

Curriculum vitae

Surname: **RIZZUTO**

First name: **ROSARIO**

Affiliation and official address: Dept. Biomedical Sciences, University of Padova, Via Ugo Bassi 58/B, 35121 Padova, Italy

Date and place of birth: Rome (Italy), April 15th, 1962 *Nationality:* Italian

Education and career

Education and training

1986: Medical degree (University of Padova, Italy) summa cum laude

1986: National Board (“Abilitazione alla professione di medico-chirurgo”)

1987-88: 2-year research stage at the H. Merritt Center for the Study of Neuromuscular disorders (laboratory of Prof. Eric A. Schon), Columbia University, New York, USA

1991: Ph.D. in Molecular and Cellular Biology and Pathology (University of Padova, Italy)

Career/Employment

1991-1992: Research Associate (University of Padova)

1992-1998: Assistant Professor of General Pathology, School of Medicine, University of Padova

1998-2002: Associate Professor of General Pathology, School of Pharmacy, University of Ferrara

2002-2008: Professor of General Pathology, School of Pharmacy, University of Ferrara

2008-date: Professor of General Pathology, School of Medicine, University of Padova

Academic and administrative duties

2002-2004: Member of the Research Council of the University of Ferrara

2004-2008: Member of the Senate of the University of Ferrara

2005-2008: Coordinator of the Genetics and Biotechnology network of the Emilia-Romagna region (ER-GenTech)

2006-2008 Dean of the Pharmacy School of the University of Ferrara

2009-2011 Director of the Department of Experimental Biomedical Sciences of the University of Padova

2012-date: Director of the Department of Biomedical Sciences of the University of Padova

2012-date: Member of the Senate of the University of Padova

Research activity

Research interests and career highlights

By developing an innovative methodology, organelle targeting of recombinant luminescent (aequorin, luciferase) and fluorescent (GFP) proteins, that allowed novel insight in the fields of calcium signalling, cellular metabolism and organelle morphology (Rizzuto et al., *Nature* 358, 325-328, 1992; *Curr. Biol.* 5, 635-642, 1995; Jouaville et al., *Proc. Natl. Acad. Sci. USA* 96, 13807-13812, 1999). These new concepts include the participation of mitochondria in cellular Ca²⁺ homeostasis and their role in translating calcium signals in effects as diverse as stimulation of metabolism and induction of cell death (Rizzuto et al. *Science* 262, 744-747, 1993; Brini et al., *Nat. Med.* 5, 951-954, 1999; Pinton et al. *J. Cell Biol.* 148, 857-862, 2000;

EMBO J. 20, 2690-2701, 2001), the occurrence of tight signalling interactions between the ER and mitochondria (Rizzuto et al. *Science* 280, 1763-1766, 1998), the identification of the Golgi apparatus as an agonist-sensitive Ca²⁺ store (Pinton et al., *EMBO J.* 18, 5298-5308, 1998), the major Ca²⁺ rises occurring under the plasma membrane upon cell stimulation (Marsault et al. *EMBO J.* 16, 1575-1581, 1997), to cite a few. In 2011, Prof. Rizzuto has identified the mitochondrial calcium uniporter (MCU), the only fundamental component of the cellular calcium signalling machinery yet to be discovered (De Stefani et al., *Nature* 476, 338-340, 2011). This result has opened the molecular era of mitochondrial Ca²⁺ homeostasis, that combines molecular insight into the structure/function relationship of MCU and its regulators (Raffaello et al., *EMBO J.* 32, 2362-2376; Patron et al. *Mol. Cell* 53, 726-37) and the possibility of manipulating mitochondrial Ca²⁺ handling in cultured cells and animal models, to clarify its role in the physiological regulation of tissues and in the pathogenesis of the most prevalent human diseases (neurodegenerative disorders, ischemic heart disease, cancer).

Publications

Prof. Rizzuto published 228 papers on peer-reviewed journals listed on Pubmed (**ISI Web of Science: total citations >20.000, h-index 74**), 14 book chapters and >200 meeting abstracts

Granted Patents:

“Method for the detection of intracellular parameters with luminescent protein probes for the screening of molecules capable of altering said parameters” (International publication number WO 2005/093429)

“Chimeric proteins for the measurement of ATP concentrations in the pericellular space and relative screening method” (International publication number WO 2006/126231).

Honours, Awards, Editorial Activity

Prof. Rizzuto is member of the Academia Europaea and of the European Molecular Biology Organization (EMBO). He was awarded scientific prizes: the Chiara D’Onofrio Prize, the Biotec award, the Theodore Bucher Medal. Prof. Rizzuto routinely acts as reviewer for international scientific journals (*Nature*, *Science*, *J. Cell Biol.*, *EMBO J.*, *J. Biol. Chem.*, *Trends Cell Biol.*, etc.) and granting agencies (European Union, Wellcome Trust, BBSRC, NIH, etc.).

