferred to the pharmaceutical company Valentia Biopharma SL.
- Addressed the challenge to establish the role of Bcl-2 transmembrane domains (Bcl-2 TMDs) in the modulation of apoptosis. The results of this project have led us to publish 6 papers, one of them in Nature structural & molecular biology (IF11.9) and other in PNAS (IF 9.4).

## Parte C. MÉRITOS MÁS RELEVANTES (ordenados por tipología)

### C.1. Publicaciones

- 1 2020. Preclinical antitumor efficacy of senescence -inducing chemotherapy combined with a nanoSenolytic JOURNAL OF CONTROLLED RELEASE. 323. ISSN 0168-3659.
- 2 2020. Real-Time In Vivo Detection of Cellular Senescence through the Controlled Release of the NIR Fluorescent Dye Nile Blue ANGEWANDTE CHEMIE-INTERNATIONAL EDITION. 59. ISSN 1433-7851.
- 3 2019. A NIR light-triggered drug delivery system using core-shell gold nanostars-mesoporous silica nanoparticles based on multiphoton absorption photo-dissociation of 2-nitrobenzyl PEG CHEMICAL COMMUNICATIONS. 55. ISSN 1359-7345.
- 4 2019. EU-OPENSREEN: A Novel Collaborative Approach to Facilitate Chemical Biology SLAS DISCOVERY. 24. ISSN 2472-5552.
- 5 2019. Janus Gold Nanostars-Mesoporous Silica Nanoparticles for NIR-Light-Triggered Drug Delivery CHEMISTRY-A EUROPEAN JOURNAL. 25. ISSN 0947-6539.
- 6 Lozono-Torres, Beatriz; Estepa-Fernandez, Alejandro; Rovira, Miguel; Orzaez, Mar; Serrano, Manuel; Martinez-Manez, Ramon; Sancenon, Felix. 2019. The chemistry of senescence NATURE REVIEWS CHEMISTRY. 3. ISSN 2397-3358.
- 7 2018. Cytochrome c speeds up caspase cascade activation by blocking 14-3-3 epsilon-dependent Apaf-1 inhibition CELL DEATH & DISEASE. 9. ISSN 2041-4889.
- 8 2018. Gold Nanostars Coated with Mesoporous Silica Are Effective and Nontoxic Photothermal Agents Capable of Gate Keeping and Laser Induced Drug Release ACS APPLIED MATERIALS & INTERFACES. 10. ISSN 1944-8244.
- 9 Llopis-Lorente, Antoni; de Luis, Beatriz; Garcia-Fernandez, Alba; Jimenez-Falcao, Sandra; Orzaez, Mar; Sancenon, Felix; Villalonga, Reynaldo; Martinez-Manez, Ramon. 2018. Hybrid Mesoporous Nanocarriers Act by Processing Logic Tasks: Toward the Design of Nanobots Capable of Reading Information from the Environment ACS APPLIED MATERIALS & INTERFACES. 10. ISSN 1944-8244.
- 10 2017. Bax transmembrane domain interacts with prosurvival Bcl-2 proteins in biological membranes PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 114. ISSN 0027-8424.
- 11 Andreu-Fernandez, Vicente; Garcia-Murria, Maria J.; Bano-Polo, Manuel; Martinez-Gil, Luis; Orzaez, Mar; Mingarro, Ismael. 2017. Differences in the Association of BH3-Only Proteins to Biological Membranes BIOPHYSICAL JOURNAL. 112. ISSN 0006-3495.
- 12 Garcia-Lainez, Guillermo; Sancho, Monica; Garcia-Bayarri, Vanessa; Orzaez, Mar. 2017. Identification and validation of uterine stimulant methylergometrine as a potential inhibitor of caspase-1 activation APOPTOSIS. 22. ISSN 1360-8185.
- 13 2017. MUC1 aptamer-capped mesoporous silica nanoparticles for controlled drug delivery and radio-imaging applications NANOMEDICINE-NANOTECHNOLOGY BIOLOGY AND MEDICINE. 13. ISSN 1549-9634.
- 14 2017. Targeting inflammasome by the inhibition of caspase-1 activity using capped mesoporous silica nanoparticles JOURNAL OF CONTROLLED RELEASE. 248. ISSN 0168-3659.
- 15 Orzaez, Mar; Sancho Medina, Monica. 2016. Cyclin-Dependent Kinase (CDK) Inhibitors Methods and Protocols Preface CYCLIN-DEPENDENT KINASE (CDK) INHIBITORS: METHODS AND PROTOCOLS. 1336. ISSN 1064-3745, ISBN 978-1-4939-2925-2.
- 16 Garrido, Maria; Corredor, Miriam; Orzaez, Mar; Alfonso, Ignacio; Messeguer, Angel. 2016. Regioselective Synthesis of a Family of beta-Lactams Bearing a Triazole Moiety as Potential Apoptosis Inhibitors CHEMISTRYOPEN. 5. ISSN 2191-1363.

