José María Valpuesta
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Education

• 1985 Ph.D. in Biochemistry- School of Biology. University of the Basque Country. Bilbao. Spain
• 1981 Degree in Biology (B.Sc). University of the Basque Country.

Positions and Employment

• 1986-1989 Postdoctoral student at the Laboratory of Molecular Biology (LMB-MRC). Cambridge.
• 1990-1993 Assistant Professor in Molecular Biology at the Centro de Biología Molecular (CBM) (Consejo Superior de Investigaciones Científicas; CSIC)
• 1993-2000 Assistant Professor in Molecular Biology at the Centro Nacional de Biotecnología (CNB)
• 2000-2003 Associate Professor in Molecular Biology at the CNB
• 2003- Full Professor in Molecular Biology at the CNB
• 2006-2007 Vicedirector of the CNB
• 2007-2013 Director of the CNB
• 2013- Head of the Macromolecular Structure Department at the CNB

Other Experience and Professional Memberships

• 1997-2001 Secretary of the Spanish Microscopy Society
• 2003-2005 Vicepresident of the Spanish Microscopy Society
• 2005-2009 President of the Spanish Microscopy Society
• 2016- Member of the executive board of the European Microscopy Society (EMS)

Awards and honors

• 2002 III Bruker award of the Spanish Biophysical Society
• 2004 I FEI award of the European Microscopy Society
• 2013- Member of the "*Academia Europaea*"

Articles

A total of 168 papers, the most relevant ones:

- L.A. Campos, R. Sharma, S. Alvira, F.M. Ruiz, B. Ibarra-Molero, M. Sadqi, C. Alfonso, G. Rivas, J.M. Sanchez-Ruiz, A. Romero, **J.M. Valpuesta,** V. Muñoz (2019) "Engineering Protein Assemblies with Allosteric Control via Monomer Fold-Switching" **Nat. Communications** *10*:5703 | https://doi.org/10.1038/s41467-019-13686-1

- J. Cuéllar, W. G. Ludlam, N.C. Tensmeyer, T. Aoba, M. Dhavale, T. Bueno, C. Santiago, R.L. Plimpton, A. Makaju, S. Franklin, B.M. Willardson*, J.M. Valpuesta* (2019) "Structural and functional analysis of the role of the chaperonin CCT in mTOR complex assembly" **Nat. Communications** *10*:2865 | doi:10.1038/s41467-019-10781-1

- P. Esteve, J. Rueda-Carrasco, M. Inés Mateo, M.J. Martin-Bermejo, J. Draffin, G.

Pereyra, A. Sandonís, I. Crespo, I. Moreno, E. Aso, P. Garcia-Esparcia, E. Gomez-Tortosa, A. Rabano, J. Fortea, D. Alcolea, A. Lleo, M.T. Heneka, **JM. Valpuesta**, JA. Esteban, I. Ferrer, M. Dominguez, P. Bovolenta (2019) "Elevated levels of Secreted-Frizzled-Related-Protein 1 contribute to Alzheimer's disease pathogenesis" **Nat. Neuroscience**. doi: 10.1038/s41593-019-0432-1.

- R. Sousa, H-S Liao, J. Cuéllar, **JM Valpuesta**, AJ Jin, EM Lafer (2016) "Clathrin Coat Disassembly Illuminates the Mechanisms of Hsp70 Force Generation" **Nat. Struct. Mol. Biol.** *23*, 821-829. doi: 10.1038/nsmb.3272.