Meeting participation and organization

Prof. Rizzuto gave >200 lectures at national and international meetings (e.g. Gordon Conferences, FASEB Summer Conferences, Keystone Symposia, FEBS, EBEC, ECDO), including >20 plenary lectures. He organized the 12th International Symposium on Calcium Binding Proteins and Calcium Function in Health and Disease (Cavalese February 2002), the EMBO Workshop on “Calcium signaling and diseases” (Capri, September 2004) (organizers: E. Carafoli, R. Rizzuto) and the Gordon Conference on Calcium Signalling (Il Ciocco, June 2013)

Awards and Academic Memberships

Prof. Rizzuto is member of the Academia Europaea and of the European Molecular Biology Organization (EMBO). He was awarded scientific prizes: the Chiara D’Onofrio Prize, the Biotec award, the Theodore Bucher Medal.

Funding ID

The research in Prof. Rizzuto’s lab is funded by grants from the European Research Council (Ideas Advanced grant), the NIA (Program Project), The Italian Ministries of Education (FIRB) and Health (Ricerca Finalizzata), the Italian Association for Cancer Research (AIRC) and Telethon-Italy, and the Cariparo and Cariplo bank foundations.

Publication list

1. Alberio T, Mammucari C, D'Agostino G, Rizzuto R, Fasano M. Altered dopamine homeostasis differentially affects mitochondrial voltage-dependent anion channels turnover. *Biochim Biophys Acta*. 2014
2. O-Uchi J, Jhun BS, Xu S, Hurst S, Raffaello A, Liu X, Yi B, Zhang H, Gross P, Mishra J, Ainsbinder A, Kettlewell S, Smith GL, Dirksen RT, Wang W, Rizzuto R, Sheu SS. Adrenergic signaling regulates mitochondrial Ca^{2+} uptake through pyk2-dependent tyrosine phosphorylation of the mitochondrial Ca^{2+} uniporter. *Antioxid Redox Signal*. 2014
3. De Stefani D, Rizzuto R. Molecular control of mitochondrial calcium uptake. *Biochem Biophys Res Commun*. 2014
4. de Bernard M, Rizzuto R. Toll-like receptors hit calcium. *EMBO Rep*. 2014
5. Patron M, Checchetto V, Raffaello A, Teardo E, Vecellio Reane D, Mantoan M, Granatiero V, Szabò I, De Stefani D, Rizzuto R. MICU1 and MICU2 finely tune the mitochondrial Ca^{2+} uniporter by exerting opposite effects on MCU activity. *Mol Cell*. 2014
6. Rossato M, Granzotto M, Macchi V, Porzionato A, Petrelli L, Calcagno A, Vencato J, De Stefani D, Silvestrin V, Rizzuto R, Bassetto F, De Caro R, Vettor R. Human white adipocytes express the cold receptor TRPM8 which activation induces UCP1 expression, mitochondrial activation and heat production. *Mol Cell Endocrinol*. 2014
7. Dyar KA, Ciciliot S, Wright LE, Biensø RS, Tagliazucchi GM, Patel VR, Forcato M, Paz MI, Gudiksen A, Solagna F, Albiero M, Moretti I, Eckel-Mahan KL, Baldi P, Sassone-Corsi P, Rizzuto R, Bicciato S, Pilegaard H, Blaauw B, Schiaffino S. Muscle insulin sensitivity and glucose metabolism are controlled by the intrinsic muscle clock. *Mol Metab*. 2014
8. Logan CV, Szabadkai G, Sharpe JA, Parry DA, Torelli S, Childs AM, Kriek M, Phadke R, Johnson CA, Roberts NY, Bonthron DT, Pysden KA, Whyte T, Munteanu I, Foley AR, Wheway G, Szymanska K, Natarajan S, Abdelhamed ZA, Morgan JE, Roper H, Santen GW, et al. Loss-of-function mutations in MICU1 cause a brain and muscle disorder linked to primary alterations in mitochondrial calcium signaling. *Nat Genet*. 2014
9. Granatiero V, Patron M, Tosatto A, Merli G, Rizzuto R. Using targeted variants of aequorin to measure Ca^{2+} levels in intracellular organelles. *Cold Spring Harb Protoc*. 2014
10. Granatiero V, Patron M, Tosatto A, Merli G, Rizzuto R. The use of aequorin and its variants for Ca^{2+} measurements. *Cold Spring Harb Protoc*. 2014
11. Hohl M, Ardehali H, Azuaje FJ, Breckenridge RA, Doehner W, Eaton P, Ehret GB, Fujita T, Gaetani R, Giacca M, Hasenfuß G, Heymans S, Leite-Moreira AF, Linke WA, Linz D, Lyon A, Mamas MA, Orešič M, Papp Z, Pedrazzini T, Piepoli M, Prosser B, et al. Meeting highlights from the 2013 European Society of Cardiology Heart Failure Association Winter Meeting on Translational Heart Failure Research. *Eur J Heart Fail*. 2014
12. Hill JM, De Stefani D, Jones AW, Ruiz A, Rizzuto R, Szabadkai G. Measuring baseline Ca^{2+} levels in subcellular compartments using genetically engineered fluorescent indicators. *Methods Enzymol*. 2014