- 17 Andreu-Fernandez, Vicente; Garcia-Murria, Maria J.; Bano-Polo, Manuel; Martin, Juliette; Monticelli, Luca; Orzaez, Mar; Mingarro, Ismael. 2016. The C-terminal Domains of Apoptotic BH3-only Proteins Mediate Their Insertion into Distinct Biological Membranes JOURNAL OF BIOLOGICAL CHEMISTRY. 291.
- 18 2015. 2,4-dinitrophenyl ether-containing chemodosimeters for the selective and sensitive 'in vitro' and 'in vivo' detection of hydrogen sulfide SUPRAMOLECULAR CHEMISTRY. 27. ISSN 1061-0278.
- 19 Gortat, Anna; Sancho, Monica; Mondragon, Laura; Messeguer, Angel; Perez-Paya, Enrique; Orzaez, Mar. 2015. Apaf1 inhibition promotes cell recovery from apoptosis PROTEIN & CELL. 6. ISSN 1674-800X.
- 20 2015. Biocompatibility Reduces Inflammation-Induced Apoptosis in Mesothelial Cells Exposed to Peritoneal Dialysis Fluid BLOOD PURIFICATION. 39. ISSN 0253-5068.
- 21 2015. Caspase 3 Targeted Cargo Delivery in Apoptotic Cells Using Capped Mesoporous Silica Nanoparticles CHEMISTRY-A EUROPEAN JOURNAL. 21. ISSN 0947-6539.
- 22 Corredor, Miriam; Garrido, Maria; Bujons, Jordi; Orzaez, Mar; Perez-Paya, Enrique; Alfonso, Ignacio; Messeguer, Angel. 2015. Efficient Synthesis of Conformationally Restricted Apoptosis Inhibitors Bearing a Triazole Moiety CHEMISTRY-A EUROPEAN JOURNAL. 21. ISSN 0947-6539.
- 23 Mingarro, Ismael; Andreu-Fernandez, Vicente; Bano-Polo, Manuel; Garcia-Murria, Maria J.; Orzaez, Mar. 2015. Insertion of the hydrophobic C-terminal domain of apoptotic BH3-only proteins into biological membranes PROTEIN SCIENCE. 24. ISSN 0961-8368.
- 24 2015. L-Aminoacid Oxidase from Bothrops leucurus Venom Induces Nephrotoxicity via Apoptosis and Necrosis PLOS ONE. 10. ISSN 1932-6203.
- 25 2014. Apaf-1 Inhibitors Protect from Unwanted Cell Death in In Vivo Models of Kidney Ischemia and Chemotherapy Induced Ototoxicity PLOS ONE. 9. ISSN 1932-6203.
- 26 2014. Cathepsin-B Induced Controlled Release from Peptide-Capped Mesoporous Silica Nanoparticles CHEMISTRY-A EUROPEAN JOURNAL. 20. ISSN 0947-6539.
- 27 Sancho, M.; Herrera, A. E.; Orzaez, M.; Perez-Paya, E. 2014. INACTIVATION OF APAF1 REDUCES THE FORMATION OF MUTANT HUNTINGTIN-DEPENDENT AGGREGATES AND CELL DEATH NEUROSCIENCE. 262. ISSN 0306-4522.
- 28 2014. Peptides Derived from the Transmembrane Domain of Bcl-2 Proteins as Potential Mitochondrial Priming Tools ACS CHEMICAL BIOLOGY. 9. ISSN 1554-8929.
- 29 Guevara, Tatiana; Sancho, Monica; Perez-Paya, Enrique; Orzaez, Mar. 2014. Role of CDK5/cyclin complexes in ischemia-induced death and survival of renal tubular cells CELL CYCLE. 13. ISSN 1538-4101.
- 30 Andreu-Fernandez, Vicente; Genoves, Ainhoa; Messeguer, Angel; Orzaez, Mar; Sancho, Monica; Perez-Paya, Enrique. 2013. BH3-Mimetics- and Cisplatin-Induced Cell Death Proceeds through Different Pathways Depending on the Availability of Death-Related Cellular Components PLOS ONE. 8. ISSN 1932-6203.
- 31 Orzaez, M.; Guevara, T.; Sancho, M.; Perez-Paya, E. 2012. Intrinsic caspase-8 activation mediates sensitization of erlotinib-resistant tumor cells to erlotinib/cell-cycle inhibitors combination treatment CELL DEATH & DISEASE. 3. ISSN 2041-4889.
- 32 Sancho, Monica; Herrera, Andres E.; Gortat, Anna; Carbajo, Rodrigo J.; Pineda-Lucena, Antonio; Orzaez, Mar; Perez-Paya, Enrique. 2011. Minocycline inhibits cell death and decreases mutant Huntingtin aggregation by targeting Apaf-1 HUMAN MOLECULAR GENETICS. 20. ISSN 0964-6906.