- M. Ukleja, J. Cuellar, A. Siwaszek, J.M. Kasprzak, M. Czarnocki-Cieciura, J. Bujnicki, A. Dziembowski, **J.M. Valpuesta** (2016) **"**The architecture of the CCR4-NOT complex from *Schizosaccharomyces pombe* provides a mechanistic insight into this multifunctional macromolecular assembly" **Nat. Communications** *7*:10433 | DOI: 10.1038/ncomms10433

- W.S. Chen, S. Drakulic, E. Deas, My.M. Ouberai, F.A. Aprile, R. Arranz, S. Ness, C. Roodvelt, T. Guilliams, E. De Genst, M.E. Welland, D. Klenerman, N.W. Wood, C. Alfonso Botello, G. Rivas, A.Y. Abramov, **J.M. Valpuesta**, C.M. Dobson, N. Cremades (2015) "Structural characterization of toxic oligomers that are kinetically trapped during α-synuclein fibril formation" **PNAS USA** *112*, E1994-2003. **(<u>selected by the "Faculty of 1000"</u>).**

- RL. Plimpton, J. Cuéllar, CWJ. Lai, T. Aoba, A. Makaju, S. Franklin, AD. Mathis, JT. Prince, JL. Carrascosa, **J.M. Valpuesta***, BM. Willardson*. (2015) "Structures of the Gβ-CCT and PhLP1-Gβ-CCT Complexes Reveal a Molecular Mechanism of G protein b Subunit Folding and Gβ□ Dimer Assembly" **PNAS USA** *112*, 2413-2418.

- S. Alvira, J. Cuéllar, A. Röhl, S. Yamamoto, H. Ito, C. Alfonso, G. Rivas, J. Buchner, **J.M. Valpuesta** (2014) "Structural characterization of the substrate transfer mechanism in Hsp70/Hsp90 folding machinery mediated by Hop" **Nat. Communications**. *5*:5484. doi: 10.1038/ncomms6484.

- S. Drakulic, L. Wang, J. Cuéllar, D. Guo, G. Velasquez, Jaime Martín-Benito, R. Sousa, **J.M. Valpuesta** (2014) "Yeast Mitochondrial RNAP Conformational Changes are Regulated by Interactions with the Mitochondrial Transcription Factor" **Nucleic Acids Research** *42*, 11246-60.

- OR Lorenz, L Freiburger, DA Rutz, M Krause, BK Zierer, S Alvira, J. Cuéllar, **JM Valpuesta**, T. Madl, M. Sattler, J. Buchner (2014). "Modulation of the Hsp90 chaperone cycle by a stringent client protein" **Molecular Cell** *3153*, 941-53.

- A. García-Trinidad, P. Muller, J. Cuellar, M. Klejnot, **J.M. Valpuesta**, K.H. Vousden (2013) "Interaction of p53 with the CCT complex promotes protein folding and wild type p53 activity" **Mol Cell.** *50*, 805-817, doi: 10.1016/j.molcel.2013.05.002

- R. Arranz, R. Coloma, J. Chichón, J.J. Conesa, J. L. Carrascosa, **J. M. Valpuesta**, J. Ortín and J. Martín-Benito (2012) "The structure of native influenza virion ribonucleoproteins" **Science** *338*,1634-1637. (**<u>selected by the "Faculty of 1000"</u>**).

- A. Peña, K. Gewartowski, S. Mroczek, J. Cuéllar, A. Szykowska, A. Prokop, M. Czarnocki-Cieciura, J. Piwowarski, C. Tous, A. Aguilera, J. L. Carrascosa, **J. M. Valpuesta***, A. Dziembowski* (2012) "Structural and biochemical characterisation of the THO complex reveals its architecture and mechanism of nucleic acids recognition" *EMBO Journal* **31**, 1605-1616.

- I. G. Muñoz, H. Yébenes, M. Zhou, P. Mesa, M. Serna, A.Y. Park, E. Bragado-Nilsson,

A. Beloso, G. de Cárcer, M. Malumbres, C. V. Robinson, **J. M. Valpuesta***, G. Montoya* (2011) "Crystal structure of the open conformation of the mammalian chaperonin CCT in complex with tubulin." **Nature Structural Molecular Biology** *18*, 14-19, doi: 10.1038/nsmb.1971 **(selected by the "Faculty of 1000").**