13. Bonora M, Giorgi C, Bononi A, Marchi S, Patergnani S, Rimessi A, Rizzuto R, Pinton P. Subcellular calcium measurements in mammalian cells using jellyfish photoprotein aequorin-based probes. *Nat Protoc.* 2013
14. Raffaello A, De Stefani D, Sabbadin D, Teardo E, Merli G, Picard A, Checchetto V, Moro S, Szabò I, Rizzuto R. The mitochondrial calcium uniporter is a multimer that can include a dominant-negative pore-forming subunit. *EMBO J.* 2013
15. Szabadkai G, Rizzuto R. Καλός και Αγαθός: how mitochondrial beauty translates into biological virtue. *Curr Opin Cell Biol.* 2013
16. Sandri M, Barberi L, Bijlsma AY, Blaauw B, Dyar KA, Milan G, Mammucari C, Meskers CG, Pallafacchina G, Paoli A, Pion D, Roceri M, Romanello V, Serrano AL, Toniolo L, Larsson L, Maier AB, Muñoz-Cánoves P, Musarò A, Pende M, Reggiani C, Rizzuto R, et al. Signalling pathways regulating muscle mass in ageing skeletal muscle: the role of the IGF1-Akt-mTOR-FoxO pathway. *Biogerontology.* 2013
17. Patron M, Raffaello A, Granatiero V, Tosatto A, Merli G, De Stefani D, Wright L, Pallafacchina G, Terrin A, Mammucari C, Rizzuto R. The mitochondrial calcium uniporter (MCU): molecular identity and physiological roles. *J Biol Chem.* 2013
18. Tarasov AI, Semplici F, Li D, Rizzuto R, Ravier MA, Gilon P, Rutter GA. Frequency-dependent mitochondrial Ca(2+) accumulation regulates ATP synthesis in pancreatic \hat{I}^2 cells. *Pflugers Arch.* 2013
19. Marchi S, Lupini L, Patergnani S, Rimessi A, Missiroli S, Bonora M, Bononi A, Corrà F, Giorgi C, De Marchi E, Poletti F, Gafà R, Lanza G, Negrini M, Rizzuto R, Pinton P. Downregulation of the mitochondrial calcium uniporter by cancer-related miR-25. *Curr Biol.* 2013
20. Ghislat G, Patron M, Rizzuto R, Knecht E. Withdrawal of essential amino acids increases autophagy by a pathway involving Ca²⁺/calmodulin-dependent kinase kinase- β (CaMKK- β). *J Biol Chem.* 2012
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24. Maltecca F, De Stefani D, Cassina L, Consolato F, Wasilewski M, Scorrano L, Rizzuto R, Casari G. Respiratory dysfunction by AFG3L2 deficiency causes decreased mitochondrial calcium uptake via organellar network fragmentation. *Hum Mol Genet.* 2012
25. Rizzuto R, De Stefani D, Raffaello A, Mammucari C. Mitochondria as sensors and regulators of calcium signalling. *Nat Rev Mol Cell Biol.* 2012
26. Drago I, De Stefani D, Rizzuto R, Pozzan T. Mitochondrial Ca²⁺ uptake contributes to buffering cytoplasmic Ca²⁺ peaks in cardiomyocytes. *Proc Natl Acad Sci U S A.* 2012
27. Raffaello A, De Stefani D, Rizzuto R. The mitochondrial Ca(2+) uniporter. *Cell Calcium.* 2012
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- controls apoptosis through the modulation of ER calcium homeostasis. *Cell Death Differ.* 2012
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 34. De Stefani D, Bononi A, Romagnoli A, Messina A, De Pinto V, Pinton P, Rizzuto R. VDAC1 selectively transfers apoptotic Ca²⁺ signals to mitochondria. *Cell Death Differ.* 2012
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 36. De Stefani D, Raffaello A, Teardo E, Szabò I, Rizzuto R. A forty-kilodalton protein of the inner membrane is the mitochondrial calcium uniporter. *Nature.* 2011
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 42. Mammucari C, Rizzuto R. Signaling pathways in mitochondrial dysfunction and aging. *Mech Ageing Dev.* 2010
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44. Mangolini A, Bogo M, Durante C, Borgatti M, Gambari R, Harris PC, Rizzuto R, Pinton P, Aguiari G, del Senno L. NF-kappaB activation is required for apoptosis in fibrocystin/polyductin-depleted kidney epithelial cells. *Apoptosis*. 2010
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