## C.2. Proyectos

- 1 PROMETEO/2019/065. 2019-2022., MEMBDEATH: Cell death and membranes: a new niche in the fight against cancer. (IP. Ismael Mingarro) Prometeo program of excellence from the Generalitat Valenciana. (Universidad de Valencia /Centro de Investigación Príncipe Felipe). 2019-2022. 197.152 €.
- 2 EU-OPENSREEN-DRIVE (IP Philip Gribbon) (Leibniz-Forschungsinstitut für Molekulare Pharmakologie). 2018-2022. 4.999.563,75 €.
- 3 SAF2017-84689-R, Understanding and drugging the Bcl-2 transmembrane interactome for tumor treatment SAF2017-84689-R (IP: Mar Orzaez) (Centro de Investigación Príncipe Felipe). 2018-31/12/2020. 181.500 €.

- 4 RED2018-102785-E, CONSOLIDACION Y POSICIONAMIENTO ESTRATEGICO DEL NODO ESPAÑOL EN LA RED ERIC EU-OPENSSCREEN (IP: Mabel Loza) (CIMUS - CENTRO DE INVESTIGACIÓN EN MEDICINA MOLECULAR Y ENFERMEDADES CRÓNICAS). 2019-2020. 60.000 €.
- 5 Exploiting Protein Complexes that Induce Cell-death. (IP: Howard Fearnhead, Subgroup IP Mar Orzaez) H2020-MSCA-RISE-2015. (Centro de Investigación Príncipe Felipe). 2016-2019. 607.500 €.
- 6 Red de Excelencia "The Spanish Channel Ion initiative" (Subgrupo IP. M<sup>a</sup> Mar Orzáez/IP. Antonio Ferrer-Montiel) Ministerio de economía y competitividad BFU2015-70067-REDC. (Centro de Investigación Príncipe Felipe). 2016-2017. 51.500 €.
- 7 The Bcl-2 transmembrane Interactome as antitumoral target (IP: Mar Orzaez) Ministerio de economía y competitividad SAF2014-52614-R. (Centro de Investigación Príncipe Felipe). 2015-2017. 100.000 €.
- 8 Modulación de interacciones proteína-proteína en apoptosis como diana terapéutica en procesos tumorales Generalitat Valenciana Proyecto Prometeo PROMETEOII/2014/061. Ismael Mingarro Muñoz. (Universitat de València). 2014-2017. 184.930 €.
- 9 Determinación de oncometabolitos mitocondriales responsables de resistencia en cáncer de endometrio (IP.: Mar Orzáez) Conselleria de Sanitat APM-09/15. (Centro de Investigación Príncipe Felipe). 2015-2015. 12.160 €.
- 10 Chemical tools that modif. Cellular fate: Molecular mechanism of action of apoptosis modulators Ministerio de economía y competitividad SAF2010/15512. Enrique Pérez Payá. (Centro de Investigación Príncipe Felipe). 2011-2014. 309.400 €.