- M. Alvarado-Kristensson, M. J. Rodríguez, V. Silió, **J. M. Valpuesta**, A. C. Carrera. "SADB phosphorylation of γ-tubulin regulates centrosome duplication. (2009)" **Nat. Cell. Biol.** *11*, 1081-92. doi: 10.1038/ncb1921 **(selected by the "Faculty of 1000").**

- J. Cuéllar, J. Martín-Benito, S. H.W. Scheres, R. Sousa, F. Moro, E. López-Viñas, P. Gómez-Puertas, A. Muga, J. L. Carrascosa, **J. M. Valpuesta** (2008) "The structure of a CCT:Hsc70NBD complex suggests a mechanism for Hsp70 delivery of substrates to the chaperonin" **Nat. Struct. Mol. Biol.** *15*, 858-864. doi: 10.1038/nsmb.1464 **(selected by the "Faculty of 1000").**

- Schuermann JP, Jiang J, Cuellar J, Llorca O, Wang L, Gimenez LE, Jin S, Taylor AB, Demeler B, Morano KA, Hart PJ, **Valpuesta JM**, Lafer EM, Sousa R. (2008) "Structure of the Hsp110:Hsc70 nucleotide exchange machine" **Molecular Cell** *31*, 232-243. doi: 10.1016/j.molcel.2008.05.006 **(selected by the "Faculty of 1000").**

- J. Martín-Benito, S. Bertrand, T. Hu, P. J. Ludtke, J. N. McLaughlin, B. M. Willardson, J. L. Carrascosa, **J. M. Valpuesta** (2004) "Structure of the complex between the cytosolic chaperonin CCT and phosducin-like protein" **PNAS USA** *101*, 17410-17415. doi: 10.1073/pnas.0405070101

- J. Martín-Benito, J. Boskovic, P. Gómez-Puertas, J. L. Carrascosa, C. Simons, S. A. Lewis, F. Bartolini, N. J. Cowan, **J. M. Valpuesta** (2002)" Structure of eukaryotic prefoldin and of its complexes with unfolded actin and the cytosolic chaperonin CCT". **EMBO J.** *21*, 6377-6386. doi: 10.1093/emboj/cdf640

- O. Llorca, J. Martín-Benito, J. Grantham, M. Ritco-Vonsovici, K. R. Willison, J. L. Carrascosa, **J. M. Valpuesta.** (2001) "The "sequential allosteric ring" mechanism in the eukaryotic chaperonin-assisted folding of actin and tubulin" **EMBO J.** *20*, 4065-4075. doi: 10.1093/emboj/20.15.4065 **(cover of the issue).**

- O. Llorca, J. Martín-Benito, M. Ritco-Vonsovici, J. Grantham, K. R. Willison, J. L. Carrascosa, **J. M. Valpuesta.** (2000) "Eukaryotic chaperonin CCT stabilizes actin and tubulin folding intermediates in open quasi-native conformations" **EMBO J.** *19*, 5971-5979, doi: 10.1093/emboj/19.22.5971 **(cover of the issue).**

- O. Llorca, E. McCormack, G. Hynes, J. Grantham, J. Cordell, J. L. Carrascosa, K. R. Willison, J. J. Fernández, **J. M. Valpuesta.** (1999) "Eukaryotic type II chaperonin CCT interacts with actin through specific subunits" **Nature** *402*, 693-696, doi: 10.1038/45294

- O. Llorca, M. G. Smyth, J. L. Carrascosa, K. R. Willison, M. Radermacher, S. Steinbacher, **J. M. Valpuesta.** (1999) "3D reconstruction of the ATP-bound form of CCT reveals the asymmetric folding conformation of a type II chaperonin" **Nature Structural Biology** *6*, 639-642, doi: 10.1038/10689

Books

- "Los peces del fin del mundo" (The fishes at the end of the world). Editorial Ópera Prima. ISBN 978-84-95461-78-0 (2015)

- "En busca del secreto de la Vida. Una breve historia de la Biología Molecular" (In search of the secret of life: a brief history of molecular biology). Editorial Hélice - C.S.I.C. ISBN 978-84-00-08704-3 (2008).

Research projects and grants (active ones)

- 2019-2022. Grant of the Madrid Regional Government P2018/NMT-4389. "NANOBIOCARGO. Nanocontenedores y nanovehículos dirigidos al transporte y liberación de agentes bioactivos". 886.650 €. Grant coordinator.

2017-2019. Grant of the Spanish Ministry of Competitivity BFU2016-75984. "Análisis estructural de chaperonas moleculares involucradas en el plegamiento y degradación de proteínas". 363000 €

- 2016-2020. Grant of the NIH (2R01EY012287-14A1) "Mechanism of assembly of photoreceptor G protein complexes". 218000 $.

PhD Theses

Supervisor of 18 PhD theses.

Teaching activities

- Honorary Lecturer at the department of Biochemistry and Molecular Biology. Autonomous University of Madrid (1995-). Organiser and lecturer in masters such as "Biophysics", "Biomolecules and Cell Dynamics", "History of molecular biology", "Structural biology"
- Occasional lecturer in different foreign universities: Crete University (Greece), Porto University (Portugal), Universidade Nova de Lisboa (Portugal), Universidad de Chile (Chile), Católica Pontificia Universidad de Chile (Chile), Medellin University (Lecturer), Tecnológico de Monterrey (Mexico).
- Occasional lecturer in different national universities: Complutense University (Madrid), Basque Country University (Bilbao), International University of Andalucía (Seville), Seville University (Seville), Cantabria University (Santander), Zaragoza University (Zaragoza)

Lectures

More than 110 lectures worldwide (25 countries).

<u>Management Activities (since 2009)</u>

- Head editor of the Structural Biology section of the *Enciclopedia of Life Sciences* (2009-2019)
- Member of the Editorial Board of *Biological Chemistry* (2015-) and *European Journal of Biophysics* (2016-)
- Grant evaluator for the National Science Foundation (USA), Wellcome Trust Foundation (UK), Human Frontiers Science Foundation, French National Research Agency, Israel Science Foundation, Biotechnology and Biological Sciences Research Council (UK), Cancer Research UK, Russian Science Foundation, Foundation for Polish Science, National Science Center Poland, Agence Nationale de la Recherche (France), Infrastructures en Biologie Santé et Agronomie (France), FONDECYT (Argentina).
- Member of the evaluation committee for the synchrotron ALBA (2016-2019)
- Member of the evaluation committee for the Institut Laue-Langevin (ILL) (2013-2016)
- Member of the evaluation committee of the Biophysics Unit (UB; CSIC/UPV; Bilbao)

and Instituto de biocomputación y física de sistemas complejos (BIFI; Zaragoza).
- Referee for journals such as Cell, Molecular Cell, Nature Structural and Molecular Biology, EMBO Journal, EMBO reports, PNAS USA, Journal of Molecular Biology, FEBS letters, Protein Science, Biophysical Journal, Molecular Microbiology, Biochimica et Biophisica Acta, Journal Biological Procedures Online, Journal of Cell Science, Journal of Structural Biology.
- Member of the "*Faculty of 1000*" (2001-)

Organisation activities (last 6 years)
- Member of the organizing committee of the 12th EBSA and 10th ICBP-IUPAP Congress, Madrid, Spain, 20-24 july 2019
- Organizer of the symposium del "25 years of cryoelectron microscopy in Spain". School of Sciences. Universidad Autónoma de Madrid. 12-13 June 2019.
- Organiser and chairman of the symposium "Molecular machines in action". 42nd Congress of the FEBS. Jerusalén, 10-14 September 2017.
- Organiser of the symposium "NanoBiosoma: design, development and production of nanocontainers and nanovehicles". Centro Nacional de Biotecnología. 10 July 2017.
- Member of the international scientific committee of "Microscopy Conference 2013" (reunión de 11 sociedades de Microscopía electrónica; Switzerland, Austria, Germany, and Croatia, Czech Republic, Slovakia, Hungaria, Italy, Serbia, Slovenia and Turkey). Regensburg, Germany. 25–30 August, 2013."