### C.3. Contratos

- 1 Contrato de Investigación Spiral Therapeutics Spiral Therapeutics. Desde 2019.
- 2 Contrato Prestación de servicios Instituto Biomar SA Instituto Biomar, S.A.. Desde 2018.
- 3 "Asesoramiento científico Yegane SL" Yegane SL. Desde 2014.
- 4 Contrato de investigación Inhibidores de Apaf-1 Laboratorios Salvat, S.A.. 2008-01/01/2012.

### C.4. Patentes

- 1 Lozano Torres Beatriz; Blandez Barradas Juan Francisco; Martínez Mañez Ramón; Galiana Guillem Irene; García Fernández Alba; Sancenón Galarza Félix; Orzáez Calatayud Mar. ES 2733357 B2. COMPUESTO PARA LA DETECCIÓN DE CELULAS SENESCENTES Y USO DEL MISMO 30/03/2020. UPV/CIPF.
- 2 Ángel Messeguer Peypoch; Ignacio Alfonso Rodríguez; Miriam Corredor Sánchez; Enrique Pérez Payá; Mar Orzáez Calatayud. PCT/ES2013/070487. Compuestos B-lactámicos Inhibidores de Apaf-1. 08/07/2013. CSIC/CIPF.
- 3 Rubén Artero Alepuz; Amparo García López; Mar Orzaez Calatayud; Beatriz Llamusi Troisi; Enrique Pérez Payá; Manuel Pérez Alonso. P201030462. Compuestos para ser usados en el tratamiento de enfermedades basadas en la expresión de transcritos tóxicos con repeticiones CUG o CCUG España. 2010. UV/Centro de Investigación Príncipe Felipe/CSIC.
- 4 Enrique Pérez Payá; Nuria Canela; Mar Orzaez Calatayud; Antonio Pineda Lucena; Oriol Bachs. PCT/ES 2007/000366. Péptidos inhibidores de la actividad catalítica del complejo ciclina A/kinasa 2 dependiente de ciclina. España. 19/06/2007. Centro de Investigación Príncipe Felipe/CSIC/UB.
- 5 s / authors / obtainers: Enrique Pérez Payá; Gema Malet Engrá; María del Mar Orzáez Calatayud; Laura Mondragón Martínez; Ángel Messeguer Peypoch; Gloria Sanclimens; María Jesús Vicent Docon; Alejandra Moure. 0457/2007. Polymer conjugate compounds for the inhibition of apoptosis. 21/05/2007. Laboratorios Salvat, S.A. Application.
- 6 Enrique Pérez Payá; Gema Malet Engra; Mar Orzaez Calatayud. PCT/IB2006/003312. Composición farmacéutica para inhibir la apoptosis. España. 23/11/2006. Centro de Investigación Príncipe Felipe/CSIC.