José María Valpuesta

Achievements in microscopy the scientific field of interest and potential of contributing to the aims of the EMS.

I did my PhD in biochemistry at the University of the Basque Country (Bilbao; Spain) where I got in contact with transmission electron microscopy, learning at that time some of standard techniques such as negative staining and freeze-fracture. This convinced me of the importance of electron microscopy in molecular biology, and successfully applied to do a postdoc at the Laboratory of Molecular Biology (LMB; Cambridge; UK) under the supervision of Richard Henderson (Nobel Prize in Chemistry 2017), one of the founders and most important figures of the field of cryoelectron microscopy (cryoEM). During this stay I learned this new technique and the necessary image processing tools for 3D reconstructing biological macromolecules, and I published a paper describing one of the first structures reconstructed with these techniques (J.M. Valpuesta, R. Henderson y T.G. Frey (1990) "A cryo-electron microscopic analysis of crystalline cytochrome oxidase" *Journal of Molecular Biology* **214**, 237-251)

After this postdoctoral stay I returned to Spain in 1990, where I introduced cryoEM at the then newly founded Centro Nacional de Biotecnología (CNB), of which I have been director (2007-2013) and I'm currently head of the Macromolecular Structure department (2013-). Since then, I have contributed to forming a large community, at the CNB and in other parts of Spain, which uses this and other electron microscopy techniques, complemented with image processing tools, to structurally characterise a large variety of biological specimens. In my case, I have worked with many different macromolecular complexes but in particular with the large family of molecular chaperones. Working with these and other biological problems, I have published more than 160 papers, some in journals such as Nature, Science, Mol Cell, Nat Cell Biol, Nat Struct Mol Biol, J Exp Med, Proc Natl Acad Sci USA, Nat. Commun., Nat. Neuroscience, EMBO J … Out of these papers, more than 110 are related to electron microscopy, in particular cryoEM, not only using single-particle techniques but also cryoelectron tomography. I have also worked with other microscopy techniques such as atomic force microscopy and scanning tunnelling and I have pioneered in Spain the use of single-molecule techniques such as optical tweezers (the first optical tweezers in Spain were established in my lab at the CNB). I have also worked with light microscopy techniques and recently I have become interested in the use of correlative techniques involving optical microscopy, scanning electron microscopy and transmission electron microscopy (for cryoelectron tomography; cryoET) or X-ray

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microscopy (for cryo X-ray tomography; cryoXT), in the latter case mostly through the use of the X-ray microscopy beamline at the Spanish synchrotron ALBA (Barcelona).

My experience and efforts in using the above mentioned techniques has led, with the help of other CNB scientists, to the creation of the CNB cryoEM facility, which is currently equipped with two state-of-the-art cryoelectron microscopes (300 kV and 200 kV) and the necessary equipment for cryocorrelative microscopy (a cryoconfocal microscope and Focused Ion Beam with scanning electron microscope; FIB-SEM). The facility forms part of different networks of European infrastructure.

Because of my experience in electron microscopy, I have organised or formed part of many different congresses, workshops, masters, lectures…, not only in Spain but also in more than 20 countries in the world.

The recognition of my work by the Spanish electron microscopy community led to my election as Secretary of the Spanish Microscopy Society (Sociedad de Microscopía de España; SME) (1997-2001), Vicepresident (2003-2005) and President (2005-2009). During my presidency I was responsible of the establishment of regular Joint Congresses between the Portuguese and Spanish Microscopy Societies that are still being held. I have a long relationship with the European Microscopy Society (EMS), and in 2004 I was awarded the I FEI Prize of the EMS. I am currently a member of the executive board of the EMS and my largest interests reside in contributing to the coordination of efforts to make the use of the microscopy infrastructure more accessible to the European scientific community, and in pushing among the EMS members the use of other microscopy techniques such as single-molecule techniques.

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